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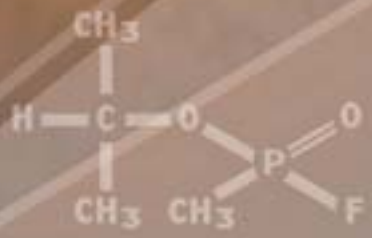
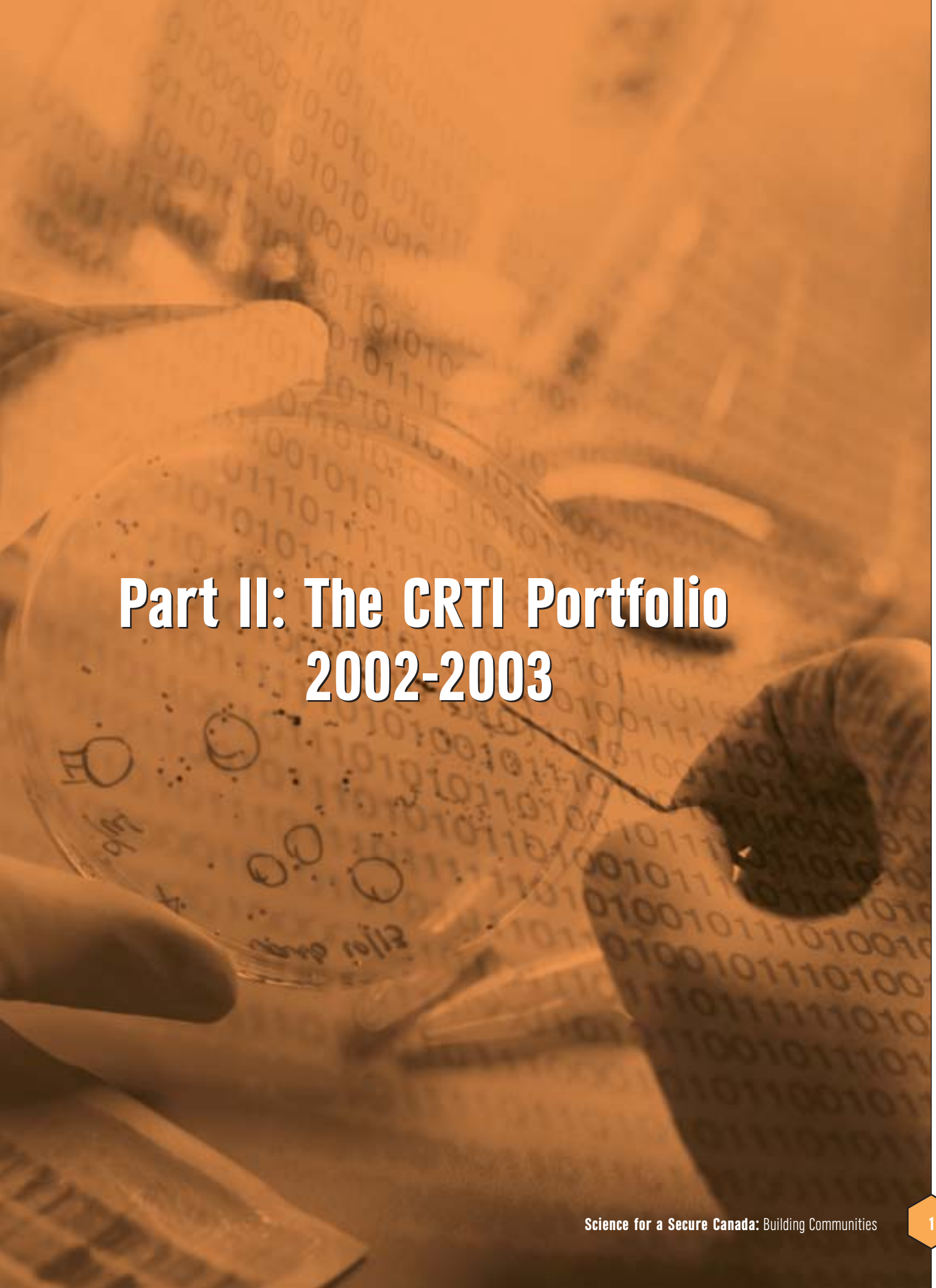


Science for a Secure Canada:
Building Communities

Part II: The CRTI Portfolio 2002-2003

Canada



Part II: The CRTI Portfolio 2002-2003

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The Chemical Biological Radiological and Nuclear (CBRN) Research and Technologies Initiative (CRTI) was announced in the December 2001 National Security Budget as one of the government of Canada's Public Security and Anti-Terrorism (PSAT) initiatives. CRTI has a five-year mandate to manage a $170 million science and technology (S&T) fund to invest in Canadian preparedness against CBRN threats. In the first round of project selection a portfolio of Technology Acceleration and Research and Technology Development Projects was chosen based on:

- Evaluation criteria (utilization, delivery, management, leveraging collaborations and contributions),
- Mandatory requirements of innovation, relevance and uniqueness,
- The funding envelope,
- CRTI Investment Priorities, and
- The CRTI framework.

The 2002 CRTI Portfolio is presented in Part II of this Annual Report.

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CRTI 0004TA

MEMS Sensor Platform

Project Lead: MEMS Precision Technology, Inc.

Federal Partners: Defence R&D Canada, Health Canada, National Research Council

MEMS Precision Technology (MPT) Corporation is a BC-registered company founded in early 2002. MPT founders and core team have extensive experience with Micro Electro-Mechanical Systems (MEMS) for precision technologies that have been developed for production. In addition, the core team has biological agent expertise and is complemented by a staff of consultants from government institutions, universities, and MEMS manufacturing. The primary focus of the business is to leverage MEMS technology into products for new biological and chemical sensors featuring unprecedented accuracy, small size, low weight, and low power consumption.

The world is facing new biological and chemical threats from terrorism and increased threats from biological epidemics. In defence situations, devices for the real-time detection of biological agents in air samples should address two main requirements. First is the requirement for an early warning indicator so that personnel operating within the threat area can put on protective clothing and respirators. Second is the requirement for clinical information in order to implement medical countermeasures at the earliest possible moment. While several existing systems address the early warning requirement by particle counting and sizing functions, the information required for intelligent medical intervention is not currently available in real time.

The core technologies of MPT are ideally suited for this emerging market for sensor platforms with improved detection capability, affordable cost for widespread deployment, and lower power and weight for person-portability. MPT has developed a comprehensive intellectual property portfolio featuring key improvements over prior art. This portfolio provides a strong position oriented towards entry into this large emerging market.

The core product development effort is to create an improved threat agent detection system that can be deployed in the field of military or civilian protection. The proposed system is simple to operate and provides real-time threat data necessary for rapid medical countermeasures. The heart of the system is a MEMS-based sensing element cartridge with the capability to accurately detect even small numbers of viruses. Several companies are attempting to achieve high accuracy with a MEMS-based sensor. Their shortfalls stem from failure to address all of the design elements necessary to achieve a fundamentally low-noise system capable of high volume manufacture. The MPT team's experience in the development of other MEMS devices of similar accuracy has produced the breakthroughs necessary to make this technology work. Comprehensive mathematical models quantify all of the noise sources, and the design has been optimized to accurately measure very small levels of captured agent with low false alarm rates.

MPT's novel approach to the design and fabrication of this MEMS detector array, on-board fluid handling systems and signal processing represents significant improvements over the prior art. The system measures the reaction to specific capture ligands such as antigens, antibodies, nucleic acids and aptamers. The small MEMS sensor array with different ligands allows for the simultaneous analysis of multiple agents in a single sample. MPT is well positioned to review nanotechnology-based sensor breakthroughs for subsequent generations.

MPT has received CRTI funding towards demonstrating its novel approach to the design and fabrication of these highly accurate sensors. This proof of concept project involves the design and manufacture of the core sensor platform, which will be fabricated and then evaluated using a test regime designed to determine the basic operational characteristics of the MEMS-based sensor. The duration of this project is approximately six months. This CRTI funding supports the validation of the basic concepts along the path to reducing initial sensor designs to practice for the first product.

CRTI 0006RD

Rapid Induction of Innate and Specific Immunity at Mucosal Surfaces

Project Lead: Veterinary Infectious Disease Organization (VIDO), University of Saskatchewan

Federal Partners: Health Canada, Canadian Food Inspection Agency

Recent events have demonstrated the threat of bio-terrorism to Canadians and to the food chain. Many highly infectious agents such as *Yersinia pestis* can infect both humans and animals, while smallpox and foot-and-mouth virus target only humans and only animals, respectively. All these agents can be dispersed through both airborne and waterborne pathways. In the case of a bio-terrorism attack, rapid diagnosis and therapy will be needed immediately, while pre-exposure prophylaxis will be required in the long-term. The goal of this project is to develop products and procedures to provide immediate short-term protection to the airways and the intestines against various organisms, while at the same time delivering vaccines that can provide long-term immunity.

Across the world there are a number of vaccines against potential threat organisms. However, their effectiveness is limited and the protection they provide is slow to develop (> 5 days). Furthermore, it is not practical to immunize all personnel and animals against potential threats of bio-terrorism. What is needed is a way to rapidly deploy vaccine formulations for use after exposure (or suspected exposure) to potentially deadly pathogens. It is now known that novel immune modulatory molecules (those based on unique bacterial sequences — CpG motifs) can act as danger signals, stimulating an extremely rapid innate immune response and resistance to some lethal infections. In addition, these molecules can act as adjuvants and enhance specific immunity if combined with specific vaccines. This project aims to unveil potentially beneficial effects of CpGs against infections with Ebola virus, poxvirus and *Yersinia pestis* in representative animal models.

Researchers at VIDO will screen a wide array of specific CpG sequences to identify those which are most effective and suitable to stimulate innate immunity in a particular animal species. They will determine optimal doses and delivery routes for CpG. The main interest will be inducing immunity at mucosal surfaces of the respiratory and digestive tracts. Researchers will also establish screening methods for measuring changes in the immune response, such as cytokine expression profiles.

At McMaster University, researchers will establish a small animal model for poxviruses. Poxviruses, especially variola major (causing smallpox), are among the most contagious and virulent infectious agents. As smallpox poses one of the most serious threats worldwide, it will be of particular interest to study the rapid induction of innate immunity in an animal model using a closely related poxvirus.

Within the Biosafety Levels 3 and 4 containment laboratories at the Canadian Science Centre for Human and Animal Health (CSCHAH), researchers will establish and carry out experimental work using Ebola virus and *Yersinia pestis*. Both agents are extremely contagious and associated with a high fatality rate in humans. In its aerosolized (that is, weaponized) form, *Yersinia pestis* is almost invariably fatal and non-treatable. Researchers will investigate the immediate effects of CpG molecules on animals exposed to either one of these deadly pathogens.

All studies will be evaluated employing clinical, molecular and microbiological parameters. In addition, the Canadian Food Inspection Agency at the CSCHAH will conduct histopathological and immunohistochemical analyses on tissues relevant to these studies.

CRTI 0011TA

Hand-Held Real-Time Biological Agent Detector

Project Lead: General Dynamics Canada

Federal Partners: Defence R&D Canada

In bio-terrorism scenarios, First Responders such as fire fighters and police officers must have real-time aerosol detectors with which to confirm an attack, isolate the contaminated area, identify potential casualties and minimize secondary contamination. Further, these detectors must be able to continuously monitor contaminated areas to determine the effectiveness of decontamination procedures. In order to be affordable they must not use expensive and delicate consumables. Finally, they must be small enough to be easily transported and deployed. The need for such detectors is exemplified in the 2001 contaminated letter event in the US, during which the inability to accurately define contaminated areas led to widespread fears among the general population, slow implementation of medical countermeasures, and excessive remediation costs. Currently no commercial technology meets these requirements, and as a result, laboratory analyses of samples collected manually from surfaces or air are slow and costly.

Chamber and field trials have demonstrated that fluorescence particle detectors (FPDs) combine reliable, generic, real-time detection with low operating costs and no need for consumables. However, most fluorescent particle detectors (such as the Fluorescence Aerodynamic Particle Sizer (FLAPS) and Biological Aerosol Warning Sensor (BAWS)) are too costly, large, heavy and delicate for widespread use by First Responders. Thus, they have been used exclusively in complex military detection systems where size and cost are less important and where environmental protection can be provided. A less expensive hand-held device based on fluorescence particle detection is clearly needed for civilian applications. In research and development efforts conducted by General Dynamics (GD) Canada for Defence R&D Canada (DRDC) and the US Department of Defense, a much smaller, lighter and less costly FPD, called Biological Agent Real-time Sensor (BARTS), was shown to perform as well as FLAPS. However, the lack of low-cost light sources prevented the extension of its development to an affordable hand-held detector. Recent advances in ultraviolet light source technologies have made possible the development of a hand-held FPD, and this project will accelerate efforts already underway between GD Canada and the National Optics Institute.

The objective of the current project is to accelerate the development of the world's first hand-held real-time biodetector based on fluorescence particle detection using the existing BARTS as a baseline detector and exploring

novel approaches to reduce size, weight, power and cost.

The project will have four stages, each stage addressing one of the limitations of the existing BARTS design. All will focus on maintaining the proven performance of the existing BARTS and FLAPS while reducing size, weight, power and cost. This approach represents the lowest-cost and least-risk approach because it allows each improvement to be made independently of the others, and each stage contains a "fall-back" option should the preferred option fail. Further, extensive testing of performance at each stage of the development will ensure that problems are promptly identified and addressed. Finally, a constant focus on reducing cost and enhancing producibility of the sensor will ensure that it meets the requirements of First Responders.

The first stage will explore alternate light sources combined with the existing BARTS optical cell. At least 5 mW of continuous power at the appropriate wavelength will be needed. The performance of a breadboard FPD with new light sources will be compared to the BARTS and FLAPS in tests at DRDC Suffield. A decision to proceed with the project will hinge on achieving performance with the new light sources.

The second stage will focus on redesigning the optical flow cell to optimize fluorescence and scatter signal-to-noise with the new light source and reduce the cost of production. Again the performance of the new optical cell will be compared against the BARTS and FLAPS. The second option will be to retain the existing optical design.

The third stage will explore novel data collection, analysis and transmission electronics options to take advantage of the new light source. In particular, the incorporation of slower and less expensive signal capture electronics will be evaluated because a continuous light source no longer requires fast capture analog-to-digital (A/D) boards.

The fourth stage will complete integration of the best options from the previous stages and a number of prototypes will be built to demonstrate reproducibility. Performance will again be compared to the FLAPS and BARTS. The prototype units will then be evaluated for performance and ruggedness in normal field operations, and may be submitted for use in the companion program to monitor biological releases in urban environments.

The project also includes funding for the construction of facilities at GD Canada to allow the sensors to be tuned against the biological warfare agent simulant, BG, as well as fluorescent polystyrene beads. This new capability will enhance the ability of GD Canada to conduct further R&D toward future generations of low cost biological agent detection technologies.

CRTI 0019TA

Real-time Rapid Detection of Biological Agents

Project Lead: IatroQuest Corporation

Federal Partners: Defence R&D Canada, Canadian Food Inspection Agency

This project proposes a breakthrough real-time biosensing technology using the nanotechnological "smart" material, Bio-Alloy™. The primary goals of this project are follow-on validation with US Critical Reagent Repository recognition elements and biological warfare (BW) simulants or agents, and prototyping a fieldable device.

IatroQuest Corporation was established to be the leader in nanotechnology-based biosensing for real-time detection and identification of biological agents. It offers a radically new platform convergence technology, called Bio-Alloy™ (global patents pending), which bridges elements of biotechnology, advanced semiconductor

[3] Annex B lists the breadth of partnerships in CRTI projects in the first round.

nanomaterials and photonics. The "smart" sensing material possesses unique attributes that allow it to recognize in real time, and without "wet chemistry," a wide range of targets with a very high degree of selectivity and sensitivity. The company has bio-defence as its initial market focus. Other markets likely to be enabled by the platform technology will include *in vitro* medical diagnostics, drug discovery, and emerging sectors of genomics and proteomics. Strategic alliances with key corporate players in each of these sectors will allow for rapid device systems integration and market channel penetration.

The practical and accurate field confirmatory detection and identification of BW agents at low concentrations in a real-time or near-time manner presents a significant challenge. Portable, reliable and cost-effective field confirmatory systems would allow for extensive device deployment in both military and civil defence environments. A technology that further provides direct interfacing with secondary techniques for unambiguous forensic evidence would be highly valuable for prosecution and attribution.

A breakthrough biosensing technology solution is proposed based on the use of Bio-Alloy™ materials. These materials are based on the discovery (global patents pending) and development of photoluminescent (PL) nanostructured (2*4 nm surface features) semiconductor materials to which bioengineered recognition elements (REs) are chemically immobilized. (The REs currently considered are antibodies or antibody fragments; nucleic acids, enzymes, and chemical ligands also possible.) The Bio-Alloy™ materials work through a low-energy 'pumping' (around 1 mW or less) of visible blue Light Emitting Diode (LED) light. If a target BW agent is captured by a RE, the event is marked by a real-time PL green emission / wavelength intensity amplification-modulation. The phenomena responsible for the real-time, and dose-specific, response of the Bio-Alloy™ materials to the presence of BW agents are related to quantum confinement and surface energy state effects. Increasing levels of agent capture results in a dose-response increase in PL (thus presenting quantification possibilities). Unique photonic array patterns could allow for multiple agents to be recognized simultaneously. The sample does not require pre-labeling or the use of reagents, further reducing storage and stability issues while simplifying device design.

The project will build upon the successful outcomes of a multi-year research program with the Department of National Defence that allowed for advancement of the Bio-Alloy™ technology to a point where technology acceleration into a device format is appropriate. This project used commercially available REs to detect target agents (bacteria, toxins, viruses) with high sensitivity and specificity. The current project will initially focus on the use of validated simulant BW agent REs and their associated "targets" from the US Critical Reagents Repository. This will enable a direct comparison with known specificity and dynamic range parameters for existing fieldable detection technologies. Representative classes of validated BW simulant agents will be tested. In conjunction with these studies, a breadboard device containing both "pumping" blue LED and a photomultiplier detector (single detection channel) will be built. As well, a breadboard-level Biosensing Cartridge (BSC) will be assembled allowing for controlled and direct interaction of the target with the Bio-Alloy™ materials.

The project team will include Micralyne (www.micralyne.com), a world leader in microfabrication of devices (including BioMEMS), and Dycor Technologies Ltd. recognized internationally for its system engineering of defence hardware and chemical-biological defence expertise. Follow-on studies employing actual "live" BW agents will be conducted at

DRDC — Suffield, an international centre of excellence in chemical-biological defence.

This project will establish the potential of Bio-Alloy™ smart materials for direct BW agent detection from food and beverage products. Select REs and their associated targets, along with material preparation protocols from the Canadian Food Inspection Agency will be used. Comparisons with current assay technologies will be conducted as well. Another part of the project will examine the direct interfacing of the Bio-Alloy™ Biosensing Cartridge, post-exposure to a BW agent (simulant), with MALDI (Matrix-Assisted Laser Desorption/Ionization)-Mass Spectrometry for direct desorption for "unambiguous" forensics identification.

The Bio-Alloy™ technology holds high potential to enable a radically new and effective approach to consequence manage chemical-biological terrorism events and to possibly even function as a deterrence.

CRTI 0027RD

Biological Dosimetry and Markers of Nuclear and Radiological Exposures

Project Lead: Health Canada, Radiation Protection Bureau

Federal Partners: Defence R&D Canada

The objective of this project is to establish a National Biological Dosimetry Response Plan (NBDRP) and develop rapid methods of radiation exposure assessment to increase throughput in large-scale events. Biological dosimetry assesses radiation exposure when physical dosimetry is not available. It can be a means of screening the general population for radiation exposure and identifying First Responders who must be restricted from further exposure. It can also be a means of assessing long-term risks following radiation exposure. In the event of a radiation emergency, timely assessment of radiation exposure and response will help guide the actions of emergency officials, First Responders and health care personnel.

The first component of this project is the development of a National Biological Dosimetry Response Plan (NBDRP). This is an emergency response plan for the coordinated delivery of dosimetry services by a network of laboratories across the country. This dosimetry service network will be able to respond to national and regional needs in a nuclear or radiological event. It will build upon a collaborative agreement among three existing laboratories to assess radiation exposure using the dicentric chromosome assay (DCA). The DCA measures dicentric and ring chromosomes that are caused by radiation. These laboratories will work towards the International Standards Organization (ISO) standard for biological dosimetry. This will require (1) standard operating procedures, (2) standard training documents, and (3) intercomparison of results from standard slides evaluated by trained staff. Other laboratories across the country will then be recruited to perform the DCA. Once established, the NBDRP will be maintained in a state of readiness for emergency response by continuing a program of intra- and inter-laboratory comparisons and participating in emergency exercises.

The second component of this project is the development and implementation of improved assays for estimating individual radiation exposure and response following a radiological incident. With a goal of achieving faster and automated methods to screen large numbers of samples, a flow cytometric version of the DCA (FDCA) will be developed. A method of premature chromosome condensation fluorescence in situ hybridization (PCC-FISH) will be investigated to determine if it can be used for the early detection of personal exposure within 4–12 hours post-irradiation. Other techniques to

be examined include a modified FDCA procedure using fluorescence in situ hybridization (F-FISH), evaluation of apoptosis, and spectral karyotyping (SKY) in lymphocytes. SKY may provide an estimate of the level of damage, and subsequently the magnitude of the dose, within 24–48 hours following exposure. SKY can also be used in follow-up investigations to monitor future health risk. Techniques will be developed to determine the exposed individual's absorbed dose directly using electron spin resonance (ESR) in tooth enamel within 24–72 hours post-irradiation. However, since collection of tooth enamel from exposed individuals could be problematic, the ESR tooth enamel assay will be developed in non-human animals that could also be involved in the exposure (e.g. mice, cats, and dogs). Once proven in the laboratory, any or all of these methods will be expanded to laboratories across the country to improve the response time to radiological or nuclear events.

In addition to the above cytogenetic assays, state of the art genomics and proteomics technologies will be used to identify specific biological markers of radiation exposure. Biological markers can be used as indicators of an individual's response to damage caused by radiation. This is more biologically relevant than a measure of exposure and may be useful in assessing the long-term risks following radiation exposure. It is expected that data on individual responsiveness will revise the traditional means of risk assessment and triage, which is based on population studies and does not take into account individual variability. Where applicable, a prototype for a field deployable assay will be developed and tested. This could be used for surveillance purposes or rapid identification of potentially exposed individuals. Moreover, individual plasma profiling has the potential of providing information about exposure to other stressors such as biological or chemical agents.

CRTI 0029RD

Protecting the First Responder Against CB Threats

Project Lead: Royal Military College of Canada, Chemical Protection Group

Federal Partners: Defence R&D Canada, Department of National Defence, Royal Canadian Mounted Police

First Responders such as firefighters, police, and emergency medical teams are in the front line of response to a terrorist event involving toxic chemicals or biological agents. To be able to do their jobs while not becoming casualties themselves, First Responders must have access to protective equipment that meets their particular needs, combining functionality with sufficient protection.

Consider an incident scenario involving chemical or biological (CB) agents. The hazardous materials team, wearing specialized fully-protective clothing, may be anywhere from twenty minutes to hours away from the scene, and so fire and rescue services are likely the first to arrive. The critical question arises: can these individuals in fact provide any response capability? Can they perform reconnaissance or quick rescues of injured individuals at the scene? Alternately, can these First Responders be provided with equipment to supplement or replace their regular equipment in order to improve the protection provided? The police may be asked to set up a perimeter around the incident area, or provide specialized tactical assistance: how much protective equipment is needed for these particular roles? Can victims of an attack be transported in ambulances when emergency medical personnel could be exposed to toxic materials by secondary contamination?

In order to address these questions, it is necessary to imagine the variety of scenarios in which exposure to toxic chemicals and biological materials

could occur, and determine the operational requirements of each potential First Responder; we must assess the type of protective equipment available to the responder and how it could be used; we must evaluate the protective capability of each representative equipment configuration; and finally, we must know how the toxic materials of concern would affect the individual under relevant exposure conditions. Only over the last few years has it become technically feasible to address many of these questions. This has resulted from the efforts of the military community to develop a new generation of CB protective clothing, needed to address the current realities of potential use of CB agents in regional conflicts. Much of the knowledge developed in these programs is now available to the First Responder community to meet their requirements in domestic terrorism response.

This project will address the issues in individual protection faced by the First Responder community in planning for and responding to a CB event. Currently, the community has very limited guidance in how to select and use existing individual protective equipment for CB event scenarios. Much of this equipment designed for other uses (occupational health and safety, spill response, protection against fire and smoke, or military CB applications), with a wide range of cost, protective ability and user burden imposed as a result. The First Responder community needs guidance in how to appropriately select and operate existing off-the-shelf equipment in order to meet their immediate needs, and should have access to information on, and input into, equipment that is under development.

This guidance will be provided by a project team that includes experts in various relevant areas, led by the Chemical Protection Group at the Royal Military College of Canada. Defence Research and Development Canada, Health Canada, and experts in the US and UK will provide additional scientific expertise in the area of toxic chemicals and biologicals. This expertise will be used to develop methods for evaluating and predicting the effective performance of protective equipment, combining user testing of equipment with modelling of equipment performance and potential toxic effects to the wearer.

The First Responder community will provide input on operational requirements, assist in equipment evaluations, and disseminate the information, with the involvement of the RCMP and the Office of Critical Infrastructure Preparedness and Emergency Preparedness, as well as various regional and military First Responder organizations.

The standards community both within Canada and internationally will be engaged in developing equipment standards recommendations. Specific expertise in the areas of standards development and protective equipment improvements will be provided by 3M Canada and DuPont Canada, industry leaders in developing and manufacturing protective materials and equipment.

The outcomes of this program will be used to develop recommendations, specifications and standards against which new equipment for a variety of First Responder users can be designed. Further, improved capabilities in the areas of respiratory protection against a broad spectrum of volatile hazards, combined CB blast protection, and body protection against a variety of chemical hazards, are also anticipated over the next few years, some in collaboration with this project. For example, in collaboration with Med-Eng Systems Inc. and Defence Research and Development Canada's CB^{plus} project, this project will assist in the design and evaluation of protective equipment designed for bomb disposal technicians that will combine effective blast and CB protection.

Ultimately, the First Responder community will be given the guidance in equipment selection and use that it requires to improve its response capabilities in the case of a CB terrorist incident. In addition, the fundamental information gathered on design requirements and approaches to equipment performance assessment will benefit a variety of other users.

CRTI 0052TA

Rapid Carbon-14 Analysis by Accelerator Mass Spectrometry

Project Lead: University of Toronto, IsoTrace Laboratory

Federal Partners: Health Canada

Carbon-14 (^{14}C) is a radioisotope that can be both dispersed in a nuclear incident, and produced in the environment from neutrons associated with such an event. Carbon-14 is readily available for dispersion. For example, CANDU reactors generate a significant amount of it during operation and hence maintain a considerable inventory of it within their working areas. ^{14}C is also widely used in biomedical (including pharmaceutical) research laboratories, as a tracer in animal and plant studies. As a result, it is readily available for use in a "dirty" bomb. ^{14}C has a long radiological half-life (5730 years) and low-energy beta emission, which make it very difficult to detect in the field using standard radiation survey instruments. Its long biological residence time (~100 years in humans) means that it causes long-term health consequences if incorporated in human tissue, even at concentrations that are too low to measure with conventional survey equipment. Both measurement techniques specific to ^{14}C, beta counting and accelerator mass spectrometry (AMS), require sample preparation times of 1-5 days. AMS provides the advantages of much smaller sample size (~ 25 mg) and shorter measurement times (< 1 hour), but the sample preparation time renders impractical the analysis of the large numbers of samples with the high throughput that would be required to assess the radiological danger of a chemical, biological, radiological or nuclear (CBRN) event.

Recently, carbon dioxide (CO_2)-fed AMS ion sources have become commercially available, through a collaborative development between Oxford University and High Voltage Engineering Europa, B.V. (HVEE). These devices, by eliminating the conversion from CO_2 to graphite required for conventional AMS, reduce preparation time by up to 50%. However, the sample preparation procedures needed for measuring ^{14}C associated with a CBRN event, where the ^{14}C levels are equal to or greater than ambient levels, are less critical than those needed for ^{14}C dating, where the levels can be up to a factor of 1000 below ambient. Hence, an auto-sampling elemental analyzer can be used to convert the sample directly to CO_2. This CO_2 can be transferred directly to the gas-fed ion source attached to the AMS spectrometer, where again, because of the higher ^{14}C levels involved, the time needed to count the ^{14}C atoms would be reduced. This combination of equipment will result in a total analysis time, from introduction of the raw sample into the elemental analyzer to data output, of less than 15 minutes. Optimization from pipelining these procedures is expected to permit sample throughputs of up to 200 per day.

This project involves the manufacture by High Voltage Engineering Europa B.V. (HVEE) of the CO_2 gas ion source and the specification and purchase of an automated combustion unit to convert raw samples (as obtained by First Responders) to CO_2 for the ion source. The work in connecting the combustion unit, the ion source and the AMS system will involve mechanical, electronic and software development.

The transport of the CO_2 gas from the combustion unit to the ion source will be carried out with established capillary tube technology, using argon to flush this line between samples. The ion source will be connected to the IsoTrace AMS system through an unused port on the existing 45° electric analyzer in the ion source region. A length of beam line, with vacuum gauges, steerers and an aperture to define the ion beam for acceptance by the 45° analyzer will be constructed. In addition, the rotation of the analyzer plates will be implemented so that the analyzer can function as a switch between the existing ion source and the new gas ion source. The combustion unit and the ion source will be delivered with their own computer control systems; for complete automation of the measurements, these will be interfaced with the existing AMS control system. This will require building some electronic hardware and modifying the AMS control software.

Once the complete system is operational, it will be tested using samples provided by Health Canada's Radiation Protection Bureau and Fisheries and Oceans Canada's Atlantic Environmental Radiation Unit to optimize the many operating parameters, as well as to determine the types and quantities of sample material that can be used. With this information, an analysis protocol will be written specifically for samples with the higher levels of ^{14}C that are expected to be associated with a nuclear event. Drafts of these documents will be exchanged with the federal partners before the final versions are produced. Information will then be provided through the federal partners to First Responders and those who would be involved in wide-area decontamination and remediation. This will be accomplished through seminars, workshops and specialized training sessions.

CRTI 0060TA

Rapid Triage Management Workbench (RTMW) Description

Project Lead: AMITA Corporation

Federal Partners: National Research Council

(RTMW) is designed by University of Ottawa and Heart Institute, National Capital CBRN Health Planning Team, Carleton University Hot Lab and AMITA Corp under the direction of Canadian Bioinformatics Resource (CBR) of National Research Council Canada (NRC). RTMW will manage the communication of medical information during a CBNR event. The system will be portable and capable of being deployed in the field in rural and urban settings with a minimum of training. A medical data capture module will provide First Responders and medical caregivers in the field with the means to record victims' medical information quickly, easily and accurately and would be particularly useful when there are a large number of casualties. This data will then be entered into a central database that will allow other Cluster members to have access to victim data. Another aspect of RTMW system is that it can be used from anywhere there is an Internet connection (RTMW will be designed with an appropriate level of access security). Clinics and family doctors could enter data if they are so authorized. This could be a very useful feature should there be a slow moving event.

RTMW will enable the response team to function as efficiently and effectively as possible by making the medical information they need immediately available to all Cluster members responders. In particular, it will provide all members of the team with accurate and up to date information on the victims' current status while avoiding the need for multiple telephone calls during a period when usual communications modalities may be significantly degraded.

The current alternative to RTMW is voice communication between providers, medical caregivers, and other response team members. This is a much less effective way of communicating the same information because it requires a large number of calls and because communications circuits will likely be overloaded. Experience has shown that traditional methods of tracking casualties from the site and while in route are not very effective, which has resulted in difficulties in trying to reconcile all casualty numbers. Many casualties cannot be tracked due to ambulances being rerouted during transit. The Red Cross has experienced many problems due to inaccurate information gathering, which leaves many concerned relatives wondering where their loved one is. Good communication of critical data between response team members has been identified as a crucial factor in minimizing the effects of a CBRN attack.

RTMW will provide the following benefits:

- Rapid triage with up-to-date medical data will increase efficiency in patient care and transportation.
- Caregivers will be providing effective and efficient care because the right people and equipment will have been triaged to where they can do the most good. This will minimize provider fatigue and unnecessarily prolonged exposure to potentially hazardous environments.
- The health care facilities receiving the victim will receive relevant patient data prior to admission.
- The safety of response team members will be improved because information on potential medical hazards will be communicated to all Custer members more quickly.
- The response team will be able to provide patients' families with accurate, up to date information.
- Public health organizations will have accurate information and will, therefore, be able to provide advice and directions to the public based on current, pertinent data.
- The RTMW will use the current triage marking (code) system used by the Emergency Management System. Therefore all First Responders will be familiar with the RTMW Triage system.
- The CBRN preparedness staff will use RTMW as a teaching tool in the art of triage and it also could be part of First Responder curriculum on a national level.

Ultimately, by facilitating a well-organized response, RTMW will maximize lead times for decision making which will ultimately minimize the overall impact of the event.

RTMW will be bilingual and include an on-line help facility and supporting documentation. The system has two major components:

1. A portable component used in the field, and
2. A stationary database accessible through Internet

RTMW makes use of the Internet as well as the latest database technology. The hardware and software components will be selected so that standard PC/Windows equipment can be used, eliminating the need to procure and maintain special equipment for this system.

RTMW is an expandable foundation module in that, once it is in place, other modules (e.g., crisis management, equipment management, First Responder management information) can be added at a later date.

The field component will be easily deployable. It will operate from within a Web browser, therefore no installation of software is required on the user workstations. The components in the portable version are at its simplest configuration – a standalone common Windows PC with a small database. It can also be expanded to be a multi workstation (including wireless) configuration, still using standard Windows based PCs. RTMW will be designed to be rugged and fault forgiving.

The field component will be connected to the Internet for communication with a central database. The connection to the Internet can be any standard mode - the simplest one being a regular modem. The field system will work even if the Internet connection is intermittent by saving information on the victims for data transmission when an Internet connection is available again.

The Internet was designed as a communications network that would remain operational during and after a nuclear war. It has massive survivability qualities built into it. In the unlikely event that Internet is not available, data can still be transported using a dedicated wire, courier, or whatever other communication means is available.

The stationary database can be set up anywhere there is an Internet connection. Once the database is online, it can be accessed from any Internet station with the proper authorization.

RTMW will store data using the Classification of Diseases standards so that entries can be related to regular health care.

User centric design methods will be used in designing RTMW. The Usability Lab of Carleton University will apply proven techniques to identify requirements and design the interface. RTMW will be designed so that it requires minimum training to use.

CRTI 0064RD

New Technologies for Surveillance of Biowarfare Agents and Identification of Engineered Virulence Genes

Project Lead: University of British Columbia

Federal Partners: Health Canada, Defence R&D Canada

An innocuous bacterium becomes a lethal weapon by the introduction of a virulence gene. The technology for gene transfer in organisms such as *Bacillus anthracis* and *Yersinia pestis* has existed for over a decade, and therefore there is an urgent need to develop the capability to identify introduced virulence genes in engineered biowarfare strains. Current methods lack resolving power to find unknown insertions. Whole-genome sequencing of all suspected biowarfare agents is impractical, and micro-array-based technologies, while powerful, are limited to genes present only in the reference strains. In this project, a novel DNA scanning technology will be adapted to rapidly identify engineered genes in order to tailor therapy and develop surveillance strategies.

The new methodology has two parts. First, the bacterial genome is resolved in two dimensions (2D) to produce a display. This display is compared against related lab reference strains. The introduced fragment of DNA can then be isolated and identified.

1. High resolution display of bacterial genome

Genomic DNA is cleaved into thousands of fragments with restriction enzymes. The fragments are resolved in two dimensions by sequential gel electrophoresis to produce a display. The separation of fragments depends on size and DNA properties (base composition) enabling comparison between specimens. For example, a pathogen

that has been engineered for drug-resistance would show novel fragments compared to the antibiotic-sensitive strain.

2. Detecting engineered DNA

To identify an unknown virulence gene, one would compare the engineered biowarfare strain harbouring the gene (strain A) against a related lab reference strain (strain B). This procedure is called Bacterial Comparative Genomic Hybridization (BCGH). The identity of the gene is then revealed by excising the novel fragment, and cloning and sequencing the extracted DNA.

The project will be carried out in the following manner:

Researchers at the University of British Columbia (UBC) labs will profile eight pathogens: *Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia), *Burkholderia pseudomallei* (melioidosis), *E. coli* O157, *Salmonella typhi*, *Shigella flexneri*, and *Yersinia enterocolitica*. Restricted pathogens and Biosafety Level 3 organisms will be cultured by National Microbiology Laboratories (NML) and Defence R&D Canada (DRDC). For these, DNA only will be provided to the UBC labs.

Display parameters (fragmentation conditions, gel composition, temperature, time, etc.) will be determined empirically for each of the organisms. The sensitivity, quality assurance and quality control of BCGH will be assessed using a panel of spiked genes representing a spectrum of sequence composition.

Standardization and refinement at federal sites will be carried out by NML and DRDC laboratories.

State-of-the-art software (BioNumerics from Applied Maths) will be used to analyze and archive the 2D-DNA profiles, as well as to communicate between partner laboratories.

Technology transfer will be jointly executed between the university and federal project partners.

In a biological terrorism event, the identification of the engineered gene will facilitate diagnosis, surveillance, vaccination and therapeutic measures to be targeted at the virulence gene to control disease outbreaks.

CRTI 0072RD

Nanodosimeters Based on Optically Stimulated Luminescence

Project Lead: Defence R&D Canada – Ottawa

Federal Partners: Health Canada

In the event of a radiological incident, tracking the spread of radioactive material will be of utmost importance. Information on the distribution of contamination will be required, both to guide evacuation and to plan responses while minimizing the risk to all involved. Clearly, the more detectors and/or detector positions that are used to map the contamination pattern, the better defined the contamination pattern will be. The aim of this research project is to create a small, inexpensive dosimeter that could be quickly and easily deployed in large numbers over a contaminated area, providing a very detailed map of the contamination pattern.

Recent development work has concentrated on a novel detector based on optically stimulated luminescence (OSL). This detector consists of a single crystal that acts as the detector's sensitive volume, a light source to stimulate emission from the crystal, and a sensor to detect the emission. The detector design lends itself well to miniaturization and system-on-chip architecture. It is anticipated that the dosimeter sensitive volume can be miniaturized and integrated with control and read-out

electronics as well as with communications. With these detectors, multiple probes could be distributed over a contaminated area and could track the level and spread of contamination in real time. Simulations have shown that this approach would produce extremely accurate contamination mapping and would be very robust: the set of detectors would survive even if there were a large number of individual detector failures.

This project will progress along two separate, but related, tracks. The first track will be the design, production and evaluation of a millimetre-scale OSL dosimeter. This track will build upon recent experimental results to produce a small, integrated version of the OSL dosimeter, complete with all of the required control, read-out and communication electronics. The second track would entail the design, fabrication and testing of a prototype chip-level OSL nanodosimeter.

Two Canadian government departments will play an active role in the execution of this CRTI project with DRDC Ottawa heading the project. The Radiation Effects Group at DRDC Ottawa is a world leader in radiation dosimetry and spectrometry research. It provides radiation protection support to the Canadian Forces and would be a key player in Canada's response in the event of a radiological incident. Health Canada's Radiation Protection Bureau will also provide technical expertise for this project. Health Canada will provide input into the design and testing of these dosimeters from the perspective of the National Monitoring Program.

The other key members of this project are Bubble Technology Industries (BTI) Inc. and the Electronic-Photonic Materials Group (EPMG) at the University of Toronto. The expertise at BTI covers many different types of radiation sensors including scintillation, gaseous, luminescent, liquid-phase, semi-conductor, and those based on reaction products. BTI has developed a radiation sensor called the bubble detector, which is sold globally. BTI has also developed a novel detector based on optically stimulated luminescence in previous work done under contract to DRDC Ottawa, and will be producing the millimetre-scale prototype OSL dosimeter and defining the parameters for the chip-level nanodosimeters. The expertise at EPMG lies in the design, production and characterization of microelectronic devices. EPMG will be performing all of the modelling, growth, processing and characterization of the chip-level nanodosimeters.

CRTI 0080TA

Information Management and Decision-Support System for Radiological-Nuclear Hazard Preparedness and Response

Project Lead: Health Canada

Federal Partners: Environment Canada

The Federal Nuclear Emergency Plan (FNEP) is administered by the Nuclear Emergency Preparedness and Response Division of Health Canada's Radiation Protection Bureau. The FNEP provides the framework for coordinating and conducting the multi-departmental federal response to a radiological or nuclear emergency affecting Canada or Canadians. The FNEP supports the provincial response to a radiological or nuclear emergency, provides the framework for radiological consequence management in support of Canada's National Counter-Terrorism Plan (administered by the Solicitor General Canada), and links to the Canada-United States Joint Radiological Emergency Response Plan. Over twenty federal departments and agencies have specific responsibilities listed in the FNEP.

Under Health Canada's lead, the national multi-department response organization established under the FNEP framework must

- Gather, coordinate and share large quantities of emergency information and data from many sources,
- Assess impacts,
- Formulate response decisions, and
- Implement protective measures that support First Responders, municipalities and provinces, federal decision makers, and international agencies.

In order to meet these responsibilities, robust information management and decision-support tools are required. Such decision-support tools assist in all aspects of radiological or nuclear emergency preparedness and response, including

- Surveillance and alerting,
- Identifying areas of increased radiation levels,
- Gathering monitoring data, meteorological information and forecasts,
- Assessing consequences,
- Visualizing data, and
- Exchanging information.

In this project, Health Canada's Nuclear Emergency Preparedness and Response Division will collaborate with Environment Canada's Canadian Meteorological Centre and work with other key federal partners to implement within Canada an international decision-support system known as the ARGOS Software Application Suite. ARGOS (Accident Reporting and Guidance Operational System) is being made available through international collaboration with the Danish Emergency Management Agency, and Prolog Development Center A/S, who are the system developer and programmer organizations.

Implementation of ARGOS as an operational radiological-nuclear emergency response tool in Canada requires Prolog Development Center to carry out specific enhancements to the core software applications in order to meet Health Canada's emergency management requirements and to interface with Canadian emergency monitoring, modelling and forecasting data sources and capabilities. Environment Canada will accelerate the development of its local and regional meteorological modelling capabilities supporting nuclear emergency response, and work with Prolog to interface these with the ARGOS core applications.

The capabilities provided by this enhanced version of ARGOS will allow the national emergency response structure established by Health Canada to handle and integrate large quantities of dynamic multi-disciplinary, multi-sourced assessment information. Included are:

- Meteorological modelling, monitoring and forecasting capabilities provided by the Canadian Meteorological Centre;
- Radiological monitoring data from Health Canada, Geological Survey of Canada and others;
- Radiation dose assessment; and
- Public information resources.

Implementation of ARGOS in Canada will improve coordination and interoperability amongst FNEP partners, and facilitate a rapid, coordinated response to a radiological or nuclear incident, effective decision-making, and provision of critical information to First Responders, the operational community, and the public.

CRTI 0085TA

Evaluation of GM-CSF for Acute Radiation Syndrome

Project Lead: Cangene Corporation

Federal Partners: Health Canada

Radiation overexposure is considered a potential threat to both civilian and military personnel in various circumstances. Radiation exposure has been reported in a variety of accidents that include accidental X-ray exposure and nuclear plant accidents, as well as a military training accident reported in 2000. Deliberate exposure in a military or terrorist situation must also be considered, due to the proliferation of global nuclear capacity and traffic in spent nuclear fuels.

In humans exposed to radiation, the use of cytokine therapy (therapy using regulating proteins) has not been systematically evaluated. However, laboratory, animal and clinical studies have suggested a role for hematopoietic stem cell modulators (cytokines that regulate the development of blood cells). In particular, animal studies have demonstrated that GM-CSF (granulocyte-macrophage colony-stimulating factor, which is known to stimulate the production of white blood cells) is useful in mitigating the effects of sub-lethal radiation exposure where some viable early stem cells remain. All currently available cytokines have proved ineffective where the dose of radiation is such that all stem cells are eliminated.

Cangene Corporation is developing a recombinant human (rh) form of GM-CSF, LEUCOTROPIN™, and will shortly submit this drug for licensure in Canada. The goal of the current project is to demonstrate the utility of LEUCOTROPIN™ in restoring the body's ability to produce white blood cells following radiation-induced damage to the bone marrow. The primary application for GM-CSF in radiation exposure would be for the early treatment of patients exposed to low- to medium-dose radiation. However, the drug may also be useful for protection of individuals likely to be exposed to radiation, such as rescue workers.

To achieve these goals, Cangene will produce LEUCOTROPIN™ according to its established cGMP process at 2,100 L scale in the company's manufacturing facility. The material will be evaluated in the pilot and full animal studies. A parallel study to evaluate a more stable PEGylated GM-CSF developed by Cangene for single-dose administration will also be conducted.

The pilot study will be conducted in cynomolgus monkeys to determine an effective low-to-medium and medium-to-high single-dose radiation cycle to compromise immune system. Confirmation of drug dose will be conducted as well. The objective of the full animal study would be to show efficacy of GM-CSF in the early treatment of low-to-medium dose radiation exposure. Monkeys will be subjected to a series of increasing levels of single exposure to radiation with recovery cycles. The placebo-controlled study will evaluate the effect of GM-CSF on relief of neutropenia. The primary end point will be a surrogate marker for immune system competence while secondary end points will include reduction in infections and transfusion requirements. Based on the efficacy results, Cangene will file a supplemental New Drug Submission for approval to add the indication of treatment for low-to-medium dose radiation exposure to the LEUCOTROPIN™ file.

CRTI 0087RD

Therapeutic Antibodies for Ebola and Marburg Virus

Project Lead: Cangene Corporation

Federal Partners: Health Canada, Canadian Food Inspection Agency

Ebola and Marburg viruses are among the deadliest known pathogens, causing severe hemorrhagic diseases with lethality rates of up to 83% for Marburg virus and 90% for Ebola Zaire virus. Since the discovery of filoviruses in 1967, outbreaks of Ebola Hemorrhagic Fever (EHF) and Marburg Hemorrhagic Fever (MHF) have been reported from several Central African countries, with the latest outbreaks reported in December 2001 in Gabon and Democratic Republic of the Congo. There is no question that the filoviruses, by virtue of their virulence and natural occurrence, represent a real threat for use as biological weapons. This is exemplified by their inclusion on the Centers for Disease Control and Prevention "Category A List" of pathogens. The former Soviet Union and Russia produced large quantities of Marburg and Ebola viruses until 1992. Soviet Union researchers quantified the aerosol infectivity of Marburg virus for monkeys, determining that no more than a few virions are required to cause infection. The Japanese terrorist cult Aum Shinrikyo unsuccessfully attempted to obtain Ebola virus as part of an effort to create biological weapons.

In a bio-terrorism incident, rapid diagnostics and therapeutics will be the first line of defence, addressing the immediate health needs of the public and military. Long-term goals will include pre-exposure prophylaxis, which will be best achieved by vaccines. The goal of this project is to bring together Canadian federal, academic and industrial partners to develop therapeutic antibodies as a front-line, short-term defence against a bio-terrorist attack with either Ebola or Marburg viruses.

Many workers in the field have suggested that therapeutic antibodies are the most promising post-exposure therapeutic strategy presently available. This approach provides short-term deliverables, which are urgently required to protect the public and First Responders. The development of effective neutralizing antibodies to Marburg and Ebola viruses has been challenging because of the limited knowledge of the viral proteins that are important targets for the protective immune response. However, recent studies have contributed to a better understanding in this area and have identified the transmembrane glycoproteins (GP) as key targets. Aspects of this work have been conducted at the Health Canada facilities in Winnipeg. Passive protection against a lethal Ebola virus challenge has been demonstrated in small animals, and post-exposure treatment with convalescent plasma seemed to have a protective effect in humans. Furthermore, antibody therapy offers immediate protection to infected individuals and may be used in either preventive or therapeutic applications. A large variety of antibody therapies have been approved by regulatory agencies and are used in a wide range of disease indications in humans, including treatment of several viral infections.

As a first step, large animal derived polyclonal antibodies will be raised and tested for efficacy and safety in Ebola and Marburg protection models. The large animal polyclonal antibody approach will provide a supply of therapeutic drugs for short-term delivery.

To provide a longer-term solution, recombinant monoclonal antibodies will be developed for both Ebola and Marburg viruses. While the lead-time to generation of the recombinant antibodies will be longer than for the polyclonal antibodies, the recombinant products will be of better-defined

specificity and will be available for indefinite supply. Researchers will evaluate soluble and membrane-bound versions of Ebola and Marburg virus glycoprotein (GP) antigens as candidates to raise monoclonal antibodies. All the recombinant proteins have already been successfully expressed and some of them are already available for immunization purposes. Currently researchers are characterizing other forms of recombinant glycoproteins and developing purification procedures for large-scale production.

Two standard technologies will be employed to develop monoclonal antibody phage display technology (PDT) and hybridoma technology (HT). These two technologies are expected to produce two different and diverse sets of potential therapeutic drug candidates. The antibody candidates will be screened, and potentially high-affinity neutralizing antibodies will be chosen for full characterization. The HT-derived drug candidates will be evaluated in viral neutralization assays *in vitro*. Subsequently, they will be tested for their *in vivo* neutralization activity in rodent models. Promising candidates will be converted into mouse-human chimeric recombinant antibodies and expressed in Chinese Hamster Ovary (CHO) cells. These recombinant monoclonal antibodies will again be tested in an *in vivo* mouse model to confirm protective efficacy. The PDT-derived antibodies will be converted from phagemid-encoded clones to a soluble Fab (antibody fragment) format. These Fab fragments will be tested in an *in vitro* assay for viral neutralization. The neutralization characteristics of the Fab will be evaluated and, if required, the most promising Fab clones will be affinity matured by error-prone PCR. Selected clones will be converted into full-length human IgG antibodies and expressed as recombinant products in CHO cells.

This project will result in the development of a panel of neutralizing antibodies for Ebola and Marburg viruses. The efficacy of antibodies will be screened initially by an *in vitro* assay of neutralization and then in rodent models of protection. It is projected that both PDT and HT will develop a minimum of 10 monoclonal antibodies. Each antibody will be purified to at least 95% purity using a laboratory scale GLP purification process. These fully human monoclonal antibodies will be tested in an *in vivo* mouse model to confirm protective efficacy, and further protection studies might be conducted. This program of work on monoclonal antibodies coupled with the short-term development of polyclonal antisera will provide federal and provincial authorities with the tools needed to protect First Responders and the public from the threat of a biological terrorism attack with Marburg and Ebola viruses.

CRTI 0091RD

The Development of Monoclonal Antibodies for the Treatment and Detection of Bio-Terrorism Agents

Project Lead: Health Canada, National Microbiology Laboratory

Federal Partners: Defence R&D Canada, Canadian Food Inspection Agency, Agriculture and Agri-Food Canada

The goal of this project is the development of protective and diagnostic monoclonal antibodies for the detection, prophylaxis and post-exposure treatment of bacterial and viral agents. This will initially be limited to antibody development for alphaviruses, foot-and-mouth disease virus, and anthrax. However, the knowledge gained in this project will advance vaccine design for other potential agents of biological terrorism (BT) and infectious pathogens of both humans and animals in general.

In a terrorist event, the public health system must deliver effective post-exposure treatment to thousands, or even hundreds of thousands, of potentially exposed persons. At present, antibiotics are available only for some bacterial agents and must be administered within hours after exposure to be truly effective. For many of the viral agents, supportive treatment is all that can be offered.

Alternatively, a cocktail of recombinant monoclonal antibodies can provide immediate protection from both bacterial and viral agents. However, to use antibodies as post-exposure treatment, rapid methods must be in place to correctly identify the microbial agent involved, since this dictates the appropriate antibodies to be used. Therefore, this proposal addresses the development of monoclonal antibodies for specific detection and identification of BT agents as well as for treatment purposes.

To be effective therapeutic agents, monoclonal antibodies must be produced rapidly, in large quantity, and at an affordable price. The scale-up production of monoclonal antibodies will make them more affordable and the high specificity of monoclonal antibodies reduces the dosage needed for protection.

While many antibody preparations are administered intravenously, the high specific activity of monoclonal antibodies allows for intramuscular delivery. This will allow First Responders to self-administer protective cocktails of monoclonal antibodies to BT agents.

Besides the human pathogens of anthrax and alphaviruses, this project also addresses the need to develop rapid diagnostic reagents for the identification of an important animal pathogen, food-and-mouth disease virus, which can have an enormous economic impact in the Canadian livestock industry. An outbreak of foot-and-mouth disease in Canadian livestock would require extensive testing before the re-establishment of international livestock trade. Validated tests with monoclonal antibodies will help to speed up the recovery of the industry after such an outbreak.

Thus, this project has as objectives:

- Develop monoclonal antibody-based treatments for the BT agents of anthrax and alphaviruses (Venezuelan Equine Encephalitis (VEE), Western Equine Encephalitis (WEE), and Eastern Equine Encephalitis (EEE)).
- Develop monoclonal antibody-based rapid diagnostic reagents for BT agents of anthrax, food-and-mouth disease virus and alphaviruses.
- Identify candidate microbe components for vaccine development against BT agents (anthrax, alphaviruses and food-and-mouth disease virus).

The total amount of funding to be expended on this project over a period of four years will be $5,730 640, administered by Health Canada's National Microbiology Laboratory (NML). Other major research partners in this project include DRDC Suffield, and the Canadian Food Inspection Agency's National Centre for Foreign Animal Diseases (NCFAD).

The project will be carried out by a team of immunologists, molecular biologists, virologists, bacteriologists, and veterinary clinicians. The majority of the work will be carried out at the Canadian Science Centre for Human and Animal Health (CSCHAH), which houses Health Canada's NML and the Canadian Food Inspection Agency's NCFAD, and at DRDC's laboratory in Suffield.

The monoclonal antibody facility will coordinate monoclonal antibody development and production, including the distribution and stockpiling of hybridoma and recombinant cell lines and purified monoclonal antibodies. DRDC Suffield has facilities, resources, and expertise for the handling of killed and live risk groups 2 and 3 BT agents. It maintains a bank of hybridoma cell lines secreting monoclonal antibodies to BT agents; has large and small animal holding facilities; has state-of-the-art molecular biology laboratories for performance of recombinant DNA techniques; and has expertise in immunoassay development.

Data mining, using World Wide Web-based tools, will be used to identify and design experimental vaccines for this project. Such candidate vaccines will be used to immunize laboratory mice for production of monoclonal antibodies, using standard procedures for developing hybridomas via fusion of mouse immune spleen lymphocytes and cancer cells. Since mouse monoclonal antibodies are not suitable for use in humans, recombinant DNA techniques will be used to clone and genetically engineer the mouse antibody molecule to a human form suitable for parenteral administration to humans. Attempts to produce human monoclonal antibodies as therapeutic agents to anthrax will be done by direct cloning of the specific antibody genes from blood lymphocytes of volunteers immunized with the anthrax toxin. The possibility of using transgenic xenomouse genetically engineered to carry the human immunoglobulin genes will also be explored for the direct production of human antibodies in experimental animals.

CRTI 0100TA

Systems Level Simulant Test Chamber for CB Personal Protective Ensembles and Equipment, with an Articulated Mannequin Capability – CB*plus* Chamber

Project Lead: Defence R&D Canada – Director Science and Technology Human Performance

Federal Partners: Department of National Defence, Royal Military College

This project will establish a world-class chemical and biological (CB) test and evaluation chamber at DRDC Suffield. The CB*plus* Chamber, equipped with a human form moving mannequin, will be used to expose personal protective clothing and other First Responder and military equipment to liquid, vapour, and aerosol hazards using non-toxic biological and chemical compounds as simulants. It will be possible to carry out these studies under temperatures ranging from 5 to 50˚C, relative humidity ranging from 10 to 90%, and sustained wind conditions of up to 7 m/s.

The CB*plus* Chamber will consist of a modular, self-contained building, which will provide additional test and evaluation capability once installed at DRDC Suffield as part of the Counter Terrorism Technology Centre (CTTC). The chamber will be capable of exposing First Responder and military clothing and equipment to biological and chemical threat simulants in liquid, vapour and aerosol forms. The chamber will be world-class and unique, presenting a leading capability in research, testing and evaluation.

Systems under evaluation will be worn by a state-of-the-art articulated human-form mannequin. The mannequin will be able to walk or march, with a breathing headform designed to allow the evaluation of respiratory protection and integrated headwear systems. The chamber will be operated

via a computer-controlled data acquisition and control system that will provide precision in the release of the threat simulant and in the manipulation of the thermal, moisture and air flow environments. The inclusion of the human-form mannequin in this test environment will permit replication of test conditions within very fine tolerances. This in turn will provide a test facility that will be capable of testing and/or certifying First Responder and military clothing and equipment.

The introduction of the chamber will allow government acquisition teams to practice "simulation based acquisition," using the facility to confirm requirements for future acquisition projects, then evaluate bid contenders, and conduct final acceptance testing of clothing and equipment items. Similarly, industrial teams wishing to sell products to the First Responder (civilian and military) community will be able to use the facility during their internal R&D cycles and to achieve product certification.

The federal lead agency for the CB Chamber project is DRDC/Director Science and Technology Human Performance (DSTHP) (funded under the CB*plus* Technology Demonstration Project), with the Directorate of Nuclear, Biological and Chemical Defence (DNBCD) of the Canadian Forces contributing. Amtech Aeronautical Limited of Medicine Hat, Alberta, will develop the chamber design and construct the facility. An international team from Canada, the Netherlands, the United Kingdom and the United States will provide scientific expertise to the development of the chamber requirements and protocols for operation. The CRTI is contributing $2.7M of the $4.5M total project cost. The chamber will be installed and operational at DRDC Suffield by the fall of 2005.

CRTI 0105TA

Mobile Real-Time Radiation Surveillance Network for the National Capital Region

Project Lead: McFadden Technologies

Federal Partners: Health Canada, Royal Canadian Mounted Police, Natural Resources Canada

Since September 11, 2001, the likelihood of future terrorist attacks is acknowledged to be higher than in the past. As a result, the Canadian public has greater expectations for security, prevention, interdiction and incident site management. Radiological agents have a particularly high potential for psychosocial impacts on political and economic systems. The malicious dispersal of radioactive materials could be used to attack civil, governmental and economic targets. Thus adequate prevention and response systems are needed.

Significant radiological sources could be acquired by terrorists through clandestine theft or low level military operations and moved, possibly undetected, to urban population areas or to targets of high symbolic value. First Responders need better tools and training to detect and report radiological incidents. There is currently a need for increased capability in Canada to collect radiological forensics, which would provide more consistent, reliable and prompt data for incident management by municipal, provincial and federal authorities.

A surveillance system of mobile radiation sensors reporting in real time will make possible early detection of illicit radiological transport and storage and increase the time available to respond.

Health Canada's Radiation Protection Bureau, the RCMP, the Geological Survey of Canada and private industry are collaborating on this project

to integrate existing cutting-edge technological solutions to develop a limited capacity to fill the radiological surveillance gap. This project will develop a system usable in routine RCMP patrol work and by Health Canada. The system will automatically transfer radiation data in real time by radio communications systems for analysis by the most sensitive available signal detection technology. Municipal, provincial and federal decision makers will, for the first time, have access to prompt, well defined and reliable radiation data for attack prevention and interdiction, incident response and management, safety, and forensics. The shared objectives will ensure development of field and command and control technology that is both relevant to terrorist attack prevention and mitigation objectives, and acceptable for routine police use. The collaborative approach will foster mutual understanding of partners' operational issues and provide the radiation information base needed for the coordination of enhanced response in complex events.

The system will detect the transport and storage of illicit radiologicals before an attack achieves target proximity, thus meeting security needs for early detection and warning. Early detection will make interdiction possible. The system, with its technology and training, provides greatly enhanced capabilities for police and command and control to assess radiation data in real time for public safety and incident management.

The mobile system brings state-of-the-art field tested radiation sensors and radio communications together with the highest-sensitivity event-detection algorithms to provide on-site rapid detection and identification of radiologicals. The system provides forensic capabilities for radiologicals by promptly deploying real-time evidence collection sensor technologies capable of gross contamination mapping and species identification.

The successful integration of these technologies into a system co-designed by law enforcement professionals will result in a system usable in routine police patrol. This use will point the way for the addition of other terrorist agent sensors for the protection of the public and First Responders.

CRTI 0120RD

Development of a Novel Molecular Imprinting Methodology for Sensing Applications

Project Lead: National Research Council of Canada

Federal Partners: Defence R&D Canada

The principal objective of this project is to enhance the capabilities of First Responders or military personnel to determine the presence of harmful agents in the environment. The use of innovative imprinting techniques to deposit artificial recognition elements on targeted surfaces will produce robust and affordable devices adaptable to a variety of detection purposes. Arrays of chemically and spatially-resolved functional groups will be imprinted onto substrate surfaces, enabling the recognition of complementary molecules and parts of molecules. When these arrays are coupled with sensors employing standard surface analytical or photonic techniques, targeted species will be detectable and identifiable in real time. Moreover, this technology in the control of surface chemistries may have various other applications, such as in the pharmaceutical and biotechnological industries.

Molecular imprinting is an emerging technology based on the use of artificial recognition elements. These artificial recognition elements provide an alternative to the use of the somewhat fragile elements (such as enzymes, proteins or antibodies) used in traditional sensing devices, which lack storage and operational stability.

* Lead Federal Department

Standard molecular imprinting is a process by which functional monomers are allowed to self-assemble around a template molecule and are subsequently crosslinked into place. The template is encapsulated in a stable three-dimensional polymer matrix. The template molecule can then be removed, leaving behind a cavity that will bind molecules identical to the template molecule. The imprint functions like a lock that is only compatible with the correct key.

Molecular recognition between a molecular receptor (host) and a substrate (guest) in a matrix containing structurally related molecules requires discrimination and binding; this can happen only if the binding sites of the host and guest molecules complement each other in size, shape, and chemical functionality. Biological systems, such as enzyme-substrate, antibody-antigen, and hormone-receptor systems, demonstrate molecular recognition properties that have developed by natural selection.

The rebinding of the target molecules can be detected by a number of optical techniques. Waveguides can be used as substrates for molecularly imprinting the recognition sites of interest. Upon the attachment of the desired molecules on top of the functionalized waveguide, changes in the effective refractive index (RI), induced by interaction between an evanescent field and the attached target molecules, can be used as the detection mechanism, leading to the development of real-time multi-analyte detection devices.

This proposal has as its first main objective the development of portable and direct sensing devices capable of equipping First Responders in their interventions and helping them in their training. The second main objective is to provide enabling technologies for use in building adequate prevention, surveillance and alert capabilities. Moreover, the availability of such real-time sensing and screening devices may have a direct effect on public confidence through the given reassurances that potential threats can not only be handled efficiently but also prevented through the use of state-of-the-art detection technologies. The main strength of this proposed methodology is the integration of the recognition and detection subsystems on a chip. The incorporation on a chip of the chemical and/or biological recognition elements along with the analytical element (such as micro-photonic analytical method) will allow the development of self-contained, compact, robust real-time sensing devices.

CRTI 0131TA

HI-6 Project

Project Lead: Defence R&D Canada

Federal Partners: Department of National Defence, Solicitor General, Royal Canadian Mounted Police, Office of Critical Infrastructure Protection and Emergency Preparedness

Recent world events have heightened the concern over the possible use of biological, chemical or radiological agents, whether in battlefield or terrorist scenarios. These threats continue to validate the requirement for research and development (R&D) programs that strive to develop new and improved drugs and biologics for prophylaxis and treatment against chemical, biological and radiological (CBR) threats. Specifically, directed R&D is needed to provide improved products and an established source of supply to facilitate immediate reaction and near-time consequence management following chemical nerve agent exposure.

Since the early 1990s, defence personnel from several nations have relied upon an auto-injector containing the nerve agent antidote HI-6 to provide immediate treatment following chemical agent exposure. HI-6 provides a broad antidote effectiveness spectrum with superior effectiveness against Soman (GD), in addition to Tabun (GA), Sarin (GB), GF and VX. This HI-6 system is comprised of auto-injectors containing an HI-6 dichloride salt and atropine, supplemented by a separate auto-injector of the anticonvulsant Diazepam. However, there are several deficiencies with the current system: (1) there is no source of supply of GMP-grade HI-6, (2) there is a cumbersome system of multiple auto-injectors, (3) the necessary range of HI-6-based drug products does not exist, and (4) there is inadequate data to support regulatory submissions. While current auto-injectors have fulfilled an immediate operational requirement, the medical countermeasure requirements staff and the scientific community within the Department of National Defence (DND) have agreed on the need for a licensed, next-generation HI-6 auto-injector system.

Defence Research and Development Canada has received core funding for the project from the federal government's CRTI. This funding and DND scientific expertise will be further supported by financial and scientific assistance through a six-nation collaboration (between Canada, Germany, the Netherlands, Norway, Sweden and the United Kingdom). This project will develop the essential components of the proposed HI-6 nerve agent antidote system and will establish a source of supply for the drug products in their final formulation. It will also provide products that are not currently available and will optimize the delivery of all three drug substances by a 3-in-1 auto-injector system that will replace the two auto-injectors currently required for treatment of nerve agent poisoning.

The HI-6 Nerve Agent Antidote (NAA) System will be comprised of the following drug products: (1) a 3-in-1 auto-injector containing HI-6 dimethanesulphonate salt, atropine and the anticonvulsant avizafone, (2) a 2-in-1 auto-injector with HI-6 dimethanesulphonate salt and atropine, and (3) HI-6 in a vial formulated for intramuscular administration by medical personnel. In addition, it will be "dual use," that is, available to both the military and to civilian First Responders in a response to a terrorist attack employing nerve agents.

The first step in the project is to develop a project management plan that considers the requirements of all countries involved, including the requirements for use in First Responder scenarios, as well as the requirements of all regulatory agencies involved. Through a series of directed contracts to industry, an optimized route of synthesis for GMP HI-6 dimethanesulfonate (DMS) will then be identified and further developed to facilitate industrial scale-up. A quantity of HI-6 DMS will then be produced, accompanied by a Drug Master File, which is required for a subsequent regulatory submission. Concurrently, a source of supply for all components will be identified and an auto-injector capable of meeting the 3-in-1 and 2-in-1 requirements will be selected or developed. The three separate drug products will be formulated to meet the requirements of the applicable regulatory agencies and a quantity of filled auto-injectors and vials of HI-6 will be provided for use in stability studies, and non-clinical and clinical trials. Following completion of these studies, the necessary regulatory submissions will be compiled.

CRTI 0133RD

New Technologies for the Rapid Assessment of Radioactive Contamination

Project Lead: Trent University

Federal Partners: Health Canada, National Research Council

Following a radiological or nuclear (RN) terrorist attack, an analytical system that can screen samples and provide results in minutes is essential to effectively assess and mitigate health, economic and environmental impacts. The quantities of specific radionuclides that are contained in a RN weapon or are released from a reactor will vary with the source of the material used to make the weapon, or the exact reactor conditions. Rapid radio-analytical techniques have very broad applicability, yet suitable methods and technologies to do this are currently limited. Traditional radionuclide detection methods are typically either slow or lacking in the ability to detect low levels of radiation.

The objective of this project is to develop innovative inductively coupled plasma mass spectrometry (ICP-MS) technologies for the rapid analysis of radionuclides of concern in a RN terrorist attack. To achieve this objective, the project must solve three problems:

1. The radionuclides must be efficiently and rapidly extracted from the sample.
2. The radionuclides must be separated from any interference and concentrated to maximize the signal.
3. The ICP-MS must be optimized so that high sensitivity is obtained especially for short-lived radionuclides, and must be equipped with hardware that can eliminate or compensate for anticipated isobaric and molecular interferences.

Solving these problems will reduce the time to analyze samples from days to minutes and increase sample throughput from tens to hundreds per day. An additional benefit produced by this work will be the ability to use the multiple radionuclide signatures from contaminated materials to help determine the origin of the nuclear material in a RN attack. This will be a valuable tool for forensic analysis. These innovations will also have spin-off benefits for Canadian government and industry. Principally, these will be better methods for measurement and monitoring of radionuclides as part of regulatory requirements for the peaceful use of nuclear materials.

The three problems outlined above will be addressed in this project by (1) developing on-line analyte vaporization and separation coupled with detection techniques that can use ICP-MS approaches; and (2) using gas phase chemistry in a dynamic reaction cell on the ICP-MS to eliminate interferences. Vaporization will involve rapid thermal decomposition of the samples, while separation will use high temperature on-line gas phase reactions and chromatography. ICP-MS optimization is required to ensure that the extractions and separations minimize problems, such as matrix loading, that degrade the ICP-MS system performance. While most of the radioisotopes of interest (or long-lived indicator isotopes thereof) are largely interference free in ICP-MS, some are isobaric with plasma ions (e.g., $^{129}I^+$ and $^{131}I^+$ are interfered by impurity Xe isotopes) and almost all are obfuscated at ultra-trace levels by hydrides, oxides or other molecular species derived from the sample or produced in the plasma (e.g., $^{238}UH^+$ interferes with the ultra-trace determination of $^{239}Pu^+$, and $^{90}Zr^+$ interferes with $^{90}Sr^+$). It has recently been recognized that specific and efficient ion-molecule chemistry can be enacted on-line (in the ion beam of the mass spectrometer) to provide chemical resolution of interferences based on the thermodynamics and

kinetics that are linked to the periodicity of the elements. For example, $^{40}Ca^{+}$ can be chemically resolved from $^{40}Ar^{+}$ by using charge transfer chemistry with NH_3, providing 9 orders of magnitude of suppression of the $^{40}Ar^{+}$ signal without significant effect on the $^{40}Ca^{+}$ signal. Development of specific ion-molecule chemistries in the dynamic reaction cell of the MS will be used to alleviate persistent isobaric and molecular interferences.

The project involves investigators at Trent University, Health Canada, National Research Council and MDS Sciex. Common instrumentation and laboratory facilities will be developed on the premises of each partner to ensure rapid method development and implementation of procedures during the project. As well, these instruments and lab facilities will provide Canada with a radio-analytical capability to respond to a RN terrorist event.

CRTI 0154RD

Rapid DNA-Based Diagnostic Tests for Two Biological Agents

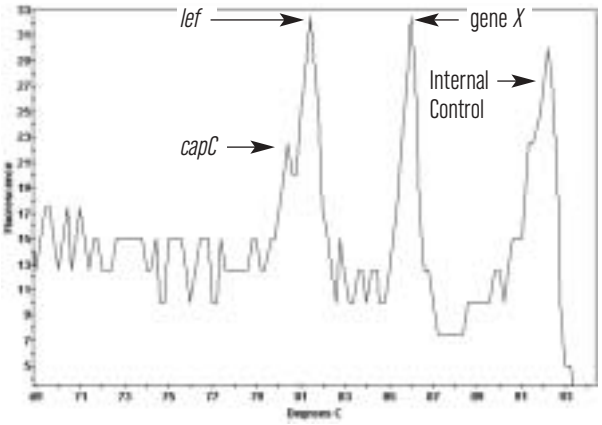
Project Lead: Infectious Diseases Research Centre, Université Laval

Federal Partners: Defence R&D Canada, Health Canada

Previously, the Infectious Diseases Research Centre of Université Laval (IDRC), in collaboration with DRDC Suffield and Infectio Diagnostic Inc. (IDI), developed a rapid, sensitive and specific test for the diagnosis of *Bacillus anthracis*, the etiological agent of anthrax, directly from clinical and environmental samples. This assay has been developed on the Smart Cycler platform as a one-tube multiplex SYBR, Green-based amplification assay, targetting two B. anthracis plasmidic genes (*capC* and *lef*) and one chromosomal gene (gene *X*). Each of the three amplicons could be distinguished by analysis of melting curves generated by the instrument (Figure 1).

It is now important to increase the list of targeted species and genes in diagnostic tests for biological threat agents. Many of these pathogens affect both human and animal hosts and therefore have the potential to impact both the public health and agricultural sectors of our country. The development of rapid identification assays for key bacterial threat agents manufactured under strict industrial standards will provide public health laboratories, agricultural laboratories and First Responders with rapid response capabilities to minimize the impact of real or suspected biological terrorism attacks, natural outbreaks or hoaxes.

Figure 1: Melting curve produced by the *B. anthracis* multiplex PCR assay



Based on proven success with the *B. anthracis* identification assay and on the need to improve biothreat response capability among First Responders, public health and government agencies, we propose to develop rapid (less than

one hour) molecular diagnostic assays for the detection and identification of the biological agents *Yersinia pestis* and *Francisella tularensis*. Classical identification of these two pathogens is slow, painstaking and risky. The new assays will be unique and innovative in their design, and performed in less than one hour directly from clinical and environmental specimens. The strategy will apply present expertise in microbial genomic rapid DNA extraction, sample preparation procedures and real-time polymerase chain reaction (PCR) technology.

To achieve this goal the following steps are required:

1. Key target genes for each agent will be identified. 1–3 target genes will be used for each species, including conserved genes for bacterial identification and virulence factors required for pathogenicity.
2. The design of optimal primers will be governed by *in silico* genomic strategies. This will be possible by sequencing selected genetic targets from several strains of the two organisms as well as from related species, and will complement the existing comprehensive sequence database.
3. The assays will be developed for detection by agarose gel electrophoresis, by SYBR, Green melting curves analysis and by fluorescent probes for real-time monitoring.
4. Using optimized reagents and PCR conditions, each assay will be tested *in vitro* for specificity, ubiquity and sensitivity. If required, primers and probes will be adjusted for optimal performance.
5. Sample preparation protocols will be established for appropriate (clinical and environmental) specimens, by using (1) spiked genomic DNAs, and (2) spiked biothreat agents using level 3 biocontainment facilities at DRDC Suffield and Health Canada.
6. Standard reagent formulations will be developed by IDI in compliance with the industrial standards and regulations of the *in vitro* diagnostic industry.
7. Tests to assess the robustness of the reagent formulations, protocols and assays will be performed in federal government laboratories.

This work will be performed by a joint collaboration between IDRC, DRDC Suffield, Health Canada (HC) and IDI. Although the previous collaboration between IDRC, DRDC Suffield and IDI was successful, the addition of Health Canada will bring complementary expertise in the field of molecular diagnostics and microbiology. HC will play an important role in the validation of the molecular diagnostic assays. In addition, this joint collaboration will permit the sharing of specific expertise between the four partners.

The end results will provide validated, specific, ubiquitous and sensitive diagnostic assays and protocols to detect and identify these two key bacterial threat agents in less than one hour directly from clinical and environmental samples. The ability to identify the causative agent(s) from a covert aerosol exposure using the diagnostic tests developed in this project, rather than tests that take days or weeks, will allow authorities to respond more rapidly to a biological terrorism incident.

CRTI 0161TA

CBRN Blast Protective Helmet

Project Lead: Med-Eng Systems Inc.

Federal Partners: Royal Canadian Mounted Police, Defence R&D Canada

One of the real emerging threats facing First Responders is chemical or biological (CB) agents attached to an explosive device. Thus, First Responders have the requirement of combined CB and Explosive Ordnance Disposal (EOD) personal protective equipment. To provide effective protection against the combined threat, chemical protective undergarments (CPU), gloves, boots, as well as respiratory protection (preferably from a self-contained breathing apparatus (SCBA)), all need to be worn in conjunction with a bomb suit ensemble.

Current blast protective helmets used for EOD provide balanced protection against the four conventional threats of an explosion (overpressure, fragmentation, impact and heat). This protection is provided through the use of various ballistic and energy-absorbing materials, aerodynamic shapes, and systems integration with an EOD suit protecting the body. However, the augmentation of conventional threats by possible CB agents necessitates a unique helmet-visor system design that provides high levels of blast, fragmentation, impact, fire and CB protection. This can be accomplished using the latest technology in processing clear thermoplastics to develop a visor that incorporates a complex curvature to protect the facemask of the SCBA.

Of the helmet systems currently available to protect against CB and blast threat, the SRS-5 helmet with a CB visor, by Med-Eng Systems, has a few shortcomings. The ballistic protection provided by the helmet shell is a compromise based on what was feasible with materials and processes a few years ago. In addition, the visor of the SRS-5 has a relatively low level of fragmentation protection. It has also become evident that the shape of the SRS-5 CB visor is too restrictive, not allowing user groups to interface the visor with the wide variety of SCBA systems in use. Finally, it has been pointed out that the interior size of the SRS-5 helmet may be too small for some end-users when a CPU balaclava and an SCBA facemask are in place.

The objective of this project is the design, development and evaluation of a new CBRN Blast Protective Helmet. This new system will be multi-purpose, using a common helmet shell with three unique interchangeable visors suited for (1) IEDD (Improvised Explosive Device Disposal) involving CB agents, (2) conventional EOD/IEDD threats, and (3) Search operations. The CB visor(s) will comprise a complex curvature visor (or visors) to accommodate a wide range of SCBA facemasks. The EOD/IEDD visor will provide the highest levels of blast and fragmentation resistance, while the visor for Search operations will be lighter, with an enhanced field of view. Current practice involves having three completely different helmet-visor systems to appropriately address these three operational environments. This is costly and logistically burdensome. In contrast, the CBRN Blast Protective Helmet system, with its various modular visors, will reduce the overall cost of head protection to the First Responder and permit on-site decisions to be made regarding the most appropriate protection to be selected, given the particular threat scenario.

The EOD visor will have an industry-leading ballistic V50 rating (employing the 17 grain chisel shaped FSP; a “V50 rating” is defined as the velocity at which a given projectile will have a 50% probability of penetrating a given material). The CB visor(s) will exhibit an intermediate V50 rating, depending on curvature complexity. The Search visor will have an adequate rating for its

purposes. The final fragmentation resistance targets for the visors will be determined based on feasibility and ergonomics. All three of the visors will make use of advances in visor processing using combinations of transparent fragmentation resistant plastics and composite materials. As a result of the creation of the new CB visor, two current deficiencies will be addressed. The first is that this visor will be designed to be used with an appropriately wide range of SCBA facemasks, thus eliminating the current compatibility problem with the SRS-5 CB visor. The second is that the new CB visor will have a much higher V50 rating than the current vulnerable SRS-5 CB visor.

For ballistic protection, the CBRN Blast Protective Helmet will be a feature a shell composed of the latest lightweight composite materials, manufactured using high-pressure compression molding. For non-ballistic impact protection, an impact liner of appropriate density and thickness will be in place. To provide a comfortable fit, designers envision a removable, customizable comfort liner that will allow for use of the helmet with or without a CPU balaclava and SCBA facemask. Moreover, this new system will allow for a comfort liner to be individually customized for different head sizes, so the same overall helmet system (minus the comfort liner) may be shared among many persons. The retention system to be put in place on the CBRN Helmet will be of a true four-point variety, to effectively balance the weight of the helmet.

The helmet will also feature an environmental awareness system (EAS) to allow the operator to hear ambient sounds. A ventilation system will be in place to supply fresh air to the face of the "non-masked" user, which prevents carbon dioxide build up, keeps the user's face cool, and prevents the formation of fog and mist on the helmet's visor (this feature can be turned off in the case of a potential CBRN threat). In order to further prevent visor fogging, an active visor demister is being considered.

The CBRN Blast Protective Helmet, with all three types of visors, will be compatible with existing personal protective ensembles by Med-Eng Systems, including the deployed SRS-5 and EOD-8 Suits, as well as being forward compatible with any suits that may be released in the foreseeable future.

Functional prototypes and alpha samples of the CBRN Blast Protective Helmet, integrated with a protective suit, will be subjected to numerous tests to assess and quantify its protective performance. Blast testing with instrumented anthropomorphic mannequins, to be carried out in cooperation with the RCMP and Defence R&D Canada, will be performed to ensure adequate blast resistance of the helmet. Chemical vapor testing will be performed at the Royal Military College of Canada, with individuals equipped with a full ensemble of protective equipment placed in an environmentally controlled chamber filled with a vapor of chemical threat simulant. Similar testing involving an aerosol simulating a biological agent will be carried out at DRDC Suffield. Limited tests will also be performed to assess the effectiveness of the system to protect against CB agents that are explosively driven. Finally, beta samples of the CBRN Blast Protective Helmet will be assessed in validation studies as part of two other CRTI projects: Standards for Personal Protective Equipment for First Responders (CRTI 0029RD) and the CB Chamber (CRTI 0100TA).

Med-Eng Systems, the lead private partner on this project, is the world leader in the design and manufacture of personal protective ensembles for EOD/IEDD roles. Since incorporation in 1981, Med-Eng Systems has tackled aggressive R&D programs with key institutions (including the RCMP, US Army NVESD (Fort Belvoir), and US SBCCOM (Natick)) to yield significant breakthroughs

in personal protective technologies. Capitalizing on these research programs, Med-Eng Systems has deployed EOD ensembles in over 130 countries and territories, worldwide.

CRTI 0196TA

Development of Rapid Detection Field Tests and Training Programs for Veterinary First Responders to Address Agro-Terrorism with Animal Pathogens

Project Lead: Canadian Food Inspection Agency

Federal Partners: Health Canada, National Research Council

Canada is currently free of major transmissible animal pathogens such as foot-and-mouth disease (FMD) and hog cholera (HC). An outbreak of an exotic animal disease caused by agro-terrorism would result in swift and severe damage to Canada. An outbreak would result in the immediate closing of Canada's borders for exports of animals and animal products. The economic and social consequences could be like those experienced during the 2001 British FMD crisis in which damage to the economy exceeded $30 billion (CDN). If agro-terrorists were to introduce a zoonosis (that is, an animal disease capable of infecting humans) such as avian influenza (AI) or Nipah virus (NV), human health would also be affected.

Agro-terrorism using an animal disease would likely present itself differently than would a natural disease incursion. A multi-focal simultaneous outbreak of an exotic or an emerging disease could occur. A disease could present with different clinical signs than usual due to aerosol exposure to the disease agent instead of the normal animal-to-animal transmission route.

The ability to mitigate the negative consequences of an agro-terrorism event depends on: being well prepared to detect signs of disease in animals early and accurately; quick differentiation between diseases that have similar signs; and managing longer-term consequences through containment and eradication. These efforts require Veterinary First Responders (VFR) in the field who are highly-trained, equipped with robust, rapid diagnostic screening tests, and able to communicate with scientific experts in real time.

Animal diseases may be diagnosed rapidly using new technologies that detect antigen (protein) or genome sequence (DNA) specific to a particular pathogen or, later in the disease process, antibodies in the blood (serum) of a recovering animal. For example, Enzyme-Linked Immuno-Sorbent Assay (ELISA) technology can produce tests that are read by a simple colour reaction and that may be suitable for use as dipstick or penside tests for either antigens or antibodies. Polymerase chain reaction (PCR) technology can detect DNA sequences unique to certain pathogens and can be used in mobile field units. DNA or protein micro-arrays can be designed to detect and differentiate multiple antigens, antibodies or DNA.

This project will focus on the development of new diagnostic tests based on the key platform technologies that have the greatest potential as field tests for VFR. These tests will be mobile and robust for use in the field. They will produce highly reliable, accurate results, support differential diagnosis, allow for automation for handling large numbers of samples, and allow for electronic collection and transmission of data. These tests will be applied to rapid diagnosis of FMD, HC, AI and NV.

Three technology groups that will be investigated:

1. Real Time Polymerase Chain Reaction (RT-PCR) for FMD, HC, and AI,
2. DNA/Protein Microarrays for FMD, HC, AI, and
3. Rapid Antigen/Antibody Detection Systems.

The last of these will include sub-projects that will:

1. Develop Fluorescence Polarization Assay (FPA) technology, dipstick ELISA or acoustic rupture event scanning for FMD, HC and AI,
2. Differentiate convalescent animals from those vaccinated against FMD by multiplex ELISA,
3. Develop Rapid Diagnostic Colloidal-Gold Immuno-Blotting Methods for HC and AI, and
4. Develop field tests for the detection of NV.

Each technology group will be led by a Canadian Food Inspection Agency laboratory equipped with biocontainment facilities (Level 3 or 4) and specialized expertise in select animal pathogens and key technologies. Federal partners include the National Research Council and the National Microbiology Laboratory of Health Canada.

Since highly trained First Responders linked to scientific experts in real time will be key to the effective use of these tests in the context of agro-terrorism, a Training and Communications group will be formed.

CRTI-0203RD

Standoff Detection of Radiation

Project Lead: Defence R&D Canada – Ottawa

Federal Partners: Atomic Energy of Canada Limited

This project aims to develop a prototype standoff radiation detector, for the detection of hazards or the characterization of hazard areas prior to personnel entry. This is a completely novel approach to radiation detection, since all existing detectors rely on more hazardous direct detection.

Many radiological terror scenarios involve the dispersal of radionuclides. In these scenarios, the greatest concerns are contamination of personnel and equipment. Thus, while First Responders may enter contaminated zones for the purpose of life saving, the response of personnel to such an incident will generally be one of hazard avoidance and containment in the early phase. Later phases will probably also include more detailed surveys, including the search for hot spots that may be indicative of larger pieces of radioactive material with more evidentiary value for criminal investigation purposes. All of these operations involve systematic measurements of the hazard with radiation survey meters.

Radiation survey meters, and in fact all radiation detectors, work on the principle of direct detection. That is, the radiation must actually enter the detector to be counted. This is a fine principle, but for one fact: in order to make a measurement of a radiation hazard with a radiation survey meter, the survey technician must be standing in the hazard itself. This is a particular problem for alpha- and beta-emitting radionuclides for two complementary reasons. First, the short range of these radiations means that the radiation field falls off quickly with distance, and so one has to approach quite closely before a conventional detector will register. Second, their short range

also means that alpha and beta emitters are also significant health hazards when inhaled or ingested, so that the hazards of walking into a contaminated area without the appropriate protective equipment are considerable. Thus, it would be highly desirable to move beyond the use of direct detection to less hazardous indirect methods.

This project builds on previous work by Defence R&D Canada – Ottawa and Bubble Technology Industries (BTI) in the indirect or standoff detection of radiation. Research in this field has been under way for approximately three years, and has had considerable success. A laboratory prototype detector has been constructed, which is capable of taking images of a scene and analyzing these images for the signature of ionizing radiation. With this instrument, alpha, beta and gamma sources have been imaged under a variety of conditions. Alpha sources of only a few millicuries have been imaged at tens of metres with high signal-to-noise ratios. The present proposal calls for the construction of a fieldable prototype standoff radiation detector. This prototype will be able to demonstrate conclusively through field trials to what extent standoff detection can aid emergency response and other applications.

The most obvious application of a standoff radiation detector is to identify radioactive sources and contaminated fields from a distance where the radiation does not constitute a hazard. This allows one to avoid the hazard, to minimize exposure by informed planning if one has to cross the hazard, or to mitigate the hazard through the use of the appropriate protective equipment, in the case of a non-penetrating radiation field. These applications of hazard detection and long-distance radiation field survey are applicable to the civilian first response, remediation, and criminal investigation communities, as well as to the military community.

This project is lead by DRDC Ottawa, with federal government partners at Atomic Energy of Canada, Limited (AECL), and Health Canada (HC). The Radiation Effects Group at DRDC Ottawa is a world leader in radiation dosimetry and spectrometry research. It provides radiation protection support to the Canadian Forces and would be a key player in Canada's response in the event of a radiological incident. AECL and HC also have considerable expertise in the fields of radiation protection and detection.

The industrial partner for this project is BTI with expertise covering many different types of radiation sensors. In particular, BTI has been involved in standoff detection research for three years. BTI's expertise with this one-of-a-kind detector makes it uniquely capable of carrying out this project.

CRTI-0204RD

Bubble Detector Film

Project Lead: Defence R&D Canada – Ottawa

Federal Partners: Atomic Energy of Canada Limited

This project aims to develop a sensitive unpowered real-time radiation exposure indicator, designed specifically for alpha and beta radiation detection. This so-called "Bubble Detector Film" (BDF) fills a long-standing gap in radiation sensing, with applications in personnel and equipment contamination detection and monitoring.

Radiological contamination is the most difficult problem following a radiological terror attack. Contaminated personnel can be susceptible to radiation burns, and contaminated personnel and equipment can become vectors for the spread of radioactive material. These realities impose two requirements on first response and remediation

operations. First, radioactive contamination must be detected as soon as possible so that further contamination can be prevented or controlled. Second, contaminated personnel and materiel must be thoroughly decontaminated before they can leave the incident scene. This project addresses both of these requirements.

There are currently two methods for contamination monitoring. One can swipe suspect surfaces, and send the swipes for lab analysis. This solution provides no real-time indication, and is thus unsuitable for most emergency response and many remediation scenarios. The second option provides real-time indication through the use of sophisticated and expensive electronic contamination monitors. These require considerable training to use, and the user cannot perform any other task while looking for contamination. Clearly, what is required is a sensitive, simple real-time indicator of contamination that requires minimal user interaction. To date, and despite decades of research, no technology has been developed that satisfies this requirement; this project marks a breakthrough in radiation detection by meeting this need.

This project aims to marry the technology of the neutron bubble detector with other chemical techniques to produce a sensitive chemical radiation sensor. This sensor will exhibit an immediate visible change in response to ionizing radiation exposure, and will be tailored for contamination detection and monitoring. Clearly, products based on this technology will have many applications in radiation safety and emergency response. For instance, this Bubble Detector Film (BDF) could be made into a disposable strip with an adhesive backing that could be stuck to the pant leg or boot of a First Responder. If the First Responder walks into a contaminated area, the strip will be contaminated and produce a visible warning that the area is contaminated. This product requires no user interaction, apart from sticking the detector on the boot, and occasionally glancing down at it. Another significant application involves making swipes from the BDF. Swipes are traditionally used to sample potentially contaminated surfaces, and are analyzed in sophisticated laboratories. Contaminated BDF swipes, however, would be instantly recognizable. The project thus addresses both near and longer term consequence management by addressing a critical gap in First Responder equipment.

This project is lead by Defence R&D Canada – Ottawa, with federal government partners at Atomic Energy of Canada Limited (AECL), and Health Canada (HC). The Radiation Effects Group at DRDC Ottawa is a world leader in radiation dosimetry and spectrometry research. It provides radiation protection support to the Canadian Forces and would be a key player in Canada's response in the event of a radiological incident. AECL and HC also have considerable expertise in the fields of radiation protection and dosimetry.

The industrial partner for this project is Bubble Technology Industries (BTI). BTI's expertise covers many different types of radiation sensors. In particular, BTI developed the bubble detector for personal neutron dosimetry. This detector is renowned worldwide for its ability to provide real-time neutron dosimetry over a wide energy range in an unpowered detector. BTI's expertise with this one-of-a-kind dosimeter makes it uniquely capable of carrying out this project.