



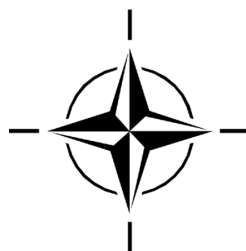
STO TECHNICAL REPORT

TR-HFM-177

Deployable Laboratory Applications of Nano- and Bio-Technology

(Applications de nanotechnologie et biotechnologie
destinées à un laboratoire déployable)

Findings of Task Group HFM-177.



Published October 2014



NORTH ATLANTIC TREATY
ORGANIZATION



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SCIENCE AND TECHNOLOGY
ORGANIZATION



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The NATO Science and Technology Organization

Science & Technology (S&T) in the NATO context is defined as the selective and rigorous generation and application of state-of-the-art, validated knowledge for defence and security purposes. S&T activities embrace scientific research, technology development, transition, application and field-testing, experimentation and a range of related scientific activities that include systems engineering, operational research and analysis, synthesis, integration and validation of knowledge derived through the scientific method.

In NATO, S&T is addressed using different business models, namely a collaborative business model where NATO provides a forum where NATO Nations and partner Nations elect to use their national resources to define, conduct and promote cooperative research and information exchange, and secondly an in-house delivery business model where S&T activities are conducted in a NATO dedicated executive body, having its own personnel, capabilities and infrastructure.

The mission of the NATO Science & Technology Organization (STO) is to help position the Nations' and NATO's S&T investments as a strategic enabler of the knowledge and technology advantage for the defence and security posture of NATO Nations and partner Nations, by conducting and promoting S&T activities that augment and leverage the capabilities and programmes of the Alliance, of the NATO Nations and the partner Nations, in support of NATO's objectives, and contributing to NATO's ability to enable and influence security and defence related capability development and threat mitigation in NATO Nations and partner Nations, in accordance with NATO policies.

The total spectrum of this collaborative effort is addressed by six Technical Panels who manage a wide range of scientific research activities, a Group specialising in modelling and simulation, plus a Committee dedicated to supporting the information management needs of the organization.

- AVT Applied Vehicle Technology Panel
- HFM Human Factors and Medicine Panel
- IST Information Systems Technology Panel
- NMSG NATO Modelling and Simulation Group
- SAS System Analysis and Studies Panel
- SCI Systems Concepts and Integration Panel
- SET Sensors and Electronics Technology Panel

These Panels and Group are the power-house of the collaborative model and are made up of national representatives as well as recognised world-class scientists, engineers and information specialists. In addition to providing critical technical oversight, they also provide a communication link to military users and other NATO bodies.

The scientific and technological work is carried out by Technical Teams, created under one or more of these eight bodies, for specific research activities which have a defined duration. These research activities can take a variety of forms, including Task Groups, Workshops, Symposia, Specialists' Meetings, Lecture Series and Technical Courses.

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HFM-177 Membership List

CHAIR

Dr. John J. SCHLAGER
Chief, Molecular Bioeffects Branch
711th Human Performance Wing, Air Force Research Laboratory
2729 R Street, Area B, Building 837
Wright-Patterson AFB, Dayton, OH 45433-5707
UNITED STATES
Email: john.schlager@us.af.mil

MEMBERS

Dr. Gürer G. BUDAK
Director
Gazi University NanoMedicine and
Advanced Technologies Research Center
Golbasi Bahcelievler District
160 Street
P.O. Box 126
06830 Golbasi-Ankara
TURKEY
Email: Gurer.Budak@gazi.edu.tr

Maj. Jiri DRESLER
(Not Appointed)
Central Military Health Institute
U vojenske nemocnice 1200
169 02 Prague
CZECH REPUBLIC
Email: Jiri.Dresler@gmail.com

Dr. Julian HOWELLS
Group Technical Lead – Reagents
Defence Science and Technology
Laboratory [Dstl]
Porton Down
Salisbury, Wiltshire SP4 0JQ
UNITED KINGDOM
Email: Jlhowells@dstl.gov.uk

Prof. Martin HUBALEK
Institute of Molecular Pathology
University of Defence
Trebesska 1575
500 01 Hradec Kralove
CZECH REPUBLIC
Email: Martin.Hubalek@sujb.cz

Dr. Mark LISANBY
Molecular Bioeffects Branch
711th Human Performance Wing
Air Force Research Laboratory
2729 R Street, Area B, Building 837
Wright-Patterson AFB
Dayton, OH 45433-5707
UNITED STATES
Email: Mark.Lisanby@wpafb.af.mil

Maj. Fe LOBO-MENENDEZ
Deputy Branch Chief, Molecular Bioeffects Branch
711th Human Performance Wing
Air Force Research Laboratory
2729 R Street, Area B, Building 837
Wright-Patterson AFB
Dayton, OH 45433-5707
UNITED STATES
Email: Fe.Lobo-Menendez@wpafb.af.mil

Dr. Brian J. LUKEY
Extramural Research Coordinator
711th Human Performance Wing
Air Force Research Laboratory
2729 R Street, Area B, Building 837
Wright-Patterson AFB
Dayton, OH 45433-5707
UNITED STATES
Email: Brian.Lukey.ctr@wpafb.af.mil

Dr. Ales MACELA
Institute of Radiobiology and Molecular Pathology
Military Medical Faculty, University of Defence
Trebesska 1575
500 01 Hradec Kralove
CZECH REPUBLIC
Email: amacela@pmfhk.cz

Prof. Robert MARKS
Department of Biotechnology Engineering
Ben-Gurion University of the Negev
POB 653, Beer-Sheva 84105
ISRAEL
Email: Rsmarks@bgumail.bgu.ac.il

Dr. Raymond MASTNJAK
Supervisor, CBRNE Support (Mobile Labs and
Kits),
Edgewood Chemical Biological Center
APG Edgewood Area, MD 21010
UNITED STATES
Email: Raymond.Z.Mastnjak.civ@mail.mil

Pr. Daniel PARZY
Directeur, UMR-MD3
GSBDD de Marseille Aubange
BP 40026, 111, avenue de la Corse
13568 Marseille Cedex 02
FRANCE
Email: D.Parzy@free.fr

Dr. Libor PISA
(Not Appointed)
Central Military Health Institute
U vojenske nemocnice 1200
169 02 Prague
CZECH REPUBLIC
Email: L.Pisa@email.cz

Dr. Sergo TABAGARI
Dean, AIETI Medical School
2/6 Ljubljana Str., Dighomi
Tbilisi 0159
GEORGIA
Email: Dean@aieti.edu.ge

Pharm. Col. François THIBAULT
(Not Appointed)
Institut de recherches biomédicales des armes
Département de microbiologie
BP 87
F-38702 La Tronche Cedex
FRANCE
Email: Fthibault@crssa.net

Dr. Roman WOELFEL
Head, Dept. Med Bio-Recon and Verification
Bundeswehr Institute of Microbiology
Neuherbergstrasse 11
80937 Munich
GERMANY
Email: Romanwoelfel@bundeswehr.org

Deployable Laboratory Applications of Nano- and Bio-Technology (STO-TR-HFM-177)

Executive Summary

The expeditionary nature of the North Atlantic Treaty Organization (NATO) Response Force requires deployable laboratory capabilities leveraging advances in nano/bio-technology. As such, the NATO Science Technical Organization Panel on Human Factors and Medicine chartered the research technical group (HFM-177 RTG) to study the “Deployable Laboratory Applications of Nano- and Bio-Technology” with a focus on deployable NATO CBRN laboratory advanced technologies. The goals were:

- 1) To survey deployable laboratory designs, construction and materials;
- 2) Analyze existing instrument technology and procedures;
- 3) Analyze emerging nano/bio-technology for instrument acquisition; and
- 4) Integrate existing and emerging technologies into a deployable laboratory design.

Over 20 representatives from eight countries participated from the Republic of Georgia, Turkey, Israel, the Czech Republic, United Kingdom, United States, France and Germany. Each country discussed their CBRN deployable laboratory capabilities and challenges. The HFM-177 RTG noted the rapidly changing evolution of analytical technologies, the different roles and mission types each country has for its specific laboratory assets, and the varying levels of funds each country allots to maintain/improve laboratory operations. When collected together, these variances provide a diverse set of applications and technologies to address multiple levels of mission requirements, if agreements are placed and leveraged by NATO forces. Consequently, the group decided that a point-in-time survey of the NATO laboratories’ capabilities, that would be used to narrow to a best standard set of instrument technologies would not be the appropriate approach. Instead, the RTG recognized the different approaches each country took to develop their deployable laboratory provided greater options for NATO to customize the level of response required. The team decided not to focus on a single NATO laboratory, but instead focus on providing knowledge to HFM on each country’s asset strength. The survey found state-of-the-art technical advances employed in current laboratories that allow NATO to best respond with a customized response team based on the threat scenario.

This RTG consisted of highly motivated, exceptionally collaborative, and extremely knowledgeable country representatives that determine great advantages in discussing each other’s capabilities and future directions. Topic discussions allowed for a much broader equipment and methodologies evaluation that would have been difficult for a single country to assess in breadth. Many countries’ lessons learned were directly applicable to most others deployment laboratory activities. Each country’s representatives agreed to continue to have frequent, open communications to address their ever-changing organization’s field laboratory needs and emerging equipment usage to facilitate NATO needs.

The HFM-177 RTG effort was a great success. We recommend these results be forwarded to the NATO Army Armaments Group, Joint Capability Group on CBRN Defence, and the Sampling and Identification of Biological, Chemical and Radiological Agents sub-group for further consideration and development.

Applications de nanotechnologie et biotechnologie destinées à un laboratoire déployable

(STO-TR-HFM-177)

Synthèse

La nature expéditionnaire de la force réaction rapide de l'Organisation du Traité de l'Atlantique Nord (OTAN) nécessite des capacités de laboratoire déployable exploitant les progrès des nanotechnologies et biotechnologies. A cet effet, la Commission sur les facteurs humains et la médecine de l'Organisation pour la science et la technologie de l'OTAN a mandaté le groupe de recherche et de technologie (RTG HFM-177) pour étudier les « Applications de nanotechnologie et biotechnologie destinées à un laboratoire déployable » en se concentrant sur les technologies perfectionnées pour un laboratoire NRBC déployable de l'OTAN. Les objectifs étaient les suivants :

- 1) Etudier les modèles, la construction et les matériaux de laboratoire déployable ;
- 2) Analyser les procédures et la technologie des instruments existants ;
- 3) Analyser les nanotechnologies et biotechnologies émergentes pour l'acquisition par les instruments ; et
- 4) Intégrer les technologies existantes et émergentes dans un modèle de laboratoire déployable.

Plus de vingt représentants de huit pays – République de Géorgie, Turquie, Israël, République tchèque, Royaume-Uni, Etats-Unis, France et Allemagne – ont participé au groupe de recherche. Chaque pays a présenté ses capacités de laboratoire NRBC déployable et les problèmes rencontrés. Le RTG HFM-177 a remarqué l'évolution rapide des technologies d'analyse, les différents types de rôles et de mission que chaque pays attribue à ses ressources spécifiques de laboratoire et les niveaux variables de financement alloué pour maintenir ou améliorer l'exploitation des laboratoires. Ces cas constituent un ensemble varié d'applications et de technologies pouvant répondre à de multiples niveaux d'exigence en mission, si des accords sont passés et exploités par les forces de l'OTAN. Par conséquent, le groupe a décidé qu'il n'était pas approprié de mener une étude ponctuelle des capacités de laboratoire OTAN pour déterminer le meilleur jeu standard de technologies instrumentales. A contrario, le RTG a reconnu que les différentes approches adoptées par chaque pays pour développer son laboratoire déployable offraient une plus large palette de possibilités à l'OTAN pour personnaliser le niveau de réponse requis. L'équipe a décidé de ne pas se concentrer sur un seul laboratoire OTAN, mais de s'efforcer d'informer le HFM sur les avantages comparés des solutions adoptées dans chaque pays. L'étude a découvert des avancées techniques, employées dans les laboratoires actuels, qui permettent à l'OTAN de réagir au mieux avec une équipe personnalisée d'intervention à partir d'un scénario de menace déterminé.

Le présent RTG se composait de représentants nationaux fortement motivés, travaillant main dans la main et extrêmement bien renseignés, qui ont décidé qu'il y avait de grands avantages à discuter des capacités et des futures orientations des uns et des autres. Les discussions thématiques ont permis une évaluation bien plus large de l'équipement et des méthodologies que ce qu'un seul pays aurait pu réaliser. Les enseignements de nombreux pays étaient directement applicables à la plupart des activités de déploiement de laboratoire des autres. Chaque représentant national a accepté que des communications fréquentes et ouvertes aient lieu pour répondre à l'évolution permanente des besoins de son organisation en matière de laboratoire sur le terrain et faire part de l'utilisation de l'équipement émergent afin de satisfaire aux besoins de l'OTAN.

Les efforts du RTG HFM-177 ont été couronnés de succès. Nous recommandons que ces résultats soient transmis au groupe armements armée de terre de l'OTAN, pour le groupe traitant de la capacité interarmées sur la défense NRBC ainsi qu'au sous-groupe d'échantillonnage et identification des agents biologiques, chimiques et radiologiques, afin qu'ils soient approfondis et développés.



Chapter 1 – FRAMEWORK AND ACCOMPLISHMENTS

Dr. John J. Schlager

Chief, Molecular Bioeffects Branch

Dr. Brian Lukey

Technical Advisor, Molecular Bioeffects Branch

711th Human Performance Wing
Air Force Research Laboratory
2729 R Street, Area B, Building 837
Wright-Patterson AFB, Dayton OH 45433-5707
UNITED STATES

john.schlager@us.af.mil

Brian.Lukey.ctr@wpafb.af.mil

1.1 BACKGROUND

1.1.1 NATO Needs and Committee Charter

The NATO Response Force provides a high-tech, flexible, rapidly deployable, interoperable and sustainable force, including land, sea, and air elements, capable of carrying out the full range of Alliance missions. The development of this high-readiness force serves as a catalyst for promoting capabilities improvements and ensuring continued transformation to meet evolving security challenges with greater interoperability for the Alliance military. The NATO Response Force requires a Deployable Laboratory to serve as another key element to create full readiness and ensure mission success of NATO operations and Defence Against Terrorism (DAT).

Consequently the NATO Army Armaments Group (NAAG), Joint Capability Group on CBRN Defence (JCGCBRN), Sub-group on Sampling and Identification of Biological, Chemical, and Radiological Agents (SIBCRA SG) identified the need for a Research Technology Group (RTG) as follows. “This RTG group will define the elements of a field-forward NBC laboratory and its full capabilities to aid in the analysis of samples received by JCGCBRN. The STANAG 4632 establishes the standards of proficiency for NBC deployable Analytical Laboratories (NBC-AL). This NBC-AL will be able to operate across the full spectrum of military land, air, and maritime operations. These operations may range from local security tasks in a relatively benign area to completely cross the operational spectrum for full collective defence. Crisis Response Operations may range from Peace Support Operations to Alliance Combat Operations. The NBC-AL will be capable of deploying as a whole, or in components, with missions tailored to the assessed threat and will be on 5 days’ Notice-To-Move (NTM) according to NRF Readiness States.”

Further, the Human Factors and Medicine Panel determined that the expeditionary nature of the NATO response force required a deployable laboratory that utilized advanced biotechnology. In 2007, Exploratory Team-066 staffed by responding country experts from the Czech Republic, Spain, Netherlands and the United States meeting in Paris tackled the task of defining specific research and technology areas necessary to develop a deployable laboratory capable of conducting theatre-level, health threat surveillance. The exploratory team identified four topics to address:

- 1) Deployable laboratory design, construction and materials;
- 2) Analysis of existing instrument technologies and procedures;
- 3) Analysis of emerging nano-/bio-technology for instrument acquisition; and
- 4) Integration of existing and emerging technologies into a deployable laboratory product.

FRAMEWORK AND ACCOMPLISHMENTS

The NATO Army Armaments Group, Joint Capability Group on CBRN Defence, and the Sampling and Identification of Biological, Chemical and Radiological Agents sub-group were all suggested recipients of this research and technology effort.

To that end, the NATO Research Technical Organization Panel on Human Factors and Medicine at the spring meeting 2008 chartered the Research Technology Group-177 (HFM-177 RTG) to study the “Deployable Laboratory Applications of Nano- and Bio-technology” with a focus on deployable NATO CBRN laboratory advanced technologies. At that time, the Czech Republic, Georgia, Germany, Hungary, Netherlands, Spain, Sweden, Turkey and the United States were Nations that were invited and/or identified as willing to participate.

1.1.2 Benefits to the Military

The North Atlantic Treaty Organization mission requires that forces be able to execute missions in Chemical, Biological, Radiological or Nuclear (CBRN) warfare environments. Operational success in such inhospitable conditions requires the earliest knowledge of the threat, region of use, active deployment, and if personnel were involved, the timely administration of preventative and curative medical responses in order to maintain the human force and provide enhanced protection of personnel. It is certain that these operational requirements both strategic and tactical combined with the effective use of life-saving measures are best applied using a deployed, dependable environmental surveillance asset with quick, reliable pre-clinical screening. Only this level of asset would provide the agility for the earliest, potentially individually-titrated administration of medical support.

The military force is currently transforming into a more responsive, deployable, agile, versatile, lethal, survivable and sustainable force (Future Force). Medical forces will have to be efficient, effective and capable of supporting the full spectrum of military operations. There exists a significant increase in novel emerging nano-/bio-technology science created coupled to advance technology development that when aligned and captured will create new and revolutionary medical systems. For the medical technology community to exploit these advances in science and technology and achieve significant field-forward gains, the technical and science research communities are required to be engaged in a coordinated effort to apply existing advances for combat support effectiveness en route to the Future Force Warrior. Specifically, prospective NATO medical applications of present nano-/bio-technology include advanced health and fitness monitoring, high-resolution imaging, new environmental sensor platforms, chemical/biological sensors, sensor networks, battle and human-centric data fusion and storage, and soldier therapeutics. Nevertheless, there are others areas where nano-/bio-technology development is needed:

- **Sensors:** Diagnostic and detection kits (gene-chips, protein-chips, lab-on-chips, etc.);
- **Electronics and Computing:** Bio-molecular hybrid devices for detection (arrays, biochips), bio-computing (biological models, bio-data treatment);
- **Materials:** Accurate monitoring device (biomarkers), self-decontaminating surfaces, selection of environmental ruggedized/resistant construction materials;
- **Logistic:** Miniaturization of biological devices and systems for lowest footprint (micro-electrical mechanical-based systems, nano-technologies); and
- **Diagnostics:** Novel discovery and use of multi-analyte technologies such as genomics, metabonomics, proteomics-based analysis and specific derived sub-platforms of marker monitors.

1.2 OBJECTIVE

The Exploratory Team-066 establish that the RTG should consider the following menu of topics regarding the detailed design and capabilities of a deployable laboratory, and application of equipment as guidelines for review of emerging nano-/bio-technologies and application to analytical and diagnostic procedures:

- a) Determine the structural features/characteristics of the deployable laboratory capability, define:
 - i) Fixed or mobile deployable unit.
 - ii) Dimensional requirements:
 - 1) Transportable by air; and
 - 2) Adequate space for equipment/work.
 - iii) Delivery by multiple means (air-droppable, tracked, etc.).
 - iv) Minimal logistics/maintenance/supportability requirements.
 - v) Versatile external power capability.
 - vi) Adequate internal power requirements to support all instruments simultaneously.
 - vii) Emergency power capability for escape.
 - viii) Deployable to multiple environments/terrains.
 - ix) Hardened/passive defence.
 - x) External sensor capability for biological, chemical and radiological.
 - xi) Easily decontaminated (both external and internal; rapid internal decontamination capability).
 - xii) Manning/personnel requirements.
 - xiii) Design for threat-based instrument modularity.
 - xiv) Design for technological and tactical upgradeability (ex. Remote detection of biomarkers in soldiers).
 - xv) Automate and remote capabilities (contained and segregated).
 - xvi) Longevity of storage (pre-deployed) and operation in theatre.
 - xvii) BSL-2/3+ Capable.
 - xviii) External sample transfer portals (to containment and/or BSL-3 sections).
 - xix) Secure internal and external communication capabilities (radio, SIPR, telecom).
 - xx) System of internal engineering controls (NBC COLPRO protection (air filtration and air-conditioning Systems): HEPA, active carbon filters, positive/negative pressure, etc.).
 - xxi) Apply applicable ergonomic design.
 - xxii) Assure ability to use in a hot (radiological)/contaminated (BSL-4) zone.
- b) Characterize and identify the deployable laboratory screening technologies:
 - i) Equipment:
 - 1) Optimize existing equipment for type of sample (environmental or clinical), agent (chemical, biological, radiological), and dimensional restrictions;
 - 2) Recommend emerging technologies;
 - 3) Maximize use of ruggedized equipment technologies;
 - 4) Capable of air transport and insertion;
 - 5) Define transport limitations/problems;
 - 6) Maximize automated, self-testing/diagnostic, high through-put and rapid analyses;

FRAMEWORK AND ACCOMPLISHMENTS

- 7) Minimize sample manipulation (whole-sample analytical capability: time save, eliminates contaminated waste generation, eliminates sample loss, promotes safety);
 - 8) Minimize use of fluid dependent equipment technologies and perishable consumables;
 - 9) Focus on equipment with minimal waste generation or creation of integrated waste management;
 - 10) Maximize resizing and application/selection of commercial-off-the-shelf technologies: Max use modular equipment in service;
 - 11) Able to be decontaminated; and
 - 12) Lowest power draw/supply requirements.
- ii) Personnel:
- 1) Number minimum needed to man, maximum for highest alert status;
 - 2) Specialty type;
 - 3) Training requirements; key to assure quality of assay completion and full lab functionality in all threat and theatre environments;
 - 4) Physical characteristics of individuals (height, weight, blended in ergonomic design); and
 - 5) Consider completely automated operations.
- iii) Procedures:
- 1) Recommend use of standardized procedures for sample collection, sample treatment, identification, and decontamination methods for deployable laboratory;
 - 2) Evaluate, develop and validate novel/emerging analytical chemistry, biotechnology/ molecular biology, and nanotechnology integrated procedures;
 - 3) Establish quality control, instrument function, result validation, and laboratory environmental control procedures (may include remote data validation);
 - 4) Maximize use of automated procedures;
 - 5) Alternative procedures (redundancy for procedure and sample assay assurance);
 - 6) Define operation time and consider through-put limitations (the number of the samples per day);
 - 7) Accepted restrictions in lab work, accepted limited sample preparation and identification capability, defined samples types to analyse (air, soil, water, liquid); and
 - 8) Ensure procedures minimize fluid use.
- iv) Data Treatment:
- 1) Real-time broadcast of data to reach-back expert laboratory;
 - 2) Establish theatre “hardened” archive system;
 - 3) Evaluate commercial-off-the-shelf clinical laboratory software (ex. Specialized Laboratory information software, LIMS);
 - 4) Fully interface instrumentation, where possible, with laboratory information system; and
 - 5) Establish stand-alone bioinformatics databases and procedures to regularly update database.

1.3 MEETINGS

1.3.1 Meeting at Edgewood Chemical Biological Center in April 2009

The HFM-177 RTG team held its inaugural meeting at Edgewood Chemical Biological Center (ECBC) in Edgewood Maryland (USA) in April 2009. Only delegates from Georgia, the Czech Republic and United States attended; the Germany representatives having planned on attending could not make this meeting date. Despite a low number of country representatives in attendance, the meeting was productive for review of both US and the Czech Republic's substantial science and engineering investments and provided a current review of deployable constructs for field laboratories and work environments. Georgia presented their position on biological agents and levied their strong support to work together to the produce deployment response applications and hardware. The meeting was opened by a welcome from Dr. Raymond Mastnjak, ECBC that was followed by a presentation from Dr. John Wade as RTG mentor who presented an RTO overview briefing. The remainder of the meeting was chaired by Dr. Schlager who followed Dr. Wade and provided a HFM-177 RTG positional briefing from the ET-066 data and the mission of the RTG. The delegates developed a professional rapport, toured multiple facilities within ECBC CBRN facilities and observed the design construction of mobile biological response laboratories utilized in the United States.

At this meeting, the delegates identified a major impediment to fulfilling the HFM-177 RTG mission. The main goal of HFM-177 RTG was to evaluate the rapid emergence of bio-and nano-technologies in NATO rapid response laboratories. However, it was quickly realized that there is no single, standard NATO response laboratory that could be used as framework to best evaluate insertion of novel technologies. The first priority objective for the RTG then became to identify the current capabilities of each Nation's laboratory to best suit these missions and determine knowledge and lessons learn to share among the Nations.

1.3.2 Meeting in Munich, Germany in October 2011

The second HFM-177 RTG meeting occurred in October 2011 and was hosted by the Chair with activities well supported by LtCol. Roman Woelfel in Munich, Germany. Seventeen representatives from seven countries met for one and a half days (October 29-30); immediately following the 2011 Medical Biodefence Conference, which had a session focused on deployable laboratory facilities and outbreak investigation teams. Dir. Schlager, the NATO HFM-177 chair, opened the RTG meeting with a review of the general concepts and rationale for the RTG. The delegates from each country then gave formal presentations on:

- 1) Deployable laboratory design and construction;
- 2) Existing; or
- 3) Emerging technologies utilized in deployable labs; or
- 4) Product integration.

Raymond Mastnjak (United States, Army ERDEC) and Libor Pisa (Czech Republic, Central Military Health Institute) each delivered talks describing their country's large, transportable, self-contained deployable laboratories presently fielded by their respective organizations. These assets shared common themes, such as compartmentalized, hard-sided container or tent-based construction, as well as the ability to process and identify samples under BSL-3+ conditions. In contrast, Roman Woelfel (Germany, Bundeswehr Institute of Microbiology) and Daniel Parzy (France, Institut de Recherche Biomédicale des Armées) presented their country's rapid deployment responsive, modular, Pelican case-based mobile labs that met commercial airline luggage restrictions, allowing rapid material and human transportability to populated sites. Such lightweight laboratories allow small, highly specialized teams to rapidly deploy and provide environmental and diagnostic analyses to many important world threat areas to include even austere outbreak locations. Key to the effectiveness of this style for these two countries and the approach for all other laboratories is having very well trained technicians that can respond to the need quickly and can perform difficult biotechnical

procedures flawlessly, even in the most difficult environmental conditions. Gurer Budak (Turkey, Gazi University) presented a spectrum of advances in the field of nano-technology with an emphasis on medical applications, while Robert Marks (Israel, Ben Gurion University) presented his research on the development of a hand-held, fiber-optic nano-sensor device for detection applications. The BIOMEDAC Chair, Francois Thibault (France, Institut de Recherche Biomédicale des Armées), also presented his committee's progress. The meeting concluded with a general discussion on:

- 1) Whether the deployable NATO laboratory would be utilized for environmental surveillance following a biological warfare attack or for outbreak diagnosis and mitigation;
- 2) The training and educational requirements of response team members;
- 3) The amount of time necessary for the laboratory to be deployable and useful for response using military or commercial air transport;
- 4) The potential need for large, transportable, self-contained laboratory facilities; and
- 5) The importance of knowing regional capabilities and possessing clearly defined CONOPs prior to NATO asset deployment.

1.4 SURVEY DEVELOPMENT

Based upon detailed discussions at the second meeting in Munich, three key HFM-177 committee members, Drs. Woelfel, Thibault and Mastnjak volunteered to develop a comprehensive, laboratory survey to disseminate not only among the committee members but also to other NATO Nations that could not attend. The survey addressed the specific objectives developed in the charter and other concerns that evolved from the two meetings (see Annex B). To ensure optimal opportunity for our NATO Allies to receive and complete the survey, we sent the survey through two routes; one through the Human Factors in Medicine Panel Executive and second pathway to the committee members' personal contacts in other NATO Nations that did not attend.

The following countries completed the survey:

- The Czech Republic, Central Military Health Institute;
- Germany, Bundeswehr Institute of Microbiology;
- France, Medical Health Services;
- Turkey, Nano-medicine and Advanced Technologies Research Center; and
- Unites States of America, the 20th Support Command, CBRNE.

Table 1-1 lists the summarized finding from the survey. Our Panel pointed out the benefits and disadvantages of a highly mobile verses transportable, fixed-site response laboratory. Briefly, the highly mobile laboratory can deploy and function more rapidly but does not have the more definitive and diverse CBRN tests compared to those within the larger fixed labs. The Panel noted that both have distinct purposes in CBRN rapid response. Because each country has its own defined mission with allies in various world regions and government funding, the range and purposed target for lab deployment assets varies with each country's laboratory functions. Most of all functional needs are based upon the inherent country's capabilities, requirements and interests throughout the world. We believe this diversity and mission variance within alliance countries provides minimally a NATO deployed laboratory approach addressing at least two laboratory designs: one a very rapid expeditionary type lab, and the other, a harden, in-place lab design for longer, more CBRN complex deployment missions. We believe both designs with potential modifications for increased agility should be readily available for NATO leadership to best customize a response team, based on the specific needs from a CBRN threat or incident.

Table 1-1: Laboratory Capability Surveys.

	Czech Republic		Germany	France	Turkey	United States
	Deployable Biological	Mobile Epi-Hygienic				20th SUPCOM (CBRNE)
<i>Permanent Field-Forward Laboratory</i>	Y		Y	N*	Y	Y
<i>Mobile Medical Laboratory</i>	Y	Y	Y			
<i>Responsible for the Technical and Operational Management</i>	Medical Service	Medical Service	Medical Service	Medical Service	CBRN Defence	Medical Service
<i>Laboratory Platform</i>	Deployable 5 Standard ISO 1C Container (L: 6058 mm x W: 2438 mm x H: 2200 mm)		Deployable: 15 packages (580 x 440 x 330 cm, 30 kg)	0,49 m ³ -90 kg; 0,49 m ³ -65 kg; 0,35 m ³ -78 kg; 0,35 m ³ -80 kg; 0,22 m ³ -53 kg (this last package is the compressor cooler); 5	Self-Mobile	Self-Mobile and Deployable: LMT V-Light Lab (LMEL) & MMTV for Heavy Lab (HMEL)
<i>Transportable by</i>	Truck, Airplane (civ/mil) Ship or Cargo Train		Airplane (civ/mil) Ship	Airplane (civ/mil) Ship	Truck or Plane	Truck, Mil Plane, Sealift
<i>Set-Up Time at Site of Operation</i>	72 hrs		2 hrs	1.5 hrs	20 min	LMEL 4 hrs; HMEL 36 hrs
<i>External Supply Requirements</i>	Water, Diesel Oil for Electric Generator Running, Diagnostic and Other Laboratory		Car Battery (Electrical Power Conversion 12V)	Fuel for Generator	Generator and Water	Water and Fuel
<i>Operational Time Without External Resupplies</i>	2 – 3 days		3 days	2 – 3 weeks	3 days	3 days
<i>Scheme for Ensuring Permanent Diagnostic Capabilities (on call or duty team)</i>	Y		Y		Y	Y
Diagnostic Tests	B-Agents of CDC List, Categories A and B		Suspected B-Agent Outbreaks			Suspected B-Agent Outbreaks
Capable of Serving Laboratory or Hospital Emergencies	Y		N	N	N	N

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	Czech Republic		Germany	France	Turkey	United States
	Deployable Biological	Mobile Epi-Hygienic				20th SUPCOM (CBRNE)
Intended to Respond to Specific Demands from a Surveillance System	N		Y			Y
National or Regional Center that Assesses the Emergency and Need for Laboratory Response	Y		Y		Y	Y
Duty Time	On alert \leq 5 days after incident		24/7		24/7	24/7
Network Duty System	NATO CBRN		Bundeswehr Medical CBRN Task Force		Y	Y
Number of People Involved	12		4	3	3	Needs Dependent
Scientists	Microbiologist (MD, VMD, Doctor of Sciences)		Clinical Microbiologist/ Virologist (MD, PhD)	PhD/MD	1	CWA and BWA Analysis, Infectious Disease / MS, PhD, MD or DVM
	Epidemiologist (MD)		Veterinarian Microbiologist (DVM)			
	Veterinary Epidemiologist (VMD)		Molecular Biologist (PhD)			
Technologists	Electrician – Engineer		Licensed Medical Technicians	Biological Technologist	2	CWA and BWA Analysis / BS, MS or PhD
	Power Generator Operator – Engineer					Quality Manager and Laboratory Operations Manager
	Machine Operator – Engineer					
	Laboratory Technician					
Biological Agent Testing	P: PCR; S: Serological; M: Microscopy; C: Culture					
Abrin			P,S			
Aflatoxins			P,S,M			
B. pseudomallei		C	P	P		P,C
Bacillus anthracis	S,M,C	P,S,M,C	P,S,M	P	C	P,S,C
Botulinum Toxine	S	P,S	P,S	S		P,S

	Czech Republic		Germany	France	Turkey	United States
	Deployable Biological	Mobile Epi-Hygienic				20th SUPCOM (CBRNE)
Brucella spp.	S	P,S	P,S			P,S,C
Burkholderia mallei	C	C	P	P		P,C
CCHF virus			P,S			P
Chikungunya virus			P	S		P
Clostridium perfringens toxin						
Coxiella burnetii	S	C	P			P,S
Eastern-Equine-Encephalitis virus			P			P,S
Ebola virus			P			P
Escherichia coli	S,M,C	S,M,C	P		C	
Flaviviruses			P,S			P
Francisella tularensis	S	P,S	P,S	P		P,S,C
Hantaviruses	S	S	P,S			P
Influenza virus	S	S	P,S			P
Junin virus			P			
Lassa virus			P			P
Machupo virus			P			P
Marburg virus			P			P
Monkeypox virus			P,S	P		P
Omsk virus						P
Orientia tsutsugamushi						
Palytoxin						
Ricin		P,S	P,S	S		P,S
Rickettsia rickettsii		S	P,S			
Rickettsia typhi		S	P,S			
Rift Valley fever virus						P
Salmonella spp.	S,M,C	P,S,M,C		C	C	
Salmonella Typhi	S,M,C	S,M,C		C	C	
Saxitoxins						
Shigella dysenteriae	S,M,C	S,M,C	P	C	C	
Staphylococcal enterotoxins	S,M,C	S,M,C	P,S	C		P,S
Tetradotoxin						

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	Czech Republic		Germany	France	Turkey	United States
	Deployable Biological	Mobile Epi-Hygienic				20th SUPCOM (CBRNE)
Tick-Borne Encephalitis (TBE) virus	S	S	P,S			P
Trichothecene			P,S			
Variola virus		P,S	P,S	P		P,S
Venezuelan-Equine-Encephalitis virus			P			P,S
Vibrio cholerae	S,M,C	S,M,C	P,S	C	C	
Western-Equine-Encephalitis virus			P			P,S
Yellow fever virus			P	P		
Yersinia pestis		P,S,M,C	P,S,M			P,S,C
Others: Dengue fever virus		S	P,S			
Others: Toxoplaxma gondii		S				
Chemical Warfare Agent	t N	N	GA, GB, GD, VX, HD, Phosgene	N	N	GA, GB, GD, GF, VX, HD, L, RVX, HN-1, HN-2, HN-3
Nuclear/Radiological Agent	N	N	SVG II Radiation Detector	N	N	Alpha, Beta and Gamma

* France collaborates with Armaments Procurement Agency (DGA) for prototype. This laboratory is in the prototype stage and has been validated for parasitological, microbial and viral pathologies. This laboratory is in course of acquisition by the Armaments Procurement Agency (DGA) for the Medical Service.

The Panel also discussed the best equipment to recommend for a NATO laboratory. After long discussions about the technology rapidly changing, the different roles that each country has for its specific laboratory and the varying funds allotted to each laboratory, we concluded that a point-in-time list of specific instruments to suggest a 'standardize' NATO laboratory (or -ies) would not be the best approach for this effort. Instead, providing a forum for frequent, open communications among the NATO laboratories about lessons learned would be best to facilitate a potential deployment and response. This approach allows an active scientific and technical address of key elements needed for the current threat combined with the ever-changing individual government organization needs, their available equipment and current country of each their laboratories. Consequently, the Chair requested that each laboratory briefly describe their laboratories in a chapter in this report as a starting point for review by the HFM Panel.

Also invited from the 2011 Medical Biodefense Conference and able to attend our meeting was Dr. Frederick Johnson from the NATO Army Armaments Group, Joint Capability Group on CBRN Defence, Sub-Group on Sampling and identification of Biological, Chemical and Radiological Agents (SIBCRA)

who participated as a SIBCRA representative. Dr. Johnson described the function/mission of his team so that we could best develop the knowledge generated from our HFM-177 RTG meetings and this report to transition to his group.

From the mission of SIBCRA, the mission is two-fold: "... to determine criteria that must be met in order to provide unequivocal proof of the first use of Biological, Chemical, and Radiological Agents to NATO political and military authorities and thus to support timely decisions concerning NATO response" and "to provide the operational commander with real time information that will lead to immediate decisions on protection that will save lives and prevent casualties".

The SIBCRA team has drafted a handbook that identifies the procedures necessary to provide NATO Command Authorities with the evidence needed for international prosecution and to maximise troop safety in cases of (suspect) B, C, or R agent exposure. Aspects of the forensic capability can also be of potential use to operational business, while these are not seen as primary tasks for SIBCRA. Potential use to operational business concerns:

- Non-forensic sampling and laboratory analysis;
- The positioning, operating posture, exposure management, tempo and manoeuvre ability of units throughout the operational spectrum;
- Support to medical services for providing the most appropriate health care to casualties and for determining the most appropriate protective actions for implementing force health protection; and
- Site decontamination and eventual remediation.

The Chair of the HFM-177 RTG sent a representative, Capt. Mark Lisanby (USAF) to present a general overview of the group's work and efforts, brief the team's progress and participate in SIBCRA's meeting on 22 May 2012 in Sweden. This NATO sub-group is working under the aegis of STANAG 4632 Deployable NBC Analytical Laboratory. This group was not aware of the HFM-177 RTG activity but appears to be the perfect recipient of this work to carry these efforts forward.

1.5 CONCLUSION

Overall, the HFM-177 collaborative effort was a great success. Over 20 representatives from eight countries participated (Czech Republic, France, Georgia, Germany, Netherlands, Turkey, United Kingdom and United States) over the term of the HFM directed work from Exploratory Team through the two activities involving the Research Technical Group. Each country discussed their laboratory's capabilities and challenges. The group clearly recognized that each deployable laboratory's personnel and equipment varies substantially, based upon the country's capabilities and mission. The group discussed varying scenarios of CBRN exposure and response and the pros and cons of different laboratory capabilities, while virtually all deep discussions remained within the Biological Warfare Agent threat area. The different approaches each country took to develop a deployable laboratory have actually provided greater options for NATO to address different mission and threat situations. The team decided not to provide a standard, forcing an organizational structure and equipment list but instead suggests that each country continue to focus on improving their laboratory mission strength. Each country agreed that they intend to follow state-of-the-art advancements in current technology that best support their laboratories and consequently allow NATO to consider the best respond with a customized team based upon the scenario.

Fruitful discussions focused on strategic, operational and tactical issues including:

- 1) The deployable NATO lab's mission after a BW attack – environmental surveillance or outbreak diagnosis and mitigation;

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- 2) The training and educational requirements of response team members;
- 3) The deployment response time using military or commercial air transport;
- 4) The requirements for large, transportable, self-contained laboratory facilities;
- 5) The importance of knowing in country or regional capabilities; and
- 6) The need to clearly defined CONOPs prior to NATO asset deployment.

The team found great advantages in discussing each other's capabilities and future directions. The meeting approach allowed a much broader evaluation of equipment and methodologies that would be far too labor-intensive for any one country to tackle alone. Also many of the countries' lessons learned were directly applicable to the entire team. The team agreed to provide platforms for more frequent and open communications among the active deployment-ready laboratories to best facilitate the every-changing organization, equipment and mission of each country's laboratory, with focused discussions on lessons learned.

This group of representatives were highly motivated, exceptionally collaborative and extremely knowledgeable. We encourage NATO to support future collaborative efforts to best share advancements in technologies among the groups and international improvements in techniques, tactics and procedures. We also recommend that NATO Army Armaments Group, Joint Capability Group on CBRN Defence, and the Sampling and Identification of Biological, Chemical and Radiological Agents sub-group, working under the aegis of STANAG 4632 Deployable NBC Analytical Laboratory, carry these efforts forward. We suggest the HFM Panel consider creating a forum for periodic meetings (yearly) with these groups involving science/technology experts (medical clinician and researcher) to discuss tactical issues that can provide knowledge of the human factors and medicine for the NATO portfolio. Lastly, the areas of chemical (e.g., nerve, vesicant, nanomaterial), nuclear, or radiological (e.g., chemical emitter and its energy) warfare were not deeply reviewed by or found key to the participating country's response with regards to their lab assets. For future considerations by the HFM Panel and NATO regarding laboratory deployments, adding sensing/detection capabilities combined with BWA sensing and well trained personnel in a deployable lab asset would be critical for providing the fully functioning theatre laboratory that could respond accurately and swiftly to these types of insidious threats.

Chapter 2 – CHARACTERISTICS OF THE CZECH REPUBLIC DEPLOYABLE BIOLOGICAL LABORATORY

Prof. Martin Hubalek
 Institute of Molecular Pathology
 Faculty of Military Health Sciences
 University of Defence
 Trebesska 1575
 500 01 Hradec Kralove
 CZECH REPUBLIC

Martin.Hubalek@sujb.cz

The Deployable Biological Laboratory (DBL) is intended for the rapid and unambiguous identification of biological warfare agents, such as pathogens registered on the United States Centers for Disease Control's category A and B select agent list, in particular. The facility is technically designed for a wide climatic range, so that it can be utilized anywhere in the world. However, it is dependent on external logistical support and therefore can only be deployed as a component of a larger operational whole. The aim of the laboratory, including selected technology, is to achieve the highest degree of protection of personnel and the environment when handling high-risk biological material in field conditions.

The layout of the facility is designed as a complex of four working sections that are connected in a unidirectional operational stream. In practice, this means that the first entry section is intended to receive samples and the preparation of laboratory personnel. The entry section also performs the function of a command and control unit. All terminals are located here. Data is collected and evaluated here. There is also a communication node located there. The core of the complex is a laboratory section. This is where laboratory tests and identification of biological agents are carried out. This space features laboratory equipment, camera system, a waste water sterilization unit and decontamination loop. Outputs are placed for air supply, allowing four people to work in pressurized protective suits. The laboratory section operates under negative pressure and airflow through the system, exhausts through HEPA and NBC filters. The air in the air conditioning unit circulates in a closed circuit.

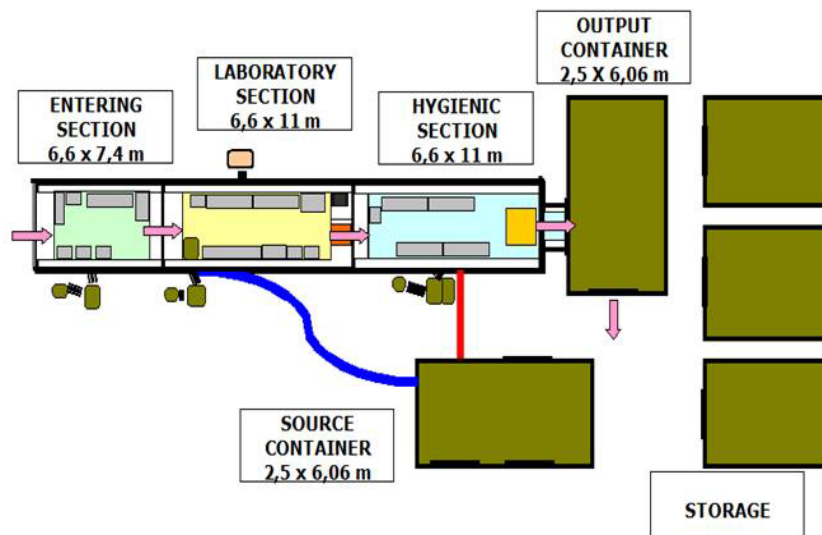


Figure 2-1: The Deployable Biological Laboratory Complex Design Scheme.



(a)



(b)



(c)



(d)

**Figure 2-2: Inside the Deployable Biological Laboratory: (a) Entry Section;
(b and d) Laboratory Section Work Benches; (c) Suited Technicians
Working Under Video Surveillance in the Laboratory Section.**

Laboratory technique allows a combination of different laboratory methods with a goal to confirm and unambiguously identify the originator. Biological agents can be identified by serological methods, by real-time PCR methods, using cultivation and subsequent microscopic and biochemical tests.

Decontamination of the laboratory section is accomplished by a combination of germicidal action of sources and application of disinfectants. The following section serves as a hygienic room where laboratory workers remove their protective suits. It is equipped with inflatable shower to perform personal hygiene.



Figure 2-3: The Hygienic Section of the Deployable Biological Laboratory.

The last part of the DBL is the output section. It is intended for storage of diagnostic and laboratory consumable materials. Its technical equipment allows us to store samples for examination, sub-samples for arbitrage or confirmatory and forensic tests in reference institutions for selected infectious pathogens.

The first three sections are designed as spacious tents with a special insert that forms the interior and also adjoining rooms that connect with lockable through-tunnels. The last section is placed in the container. The tents are reinforced with inflatable ribs. The insert is suspended on an aluminium frame. The floor is resistant to mechanical stress and composed of a segment system that allows for quick assembly.

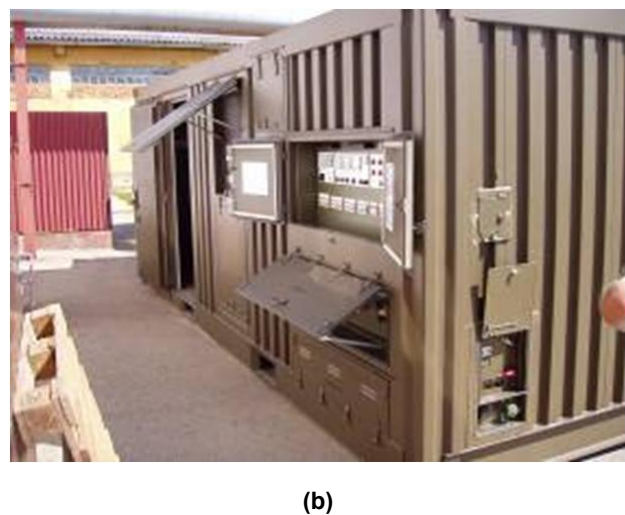
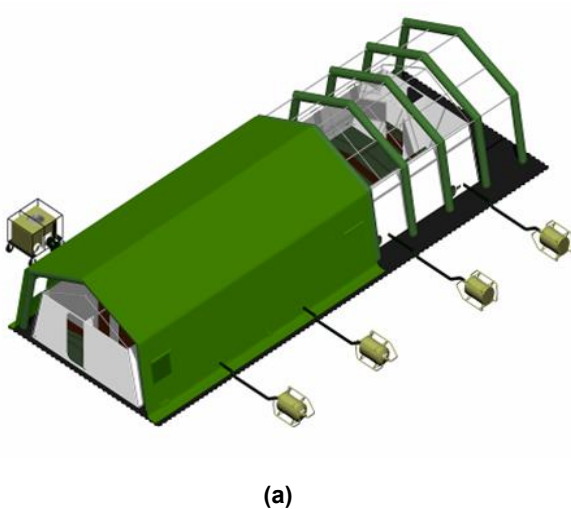


Figure 2-4: Construction of the Deployable Biological Laboratory: (a) Inflatable Rib Reinforced Tents of the Entering, Laboratory and Hygienic Sections; (b) "Source" Container that Houses the Electric Generator, Fuel Tank and Compressor.

During full operation, pressure modes are set so that the entry and hygiene sections are protected by controlled positive pressure, whereas the laboratory section is maintained under negative pressure. The heart of the facility is an energy container with a power generator unit that is equipped with a diesel motor. A compressor station provides production and storage of compressed air for the laboratory section. Although the energy unit is fully automated, it requires supervision by an engineer for each working shift. Another technician must be present to supervise the activities of air and water management. A specialist in the field of electrical devices and power distribution is essential to the operation of the DBL.

The Deployable Biological Laboratory has a 12-member staff: the Commander; 4 specialists in hygiene, microbiology, epidemiology or veterinary epidemiology; 3 laboratory technicians and 4 engineers. Designation of special laboratory equipment to field conditions requires that each staff member be completely independent and sufficiently competent in their field and at the same time be able to work as a team, especially in the construction of the complex, in full operation, in dealing with accidents or maintenance and care of some larger technological units. Construction of the complete facility can be completed within 72 hours, at which point the laboratory can be brought into a state of alert and initiate action. The deployable biological laboratory is stored in 5 standard ISO-type containers. This packaging format allows for a wide range of transportation means.

Table 2-1: Personnel Required for Staffing the Mobile Deployable Laboratory.

	Post	Number
1.	Commander	1
2.	Medical/biological experts (microbiologist, epidemiologist, veterinarian, doctor of natural sciences)	4
3.	Laboratory technician	3
4.	Engineer	4
Total		12

Chapter 3 – THE FRENCH TRANSPORTABLE MICROBIOLOGY LABORATORY

Pr. Daniel Parzy

Directeur, UMR-MD3
IRBA, Antenne Marseille
GSBDD de Marseille Aubagne
B.P. 40026, 111, Avenue de la Corse
13568 Marseille Cedex 02
FRANCE
(33) 4 91 15 01 14

d.parzy@free.fr

Pharm. Col. Francois Thibault

Institute de recherches biomédicales des armées
Centre de recherches du service de santé des armées
Département de microbiologie
B.P. 87
F-38702 La Tronche Cedex
FRANCE
(33) 4 76 63 6

fthibault@crssa.net

3.1 CHALLENGES AND ISSUES

Our troops deployed in tropical area are exposed to major health risks likely to reduce their operational capacity. Facing the risks of natural disasters and terrorism, France has the means specific usually entrusted to civil security, but does not have all the capabilities to deploy the biological means of investigation. The Direction of the health service of the armed forces intends to strengthen its expertise on the infectious risks, in particular in the context of emerging disease, and to develop its operational research in more close proximity to the forces. This is the reason for which the military component of biological and epidemiological investigation (EMIBE) has been created. This structure should include a laboratory of microbiology developed from the experiences in field campaigns of the research teams, the concept must offer a rapid deployment regardless of the place of investigation. In the difference of laboratory shelters, it should also reduce the duration and the cost of missions. The goal is to get a quick diagnosis for a fast and appropriate response.

3.2 OBJECTIVES

The objective of this project was to develop a transportable, autonomous field laboratory that is quickly deployable in degraded environments. It must integrate elements for microbiological techniques, but its modular design should allow its adjustment to all situations and evolve with technological progress.

3.3 RESPONSES

The system is actually composed of four suitcases that are small enough and light enough to transport by car, truck, or civilian or military airplane (complies with the IATA standards). To meet the cold requirements a cooler is added to the equipment. It provides reliable service in severe-duty environments, with low maintenance.

Its design allows deployment in a short period of time (< 30 minutes) without tools. The layout of the different elements offers good ergonomics for optimal work. All the procedures and embedded software allow quality control found in the reference laboratories. Self-sufficiency in energy is provided by a generator (fuel tank capacity 4,2 L, approximately 13H00).

3.3.1 Constitution

- 4 composite carbon fiber cases (0,49 m³-90 kg; 0,49 m³-65 kg; 0,35 m³-78 kg; 0,35 m³-80 kg) [see Figure 3-1].

THE FRENCH TRANSPORTABLE MICROBIOLOGY LABORATORY

- 1 compressor cooler (- 20°C and +4°C; 0,22 m³-53 kg).
- Total weight and volume: 366 kg, 1,9 m³.

NB: The weight of different cases is variable depending on the supplies provided for the mission.



Figure 3-1: The 4 Cases.



Figure 3-2: The Laboratory in Operation.

3.3.2 Deployment



Figure 3-3: The Laboratory's 5 Step Assembly.

3.4 MAJOR EQUIPMENT

- Laminar flux hood that ensure the protection of the biologist and samples (with a self-test security).
- Microbiology trigaz incubator with a maintenance of set-point temperature whatever the outside temperature (control of CO₂ and O₂ level by using CO₂ and N₂ compressed bottle, storage of data culture conditions).
- Micro-plaque absorbance reader and micro-plaque washer.
- Mini real-time PCR apparatus.
- Centrifuge.
- Microscope.
- Electrical board with UPS top line.
- Generator 1 kw.

The consumables and reagents are chosen according to the objectives of the mission.

3.4.1 Examples of Use

This laboratory has already been used in various field studies and is the subject of continuous improvement.

- Carpiagne – France

Climate: Mediterranean / Transport: Road / Energy: Portable Generator / Analyses: Bacteriology, Virology, Parasitology



Figure 3-4: Carpiagne – France.

- N-Djamena/Abeche – Chad

Climate: Semi-arid / Transport: Civil and Military Airway / Energy: Portable Generator / Analyses: Bacteriology, Virology



Figure 3-5: Chad.

- Bom-Bô – Vietnam / Kinshasa – DRC

Climate: Tropical wet / Transport: Civilian Airway and Road / Energy: Sector 110/230W-Portable Generator / Analyses: Parasitology



Figure 3-6: Vietnam.

3.5 PERSPECTIVES

- Energy autonomy: Development of a hybrid power source integrating both a fuel cell and photovoltaic panels.
- Development of bioassays based on the luminescence technology and automated pipetted bioluminescent plate reader.
- Development of new module with integration of haematology and biochemistry devices.

Chapter 4 – THE BUNDESWEHR RAPIDLY DEPLOYABLE BIO LAB

LtCol. Dr. Roman Wölfel

Head, Dept. Med Bio-Recon. and Verification
Bundeswehr Institute of Microbiology
Neuherbergstrasse 11, 80937 Munich
GERMANY

romanwoelfel@bundeswehr.org

Rapid and reliable identification of biological agents and other dangerous pathogens is one of the major tasks of the Department for Medical Bio-Reconnaissance and Verification at the Bundeswehr Institute of Microbiology in Munich. To fulfill this task outside of Germany a modular, rapidly deployable, microbiological laboratory was developed for field operations.

Because modern microbiological methods place high demands on the infrastructure of a lab – particularly when employed for medical or bioforensic purposes – a core capability of the rapidly deployable bio lab consists in utilizing very basic facilities for modern diagnostic investigations. By virtue of the system's modular design it is possible to bring only the equipment needed to fulfill a specific mission.

All equipment in the deployable bio lab is packed in waterproof rollable boxes. It is deployable within 72 hours in an aircraft as passenger luggage and depending on local conditions, it is operational six to twelve hours after arrival in the area of operation. The typical space requirement for the lab is approximately 20 square meters. Using different materials, several separate working areas can be created in the deployed environment. For transportation and storage of laboratory reagents and clinical samples both active and passive freezers are available. To increase safety of lab personnel, preparation of unknown biological samples can be conducted in a mobile glove box up to prevent exposure to potential pathogens.

The modular design of the deployable lab allows a mission specific tailoring of equipment and personnel to meet the needs on-site. Key features of the rapidly deployable bio lab are:

- **Modular laboratory equipment:**
 - 8 – 15 milspec boxes;
 - Weight per box: max. 31 kg;
 - Cleared as passenger baggage in commercial aircrafts; and
 - Waterproof packaging.
- **Main focus:**
 - Real-time PCR techniques; and
 - Conventional PCR as backup method.
- **In addition:**
 - (Immunofluorescence-) microscopy;
 - ELISA and immunochromatography;
 - Transport and set-up by lab personnel; and
 - Operational under resource-limited conditions.

THE BUNDESWEHR RAPIDLY DEPLOYABLE BIO LAB

The deployable bio lab allows the identification of bacteria, viruses, certain toxins and parasites with the aid of conventional and real-time PCR, immunological tests (ELISA and immunochromatography), as well as light and immunofluorescence microscopy. The laboratory mission, as well as all methods and documentation techniques, adhere to NATO requirements regarding rapid outbreak investigations (RDOIT) and handling and confirmed identification of biological warfare agents (SIBCRA).

At present the diagnostic spectrum of the lab covers more than twenty-eight diseases, among them anthrax, plague, tularemia, Q-fever, brucellosis, Crimean-Congo-Haemorrhagic-Fever, Ebola fever, smallpox, influenza and malaria.

The operation capacity of the lab is limited by the amount of consumables and by the number of personnel. In total approximately 50 tests can be run, with up to three different tests with 14 samples each per day. Both conventional and real-time PCR investigations can be conducted in the deployable bio lab abroad. For the confirmation of conventional PCR products DNA hybridization assays are used in the field.

By addition of modular packed supplementary equipment, it is possible to further extend both the diagnostic spectrum of the lab and also its duration of operation. This increased spectrum of application may include diagnostic methods (e.g., basic blood chemistry), additional lab equipment, and more personnel abroad to allow shift work. All necessary equipment is packed on aircraft pallets and can be deployed within a few days as air freight.



Figure 4-1: The Deployable Bio Lab, Packed in Robust and Waterproof Transport Boxes.



Figure 4-2: Modern Real-Time PCR Allows Molecular Detection of Different Pathogens Within a Few Hours.

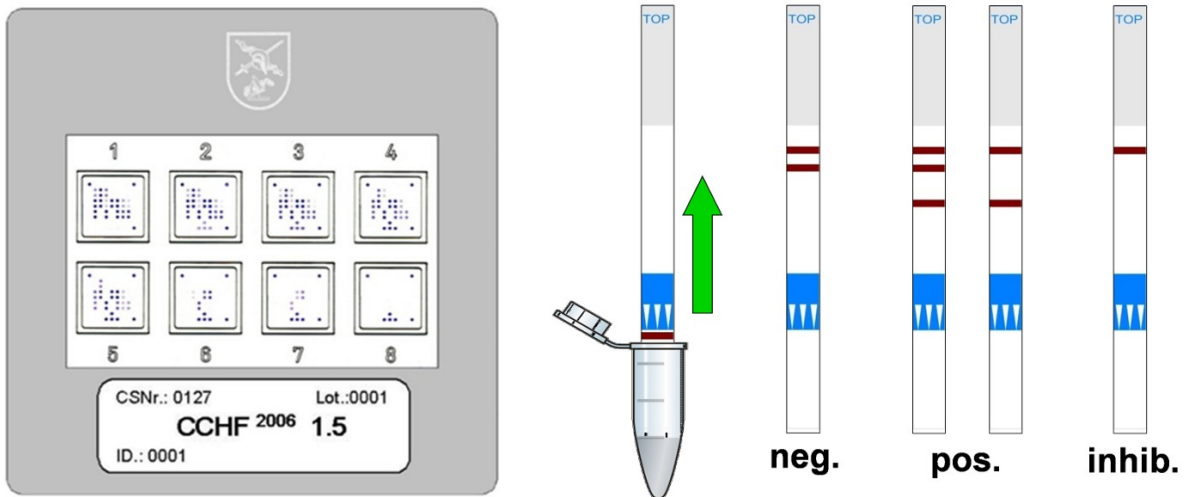


Figure 4-3: Conventional PCR Products are Visualized and Confirmed by Either Hybridization Chip Technology (Left) or Lateral Flow Dipstick Assays (Right).

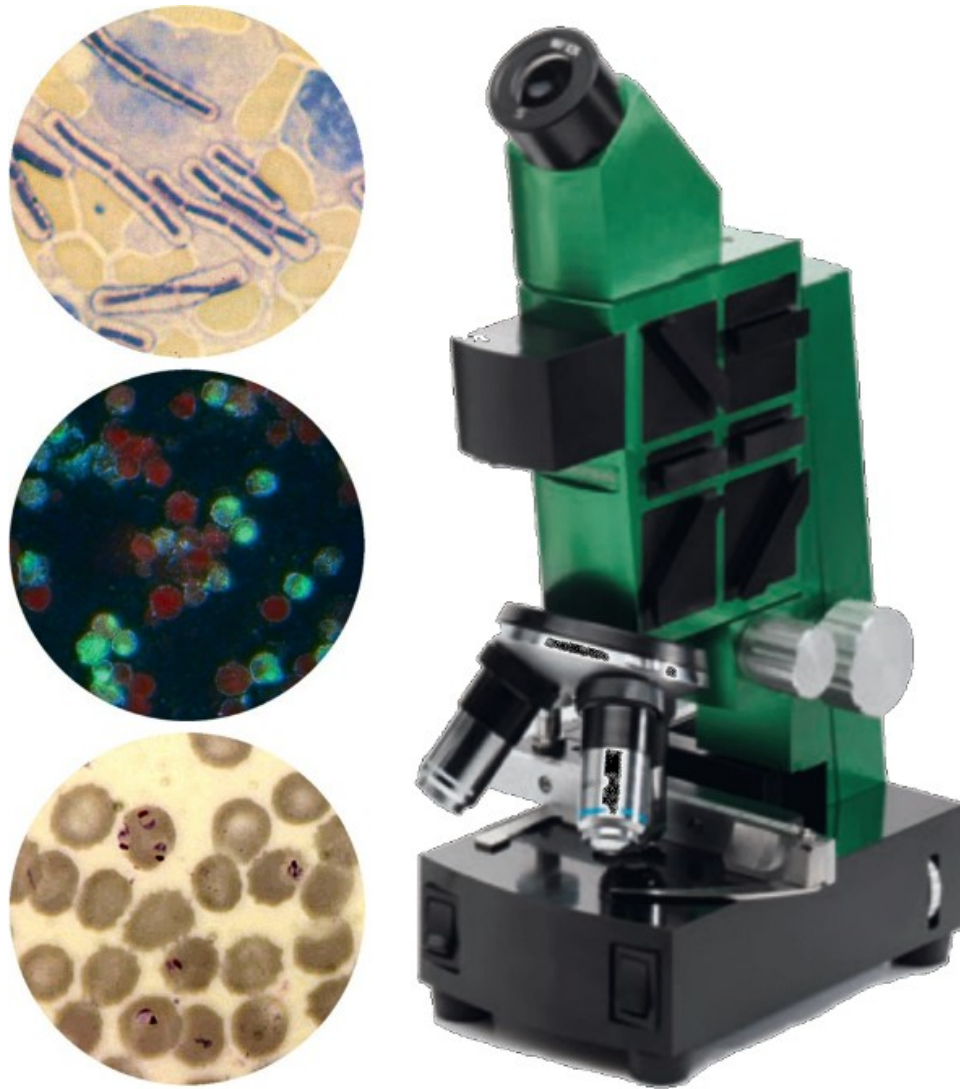


Figure 4-4: A Mobile, Battery-Operated Microscope Allows Microscopically Investigations (e.g., Capsule Staining of *Bacillus Anthracis*, Malaria Diagnostics) as well as Serological Diagnostics by Immunofluorescence Assays.

Chapter 5 – NANO-MEDICINE AND NOVEL ANALYTICAL APPROACHES

Dr. Gürer G. Budak (MD, PhD, EMBA)

Director, Nanomedicine and Advanced Technology Research Center, Ankara-Turkey

Member, European Technology Platform on Nanomedicine

President, International Society for Nanomedical Science

+90 312 485 1519

TURKEY

drgurerbudak@yahoo.com

5.1 INTRODUCTION

Developments in nano-technology have revealed that macroscopic and nano-metric forms of organic structures possess different features in physical, chemical and biological aspects. By proving that nano-devices, which are produced at laboratory, can interact with biomolecules, both physiological processes in healthy tissues and patho-physiologic basis of diseases begin to be understood.

“Nano-medicine,” which appeared as a new scientific interest parallel to the above-mentioned developments in nano-technology, became one of the most studied topics in the world by the reason of the fact that it leads conceptual changes in accepted and applied medical methods up to now and presents different diagnosis-treatment alternatives.

Although nano-technology is a commonly studied field all around the world, there is still no clear consensus about what nano-scale really is. One nano-meter is calculated as one billionth (10⁻⁹). It is possible to fit 5 carbon atoms in this scale as in three dimensional forms. According to BSI (PAS 71) applications, less than 100 nm or even smaller scales are evaluated within the concept of nano-technology. While at the beginning of 2000 s, studies less than 200 nm and in smaller scale were considered as nano-medicine, today this range is accepted between 5 – 100 nm.

5.2 CLINICAL NANO-MEDICINE PERSPECTIVES

Currently the goal is to approach patients with diseases and diagnose and start treatment, when pathologic change is only at single-cell level. However, this is only possible by increasing the efficiency of *in-vivo* and *in-vitro* diagnosis methods. Although nano-medicine is a field presenting great opportunities in this regard, it also brings along disadvantages because it is a new, developing discipline.

In the literature, there is a wide range of research topics: everything from the discovery of new nano-biomaterials to using these materials in clinics. While searching for physical, chemical and biological applications for nano-materials it is also attempted to be understood how to use these materials on living creatures. Research want to know what adverse effects might be caused by the use of these materials specifically, effects of nano-materials on human health and environmental health. In addition, possible social and legal problems have been discussed and new ethical rules have been introduced.

Some studies are detailed, more specific and more focused on developing safer diagnostic devices. There are studies investigating different biological measuring methods with one integrated device. By using biosensors which are developed with the use of nano-electronic circuits, researchers would be able to establish micro mobile laboratories which could easily be used by patients and, if necessary, could transmit data to an external user.

Another related area of nano research studies the combination of *in vitro* monitoring techniques and *in vivo* nano-medical devices. In those studies, researchers are attempting to develop nano-structures which are able to carry specific contrast substances which will be directed from the outside. Thus, it will be possible to take detailed molecular images of target tissues.

In another study, it was researched how to combine nano-structures with pharmacological agents. Nano-structures which carry therapeutic and diagnostic agents at the same time, would be especially groundbreaking in cancer cases making it possible to administer a treatment directly on target. This cancer treatment, known as theragnostic (therapy + diagnose), is aimed to improve efficiency of cancer treatment by taking images of the target tissue at different times.

Lastly, intense studies have been conducted on the successful regeneration of diseased or injured tissues by means of nano-grafts and reproducing needed artificial organs by means of nano-scaffolds in *in vitro* conditions and then replacing diseased or injured organs with the artificial ones.

Methods which have been developed by using nanotechnology have the potential to be effective on all medical equipment. For example, developing new materials to be used in surgical implants. Nano-metric systems or minimal invasive sensors, which can be used in monitoring metabolic activities, can be considered within this regard. Nano-pumps, injectable/implantable polymer systems, liposomal drug applications and cell/gene therapy methods, can be considered for controlled drug delivery systems. Currently, half of the improvements related to new molecules all around the world are made by biotechnology companies. Therefore, over 4000 companies in the world work in an area related to drug delivery systems, tumor targeted therapy methods, or drug carrying implants.

5.3 INTERDISCIPLINARY FRAMEWORKS

All those efforts for understanding the development of disease at the molecular level and for treatment are very important to spread all the developments in nano-medicine to the society. Since the topic has a wide scale, different disciplines have to work together in the nano-medicine area. It can be said that for now, neither any scientific field nor areas of expertise possesses the capacity of scientific and technical infrastructure to conduct such a research by itself. To manage scientific research in such a field, it is a must to establish a well-organized 'team'. Within such a team, conventional disciplines such as basic-clinic medical scientists, pharmacologists, physics-chemistry-electric-electronic-biomedical-computer engineers, etc., and new fields such as genome-proteome science, pharmacokinetic modeling and microscope designing, etc., should be included.

In addition to self-disciplinary nature of nano-medicine, the more the numbers of studies increase in this field the better new sub-disciplines appear. Some of these sub-disciplines are mentioned below and many studies have been conducted on each specific topic:

- Imaging: molecular, vascular, neurological, etc.;
- *In vitro* diagnosis;
- *In vivo* diagnosis and biosensors;
- Advanced biomedical materials, including "smart" and functionalized materials and surfaces;
- Regenerative medicine and tissue engineering;
- Infection control;
- Drug design and targeted drug delivery;
- Gene and cell therapy;
- Man-machine interfaces;

- Nano-toxicology;
- Nano-medicine and risk management; and
- Nano-medicine and ethics.

5.4 CLINICAL NANO-MEDICINE APPLICATIONS

Today, big scaled centers which conduct experimental and clinical studies are focused mainly on three fields.

5.4.1 Regenerative Nano-Medicine

Current ‘traditional treatment’ approaches seem to have limited results in many diseases or cause success of training to change from patient to patient. Both for improving the efficiency of the treatment and minimizing the side effects, methods to be used should be patient-specific characteristics.

As a result of “tissue engineering” studies, the basis of patient-specific treatments, which can be used in the regeneration and reparation of *in situ* tissues, has started.

Main implementation fields of tissue engineering, which is an interdisciplinary field, are maintaining, improving and repairing the functions of biological structures through collaboration of engineering and life sciences. By means of tissue engineering, future therapy methods will be more focused on treatment of chronic disorders by use of self-healing mechanisms of the body than targeting symptoms or reducing the development of diseases.

It is possible to evaluate regenerative nano-medicine studies into two topics as therapy and biomimesis.

5.4.2 Diagnosis and Imaging Methods Based on Nano-Medicine

The most important aim in the diagnosis of diseases is to diagnose disease when it is at the earliest stage, at one-cell level. To reach this aim, we must develop new *in vivo* and *in vitro* diagnosis methods based on nanotechnology. Within the scope of *in vitro* applications, studies on chemo-bio nano-sensors, ultra-sensitive biochips (“lab-on-a-chip” and “cells-on-chips” devices) have been prepared for routine medical applications.

Yet-to-be-produced nano-analyser devices will be used by patients and, at the same time, will transmit multiple types of data to clinicians. More important than that, by means of nano-biosensors, it will be possible to increase the accuracy of already used test methods. Biosensors (such as photonic crystal nano-biosensors, magneto nano-immunosensor, piezoelectric nano-sensors, resonating beam sensors, and ion-channel biosensors) harness the immensely powerful molecular recognition properties of living systems and engineer these into electronic devices to provide easy-to-use sensing devices. The most successful biosensor developed to date, is the home blood glucose sensor which is now ubiquitous world-wide. Biosensors can be used to measure disease markers, food safety, and environmental quality, to ensure safety and security.

Developments in microscopic scanning-imaging methods (quantitative-PET, MRS, d-MRI, and f-MRI), spectroscopic-spectrometric techniques (Fourier Transforms Infrared Imaging Spectroscopy – FTIR, High Performance Liquid Chromatography – HPLC-MS / HPLC-UV-Vis, and Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry-MALDI-TOF) and advanced genetic analyses (Real-Time Polymerase Chain Reaction – PCR) provide ultra-high spatial resolutions and give detailed molecular information about the complex ‘functionality’ of cells. Data acquired by use of quantum dots and fluorescent nanoparticles will lead developments of more innovative and stronger *in vivo* diagnosis devices. Nano-devices produced as accompanying this functional molecular imaging will be more effective and much safer.

5.4.3 Targeting Delivery and Releasing

Long-term aims of controlled drug delivery systems are to develop diagnosis agents with a high level of efficiency and safety, and to perform treatment, application and follow up with the same nano-system. 'Find, fight and follow', as is the concept; includes early diagnosis, treatment and monitoring of the results and also is stated as "theragnostic" (diagnosis + treatment).

Drug delivery techniques suitable for theragnostic definition are prepared in accordance with two needs. First is drugs targeting more effectively where the disease is located, with high patient tolerance and cost effectiveness, the other is to detect new methods for distribution of new types of pharmacologic agents which cannot be distributed effectively by conventional methods.

The main aim of pharmaceutical studies in this regard is to target medication to specific target tissues, at the right time, in the necessary amounts and with safe, repeatable, and controllable methods. Currently, 13% of products on the pharmaceuticals market are related to controlled drug distribution systems. Nano-particle formulations are still used to increase activity without increasing surface/volume proportion. In addition, nano-particles act as drug carriers to effectively transmit therapeutics which have weak liquidity. If a therapeutic active substance is suitably encapsulated in a nano-particle, carrying this drug anywhere requested, controlled oscillation of the drug and protection from early stage activity decreases can be managed. These results will both increase the efficiency of drugs and decrease side effects dramatically. These types of nano-particle delivery systems can be used for the treatment of cancer and many other diseases.

Controlled drug delivery is based on the principle of turning pathophysiological changes, which appear basically in diseased tissue, into advantages for treatment. Because in tissues in which pathological process has already started, all physiological functionality disorders related to cell homeostasis are observed, accumulation of carriers which distribute drugs in a controlled manner will be easier. Anatomic barrier between normal and pathologic tissues and vascularisation differences will make it easier to deliver nano-carriers to diseased tissue. Thus, nano-carriers which carry therapeutic agents will reach much higher concentration in target tissue compared to doses applied with normal drug treatment.

As a result of decrease in vascular permeability and lymphatic drainage appeared especially in tissue which developed tumor and inflammatory diseases, on one hand reach of nano-structures to target tissue will be facilitated, on the other hand it will be more difficult to withdraw. By means of the opportunity created by this pathophysiological change, nano-structures can easily be accumulated in extravasations and target tissue.

By means of localization tendency of nano-carrying systems especially in RES will be considered as a huge advantage in terms of both controlled and passive distribution of drugs. This natural distribution method managed by macrophages can be used for intracellular infections of liver and spleen.

Patient-specific therapies and diagnosis have a critical role on nano-systems performing controlled distributions to reach the target. It is possible to find many nano-carrying systems having such an aim in the literature (liposomes, micellar and micro-emulsion systems, liquid crystal based formulations, nano-crystals, antibodies and conjugates, naturally occurring proteins as delivery systems, polymer conjugates and bio-conjugates, biodegradable nanoparticles/nano-capsules, virus-like particles for gene delivery, delivery of small nucleic acids or mimetics, delivery of vaccines, synthetic biomimetics, dendrimers, carbon nano-tubes, etc.).

Although there have been many successful experimental studies on the topic existing today, strategies for developing new drug carrying systems aren't completely accepted yet. Efforts on this topic have been proceeding slowly because of the uncertainties about regulation and toxic side effects. It should be accepted that drug safety has to be attached as much importance as drug efficiency considering all nano-particles.

Chapter 6 – CHARACTERISTICS OF THE UNITED STATES MILITARY DEPLOYABLE CBRNE LABORATORY

Richard Trombly
 20th Support Command
 FORSCOM
 5183 Blackhawk Rd, E-1042
 Aberdeen Proving Ground, Maryland 21010
 UNITED STATES
 (410) 436-0088

richard.trombly@us.army.mil

6.1 INTRODUCTION

The United States Military Deployable CBRNE Laboratory interfaces with numerous units to provide Field Confirmatory and Theater Validation results. A graphic representation of the various levels of analysis is displayed below. In a field environment, rapidly deployable units are tailored to the incident and involve specialized teams with a tactical focus. These teams provide presumptive and field confirmatory results for consequence management. Mobile “Theater Validation” labs provide theater/operational level support by scientific experts to major combatant Commanders. Fixed site laboratories located in continental United States provide definitive analyses for national command authorities for strategic level decision-making. This chapter will focus on mobile laboratories providing Field Confirmatory and Theater Validation results.

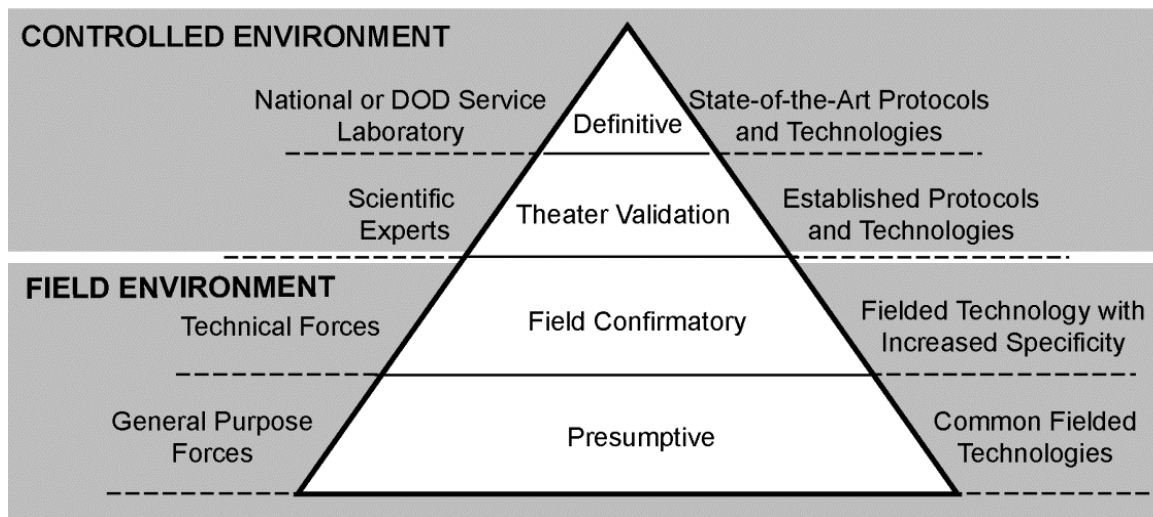


Figure 6-1: Overview of CBRN Identification Levels.

U.S. Army Forces Command tasks the 20th Support Command to provide specialized CBRNE solutions for DoD challenges. The CBRNE Analytical and Remediation Activity (CARA), subordinate to the 20th Support Command, deploys and conducts operations in support of regional combatant Commanders or other government agencies in order to counter CBRNE and WMD threats in support of National Combating WMD objectives.

The CARA typically deploys elements in a general support role to a theater Commander under the mission command of the JTF-HQ or mission dependent direct support allocation to designated Commanders on an

area/site specific basis. Each of these elements can also deploy separately from the JTF. In this case, these elements will most often be placed in the operational control of the supported command.

The MEL mainly operates in a permissive environment but under certain conditions can operated in uncertain environments while conducting field confirmatory identification. The MEL cannot sustain 24-hour operations unless augmented by additional technical laboratory personnel. RRTs are capable of conducting non-intrusive assessment of munitions; presumptive identification of CB materials and may collect CBRN samples if required. All of CARA deploy in mobile, modular, tailorable teams depending on the mission requirement.

6.2 REMEDIATION RESPONSE

CARA has four Remediation Response Teams, located at Pine Bluff Arsenal, Arkansas and Aberdeen Proving Ground, Maryland. They provide:

- Response, remediation and escort support to combatant Commanders and other Government Agencies to counter the CBRNE and WMD Threat;
- Emergency response to discoveries of suspect Recovered Chemical Warfare Materials (RCWM) in support of the Army Chemical Materials Agency's, Non-Stockpile Chemical Materiel Project;
- Remediation operations involving chemical warfare materials found at formerly used defence sites and base realignment and closure sites in support of the Army's Corps of Engineers and active military installations in support of installation Commanders;
- Stockpile and non-stockpile operations in support of the Army Chemical Materials Agency; and
- Conduct technical escorts to transport chemical and biological surety and non-surety material for various Army laboratories.

The Mobile Munitions Assessment System (MMAS) Team conducts emergency response assessments of recovered chemical warfare materiel. The MMAS serves as a command center. It has an equipment storage area and weather monitoring system. It utilizes satellite communications to transmit data back to headquarters for analysis and can remain on site for months, with a constant power supply and redundant computer systems providing added data protection.

The MMAS Operators are trained and proficient with the MMAS equipment set:

- A Portable Isotopic Neutron Spectroscopy (PINS) system: PINS accurately detects the presence of chemical elements using neutron particles to produce a unique energy spectrum given off by chemicals inside a munition;
- A Digital Radiography and Computed Tomography (DRCT): DRCT uses X-ray photography to produce high-quality images of an item's interior to show if the munition contains a liquid fill and explosive potential; and
- A Raman Spectrometer: Using a fiber optic probe and laser, the Raman identifies the contents of glass Chemical Agent Identification Sets (CAIS) bottles containing various agents and industrial chemicals once used to train Soldiers.



Figure 6-2: Pictures of the Mobile Munitions Assessment System (from Top Left to Bottom Right): RAMANS Spectrophometer; MMAS Phase 2 System 2; Portable Isotopic Neutron Spectroscopy System; Digital Radiography / Computed Tomography.

6.3 MOBILE EXPEDITIONARY LABS

The Mobile Expeditionary Laboratory is staffed with credentialed, deployable civilian scientists, both chemists, and microbiologists. It can deploy using several different packages three tactical platforms, Light Mobile Expeditionary Lab (LMEL), Heavy Mobile Expeditionary Laboratory (HMEL) and Chemical Air Monitoring Suites (CAMS). This laboratory can detect, identify, quantify and provide field confirmatory/theater validated analysis of Chemical Warfare Agents (CWA), Toxic Industrial Compounds (TIC), biological agents and select explosives; and conduct near real time air monitoring of chemical warfare agents. It supports Sensitive site exploitation, crisis and consequence management, and mitigation operations. The tactical platforms are deployable by military aircraft and ruggedized for field deployment. The modular configurations can be tailored to support needs of combatant Commanders.

6.3.1 Light Mobile Expeditionary Labs



Figure 6-3: The Light Laboratory Capability.

The light configurations are two rugged, rapidly deployable suites of modular and tailored laboratory instruments for rapid operations at the request of a ground force Commander. The platforms use a standard military Light Medium Tactical Vehicles or LMTVs and a High Mobility Multipurpose Wheeled Vehicle, better known as a HMMWV. A vestibule connects the two vehicles. The actual “lab” is inside the shelter on the back of the LMTV. The package includes one Light Medium Tactical Vehicle (LMTV) with mounted lab shelter, an environmental control unit, trailer mounted 30-kW generator, and a shelter-installed glove box; one High Mobility Multi-purpose Wheeled Vehicle (HMMWV) with tactical shelter. This package is air transportable by a C-130 or larger aircraft.

Light Lab Chemistry



Light Lab Biological



Figure 6-4: Inside of the Flyaway Laboratory with a Chemistry and Biology Configuration.

The inside of the light laboratory has two configurations, chemistry and biology. The analytical components include a chemical package consisting of a:

- 1) Gas Chromatograph Mass Spectrometer (GC/MS) to separate and identify chemical and some explosive agents in air, vegetation, solid and liquid samples;
- 2) Fourier-Transform Infrared (FT-IR) Spectroscopy for bulk screening of chemicals and explosives (liquid, solid, thin film);
- 3) Raman spectrometer for bulk screening of chemicals and explosives (liquid, solid); and
- 4) Radiological screening capability.

The biological package consists of a:

- 1) Joint Biological Agent Identification and Diagnostic System (JBAIDS) [Polymerase Chain Reaction (PCR)] for identifying specific DNA/RNA of biological weapon agents;
- 2) Microscope used with specific stains to determine the presence and characteristics of microorganisms; and
- 3) Radiological screening capability.

The light laboratory can be configured in a combined package consisting of a GC/MS, FT-IR, PCR, and Antibody Assay, and a radiological screening capability.

6.3.2 Heavy Mobile Expeditionary Labs

The heavy MEL configurations are two 20-foot expandable shelter/containers that are deployed into a theater sanctuary area. The heavy MEL configuration brings a full brick and mortar lab-like facility with theatre-level confirmatory standard capabilities. A robust suite of analytical instrumentation allows for a high confidence identification of unknown hazards. The heavy MEL is deployed via C-17 and deploys with a family of medium tactical vehicles for ground transport with a 60-day supply of consumables. Each platform brings ten large containers and two refrigerators for shipment and storage.



Figure 6-5: The Heavy Laboratory Capability.



Figure 6-6: The Heavy Laboratory Engineering Controls Include Fume Hood, Class II Biosafety Cabinet and Glovebox.



Figure 6-7: The Heavy Laboratory Images Inside the Sample Receipt Tent and 20' ISO Shelter.

The HMEL deploys with a robust suite of analytical equipment to analyze CWA's, precursors, degradation products, TICs, explosives, toxins, viruses and bacteria. The chemist use the following analytical instruments:

- 1) Gas Chromatograph Mass Spectrometer (GC/MS) to separate and identify chemical and some explosive agents in air, vegetation, solid and liquid samples;
- 2) Fourier-Transform Infrared (FT-IR) spectroscopy for bulk screening of chemicals and explosives (liquid, solid, thin film);
- 3) Raman spectrometer for bulk screening of chemicals and explosives (liquid, solid);
- 4) Capillary electrophoresis to separate and detect chemical degradation products;
- 5) Liquid Chromatography Mass Spectrometer (LC/MS) for the detection of trace level explosive compounds and proteomics analysis;
- 6) X-Ray Diffraction (XRD) identifies explosive, TICs compounds with crystal structures; and
- 7) X-Ray Fluorescence (XRF) for post blast analysis and identification of metal alloys and elemental analysis.

The microbiologist use the same equipment listed in the LMEL but the HMEL also include limited culture capability.

6.4 CHEMICAL AIR MONITORING SUITES

The chemical air monitoring suites configurations are four light medium tactical vehicles with shelter and towed generator sets. The chemical air monitoring suites provide the ground force Commander with the data on occupational exposure limitations as defined by Occupational Safety and Health Administration, CDC, U.S. Army Center for Health Promotion and Preventive Medicine, and the U.S. Surgeon General during CBRN material recovery or long-term site remediation. The chemical air monitoring MEL is deployed via C-130 and carries a 90-day supply of consumables.

The CAMS equipment is transported by a 2.5-ton M1079A1 shelter-equipped Light Medium Tactical Vehicle (LMTV) towing a 30-kW trailer-mounted generator set. The term CAMS refers to the entire system, which consists of the LMTV van and on-board chemical air monitoring equipment.

The CAMS equipment consists of MINICAMS (Gas Chromatography (GC) with a Flame Photometric Detector (FPD) and GC with Halogen Specific Detector (XSD), which employs analytical and surveillance methods to continuously evaluate for the presence of low-level Chemical Warfare Agents (CWAs) in order to comply with established Short-Term Exposure Limits (STEL). Depot Air Monitoring System (DAAMS) for GC/MS monitoring of air/gas/vapor samples captured on the DAAMS tube.

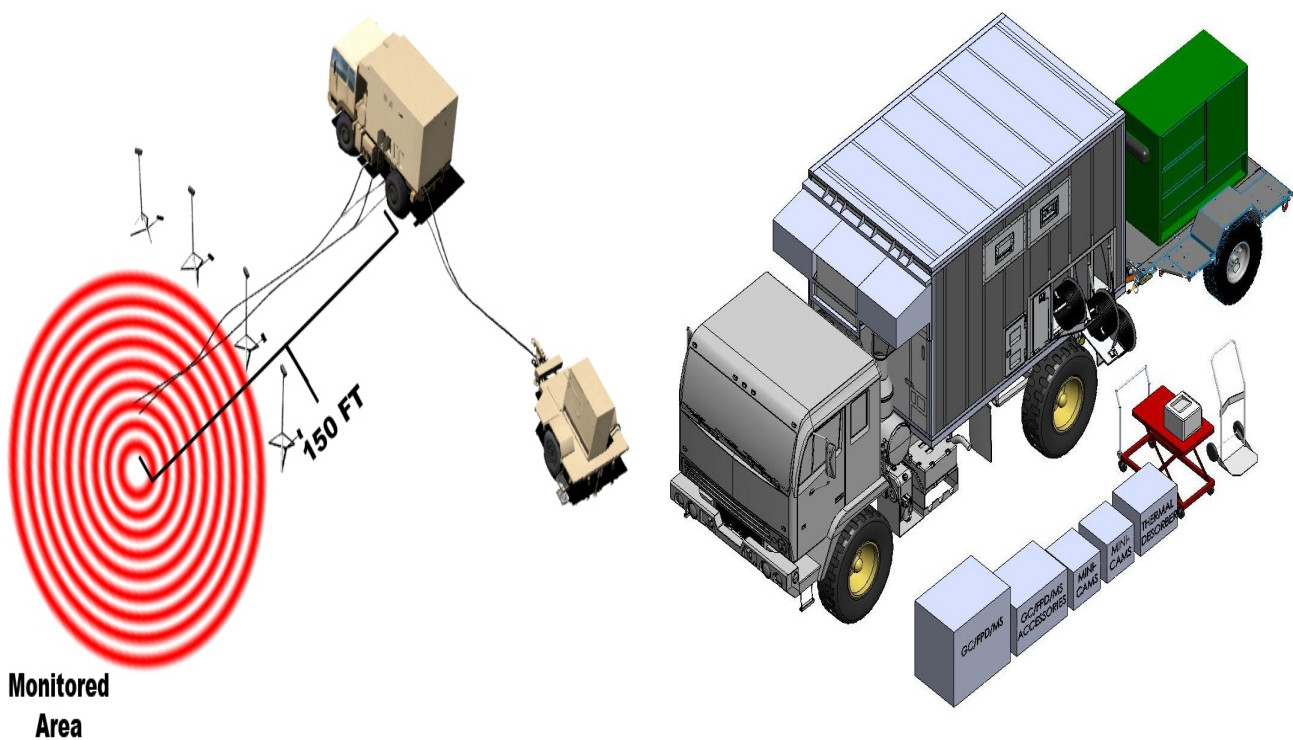


Figure 6-8: Light Medium Tactical Vehicle with Shelter and Towed Generator.
Left: Deployed air monitoring arrangement with generator; Right: Mobile configuration with stored analytical equipment removed.



Figure 6-9: Internal Laboratory and Storage Configuration of Light Medium Tactical Vehicle.

The MEL brings the following capabilities to the supported Commander:

- Receipt and storage of solid, liquid, and vapor/gas samples;
- Field confirmatory or theater validation identification;
- Identification of the constituents of the solid, liquid, and vapor/gas sample;
- Characterization of the sample;
- Quantification of the sample;
- Security and positive control of samples and sample related data;
- Split samples for additional analysis as needed;
- Sensitive analytical data and results transmission; and
- Safe (and according to applicable laws, regulations, and customs) storage, transportation, and/or treatment and destruction (as needed) of any hazardous materials resulting from the laboratory operations.



Chapter 7 – NATO JOINT CBRN DEFENCE BATTALION

Dr. Frederick Johnson

Chief, Biology Branch
CWMD Analysis Division
United States Army Nuclear and
CWMD Agency, G-357
Fort Belvoir, VA 22060
UNITED STATES
703-806-7878

frederick.johnson8.civ@mail.mil

Dr. Brian J. Lukey

Chem/Bio Research Coordinator, HJF
711 Human Performance
Wing/RHDJ
Wright Patterson Air Force Base
OH 45433
UNITED STATES
937-904-9543

brian.lukey.ctr@wpafb.af.mil

7.1 NATO REQUIREMENT/OBJECTIVE FOR A CBRNE DEPLOYABLE LABORATORY

The ever-growing threat of unconventional warfare requires NATO countries to be best prepared for a rapid response to a potential CBRNE event. The threat has elevated recently with the unrest in the Middle East, where terrorists and even host Nations may access CBRN stockpiles to use on their adversaries to gain the advantage. Past events that underscore the threat include the sarin attacks in the Tokyo subway, the anthrax letters in the US, and the sulfur mustard attacks on the Kurdish villages in Iraq. Most strategic analysts believe that the likelihood of such future CBRN events occurring no longer becomes a question of “if” but “when”.

For CBRNE events, military Commanders need timely confirmatory analyses for crisis management to appropriately handle the immediate situation, with emphasis on appropriate decontamination, site evacuation and medical treatment for those exposed and also on avoiding exposure for anyone else. Senior political leaders require forensic confirmatory analysis for consequent management to take appropriate action on the identified perpetrator. All involved want to ensure the results are precise and accurate to make key strategic, operational, and tactical decisions in the most expeditious manner. Consequently, the need for a rapid-response CBRNE laboratory has never been more urgent.

The challenge for a NATO laboratory is complicated on several fronts. For consequence management decisions, most countries prefer obtaining advice from their own scientists/subject-matter experts. However, the skills to appropriately collect and analyze samples for a suspected CBRN incident require much training and time. As a result, forward-deployable military scientists and technicians with these required, highly-developed analytical skills are very limited in number. Maintaining a pool of military scientists for each NATO Nation with standardized, highly-technical skills would be most challenging. In addition, many countries have developed different requirements and approaches for the personnel, equipment, and missions for a deployable laboratory. The approaches are dependent upon a variety of factors to include the country’s military size, political interest in the degree of retaliatory actions to be taken, and the appropriated budget to support such a laboratory. A single, standardize approach would be difficult to obtain with consensus. Consequently, the NATO deployable CBRNE laboratory has been designed to be flexible in its composition, reflecting each country’s interpretation of their deployment need.

NATO’s new Strategic Concept adopted at the 2010 Lisbon Summit confirmed the Alliance’s commitment to further develop its capacity to defend against the threat of CBRN weapons of mass destruction and protect its populations, territory and forces. NATO developed the Combined Joint CBRN Defence Task Force (CJ-CBRND-TF) as one of NATO’s key defences against CBRN events.

7.2 COMBINED JOINT CBRN DEFENCE TASK FORCE

The NATO CJ-CBRND-TF consists of CBRN Joint Assessment Team (JAT) and CBRN Defence Battalion. This NATO body is specifically trained and equipped to deal with CBRN events and/or attacks against NATO populations, territory, or forces.

The Battalion and the CBRN JAT, created in 2003 and declared operational the following year, is a multi-national, multi-functional team, able to deploy quickly to participate in the full spectrum of NATO operations.

The Battalion's mission is unique in that it is not only trained for armed conflicts, but is also able to be deployed to crisis situations such as natural disasters and industrial accidents, including those involving hazardous material. The CJ-CBRND-TF can also be deployed in order to support the protection of High Visibility Events (HVE) such as Olympic Games or NATO Summits.

The realization of the CJ-CBRND-TF fulfils two of the capability commitments made by Allies at the 2002 Prague Summit: a Prototype Deployable Nuclear, Biological and Chemical (NBC) Analytical Laboratory and a Prototype NBC Event Response Team. These capabilities greatly enhance the Alliance's defence against WMD.

The Battalion's mission is to provide a rapidly-deployable and credible CBRN defence capability to maintain NATO's freedom of action and operational effectiveness in a CBRN threat environment.

The CBRN Battalion may be used to provide military assistance to civil authorities when authorized by the North Atlantic Council, the Alliance's principal political decision-making body. For example, they played a key planning role during the 2004 Summer Olympics in Greece, and the 2004 Istanbul Summit, where they supported any CBRN-related contingency operations.

The CBRN Defence Battalion is capable of conducting the following tasks:

- 1) CBRN reconnaissance and monitoring operations;
- 2) Sampling and Identification of Biological, Chemical, and Radiological agents (SIBCRA);
- 3) Biological detection and monitoring operations;
- 4) Provide CBRN assessments and advice to NATO Commanders; and
- 5) CBRN hazard management operations, such as decontamination.

7.3 NATO NATIONS PARTICIPATING IN THE DEFENCE TASK FORCE

Following the agreement at the 2002 Prague Summit to enhance the Alliance's defence capabilities against weapons of mass destruction, the North Atlantic Council, in June 2003, decided to form a Multi-national CBRN Defence Battalion and JAT.

The structure of the Battalion was established at a planning conference on 17-18 September 2003. The following month, on 28 October 2003, a force generation conference was held at Supreme Headquarters Allied Command Europe (SACEUR). On 18-21 November 2003, a follow-up conference was held in the Czech Republic, the first volunteer lead country. Twelve other nations (Belgium, Canada, Hungary, Italy, Norway, Poland, Portugal, Romania, Spain, Turkey, United Kingdom and United States) have offered to provide forces for this first Multi-national CBRN Defence Battalion.

The Battalion reached its initial operational capability on 1 December 2003. Full operational capability was achieved on 28 June 2004 as declared by SACEUR at the Istanbul Summit, and responsibility was transferred into the strategic command of Allied Command Operations. From then on, the Battalion was included in the six-month rotation system of the NATO Response Force.

Some 21 NATO Nations now contribute to the Combined Joint CBRN Defence Task Force on a voluntary basis. National commitments vary depending on the rotation, but there are usually 8 – 10 Nations involved per rotation.

For the very first time a non-NATO Member Nation participated in 2010. Ukraine contributed a decontamination platoon after having accomplished a NATO evaluation and certification process very successfully.

7.4 OPERATIONAL PROCESS

The CBRN JAT and CBRN Battalion fall under the strategic command of the SACEUR. Operational control is delegated to a subordinate command as required.

NATO's Allied Command Transformation provides evaluation standards, supports training and determines future NBC defence requirements and develops capabilities.

The Battalion level organization is composed of personnel from a number of NATO Nations. Like the NATO Response Force, dedicated personnel are based in their countries, coming together for training and deployment.

A voluntary lead country is identified for each rotation. The lead country hosts the CBRN Joint Assessment Team and Battalion headquarters, responsible for command and control arrangements, maintaining standard operational procedures, sustaining readiness levels and for planning and conducting training. Contributing countries supply functional capabilities. This includes providing requisite troops, equipment and logistical support in accordance with mission requirements. The Defence Task Force is composed of separate but complimentary components, which can be deployed in different stages and different combinations to suit each mission.

The components are:

- 1) **Joint Assessment Team** – Comprised of specialists that provide CBRN-related advice and support;
- 2) **Headquarters Command and Control** – Tailored command and control capabilities with a robust communications package to support assigned and attached organizations;
- 3) **Reconnaissance** – Designed to provide route, area and point detection and identification of agents;
- 4) **Decontamination** – Maintains the capability to decontaminate personnel and equipment; and
- 5) **Deployable Analytical CBRN Laboratories.**

Designed to provide expert sampling, analysis, and scientific advice to support operational Commanders.

The Battalion has a close relationship with the NATO Response Force. While it can be deployed independently, it is consistent and complementary to the NATO Response Force. Its strength is included within the NATO Rapid Force structure, and it can deploy within 5 to 30 days.



Annex A – HFM-177 MEETING ITINERARIES

A.1 6-8 APRIL 2009 MEETING IN EDGEWOOD, MARYLAND, USA

NATO RTG/HFM-177
Deployable Application of Biotechnology
6-8 April 2009
Conference Room 229, Building E3330
US Army Edgewood Chemical Biological Center
Edgewood, MD 21010-5424
United States

Center Host: Mr. Raymond Mastnjak, X5-2516
Visit POC: Ms. Marlena Long, X5-0987

Mil Uniform: Duty Uniform
Civilian: Business Attire

ARRIVAL DATA:

Date: Mon 6 Apr 09
 Time: 0800
 Mode: POV
 Loc: Bldg E3330

DEPARTURE DATA:

Date: Wed, 8 Apr 09
 Time: 1200
 Mode: POV
 Loc: Bldg E3330

ITINERARY

Time	Event	Mode/Location	POC
Monday, 6 April			
0830	Arrive at ECBC	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
0900 – 0930	Introductions and Opening Comments (Mastnjak)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
0930 – 1000	Overview Presentation of the HFM-177 (Schlager/Wade)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1000 – 1030	Overview of Czech Republic Lab Technology (Hubálek)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1030 – 1045	Break and Informal Discussion	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1045 – 1115	Overview of the Turkey Lab Technology (Budak)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1115 – 1145	General Overview of Georgia Lab Technology (Tabagari)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1145 – 1300	Lunch Break	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1300 – 1330	Overview of US Lab Technology (Mastnjak/Schlager)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1330 – 1430	Tour, STORM High Throughput Mobile Bioanalytical Lab	Bldg E3330	Mr. Raymond Mastnjak
1430 – 1445	Break	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1445 – 1600	Open Discussion, Deployable Bioanalytical Laboratories	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1700 – 1800	Drinks / Happy Hour / Ongoing Discussion (Optional)		Mr. Raymond Mastnjak
1800 – 2000	Dinner Outing (All)		Mr. Raymond Mastnjak
Tuesday, 7 April			
0900 – 0930	Coffee and Open Discussion (All)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
0930 – 1000	Triage of Uncharacterized Samples (Unknowns) (Mastnjak)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1000 – 1030	Field Operations in a Mobile Bioanalytical Laboratory	Bldg E3330 / Rm 229	Dr. Carrie Poore

ANNEX A – HFM-177 MEETING ITINERARIES

1030 – 1045	Break and Informal Discussion	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1045 – 1145	Tour, Mobile Bioanalytical Lab at Bldg E5830 (All)	Bldg E5830	Mr. Raymond Mastnjak
1145 – 1300	Lunch	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1300 – 1430	Tour, US Army / FBI Sample Receipt Facility (Mastnjak)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1430 – 1445	Break		Mr. Raymond Mastnjak
1445 – 1600	Open Discussion (All)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
	* Presentation of new and existing bio- and nano-technologies		
	* Discussion and consideration deployable mobility aspects, structures and technologies for lab systems		
	* New concepts and consensus for mobile platforms labs		
1700 – 1800	Drinks / Happy Hour (Optional)		Mr. Raymond Mastnjak
1800 – 2000	Dinner Outing		Mr. Raymond Mastnjak

Wednesday, 8 April (Morning only)

0900 – 0930	Coffee and Open Discussion (All)	Bldg E3330 / Rm 2299	Mr. Raymond Mastnjak
0930 – 1045	Wrap-up and discussion of preparation meeting minutes and results for NATO HFM submission (All)	Bldg E3330 / Rm 229	
1045 – 1100	Break	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak
1100 – 1130	Concluding Comments / Open Discussion (All)	Bldg E3330 / Rm 229	Mr. Raymond Mastnjak

A.2 29-30 OCTOBER 2011 MEETING IN MUNICH, GERMANY**NATO RTG/HFM-177
Deployable Application of Biotechnology****29-30 October 2011
Theresa Conference Room
Holiday Inn Munich – Schwabing
Munich, Germany****Saturday, 29 October**

- 0900 – 0930 Introductions and Overview Presentation of the HFM-177 (Schlager/Lukey)
– *With coffee & bagels*
- 0930 – 1000 Deployable Biological Laboratory of the Armed Forces of the Czech Republic
(Hubálek/Pisa/Dresler)
- 1000 – 1015 US Army Bio-Environmental and Public Health Mobile Analytical Laboratory
Capabilities (Walker)
- 1015 – 1030 Construction of Deployable Laboratories During Times of Reduced Funding (Mastnjak)
- 1030 – 1045 Break and Informal Discussion
- 1045 – 1100 The Role of Triage in Sample Analysis (Mastnjak)
- 1100 – 1130 The Bundeswehr Rapidly Deployable Bio Lab – Microbiological High-Tech Diagnostics
for Outbreak Investigations Abroad (Woelfel)
- 1130 – 1300 Lunch Break (at the hotel)
- 1300 – 1330 Defence Nano-Biotechnology Applications in Turkey (Budak)
- 1330 – 1400 General Overview of Israel Lab Technology (Marks)
- 1400 – 1415 Break and Informal Discussion
- 1415 – 1445 General Overview of Georgia Lab Technology (Tabagari) (Optional)
- 1445 – 1500 Introduction to the “Biological Surveillance Collector System (BSCS)” (Howells)
- 1500 – 1530 NATO’s Rapidly Deployable Outbreak Investigation Team (RDOIT) – From Concept to
Development, from Implementation to Deployment (Wojtyk/Thibault/Chickery)
- 1530 – 1630 Discussion of Presentations and Initial Ideas on NATO Lab Design Elements:
- Development of the deployable laboratory design, construction, and materials
 - Analysis of existing instrument technology and procedures
 - Analysis of emerging nano-/bio-technology for instrument acquisition
 - Integration of existing and emerging technologies into a deployable laboratory product
- 1830 – 1915 Drinks / Happy Hour at the hotel (Optional)

ANNEX A – HFM-177 MEETING ITINERARIES

1930 – Ends Dinner at “Wirtshaus zur Brezn” (All)
Leopoldstr.72, D-80802 München
<http://www.zurbrezn.de/>
+49 89 390092

Sunday, 30 October

0900 – 0930 Coffee and Continue Open Discussion (All)

0930 – 1000 Complete Open Discussion: Development of the Deployable Laboratory Design,
Construction, and Materials (All)

1000 – 1030 Complete Open Discussion: Analysis of Existing Instrument Technology and Procedures
(All)

1030 – 1045 Break and Informal Discussion

1045 – 1115 Complete Open Discussion: Analysis of Emerging Nano-/Biotechnology for Instrument
Acquisition (All)

1115 – 1145 Complete Open Discussion: Integration of Existing and Emerging Technologies into a
Deployable Laboratory Product (All)

1145 – 1300 Lunch (at the hotel)

1300 – 1430 Discussion / Concluding Comments (All)

1800 – 1900 Drinks / Happy Hour at the hotel (Optional)

1930 – Ends Dinner at “The Big Easy”
Frundsbergstr. 46, D-80634 München
<http://www.thebigeasy.de/>
+49 89 15890253

Annex B – NATO HFM-177 DEPLOYABLE LAB SURVEY

B.1 TEMPLATE

Country:

Institution:

Point of Contact:

Telephone:

Email:

- | | | | |
|---|--------------------------|--------------------------|--------------------------|
| 1. Does your Ministry Of Defence (MOD) possess permanent field-forward or mobile/deployable medical laboratory facilities for biological or chemical defence? | Yes | No | Don't Know |
| | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

→ If yes, please provide descriptive information and/or documentation using an attachment. If your country has more than one deployable system, please complete this Survey for each system.

2. If your MOD does NOT possess medical biological and/or chemical defence facilities:

Does your MOD coordinate with any other responsible/responsive government agency (i.e., Ministry of Health) concerning the detection of infectious disease outbreaks in field containment?	Yes	No	Don't Know
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

→ If so, please briefly describe the arrangement:

3. Who is responsible for the technical and operational management of these field-forward or mobile/deployable medical laboratory facilities?

- Medical Service
- CBRN Defence
- Others?

4. The laboratory is:

- Self-mobile
→ Platform/type of vehicle:
- Deployable
→ Typical size and weight of single package:
→ Total number of packages:
- Others?

ANNEX B – NATO HFM-177 DEPLOYABLE LAB SURVEY

Country: **Institution:** **Point of Contact:**

5. The laboratory can be transported:

- By car
- By truck
- In a civilian airplane as passenger luggage
- In a civilian airplane as cargo only
- In a military airplane
- Others?

6. How long does it take to set up the lab after arrival at the site of operation?

7. What kind of external supplies (water, electricity, etc.) are needed to operate the laboratory?

	Yes	No	Don't Know
8. Is the laboratory able to work autonomously without external supplies? → If your answer is yes, how long is the laboratory operational before external supplies are needed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Yes	No	Don't Know
9. Does your laboratory participate in any scheme for ensuring permanent diagnostic capacity, such as an on call or a duty team regimen?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

→ If your answer is yes, is this restricted to specific diagnostic tests, or specific diseases?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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→ If yes, which are they?

	Yes	No	Don't Know
10. Is this call system also designed to serve laboratory or hospital emergencies?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Yes	No	Don't Know
11. Is it intended to respond to specific demands from a surveillance system?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Yes	No	Don't Know
12. Is there a filter, at any level (national or regional), that will receive the demand and call the system only after assessment, deciding whether or not this is needed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Country: **Institution:** **Point of Contact:**

13. What is the timing of the duty?

- 24 hours a day, 7 days a week?
- Non-working hours of the day and non-working days of the week?
- Any other schedule?

Yes	No	Don't Know
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

14. Is the duty system part of a network?

- National?
- Regional?
- International?
- Other?

Yes	No	Don't Know
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

15. If your answer to #14 was yes, does the duty call system include a whole team?

- How many people are involved?
- Scientists (Experience/Degree type)?
- Technologists (Experience/ Degree type)?
- Others?

Yes	No	Don't Know
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

16. Are there other relevant capabilities or features of your field-forward or mobile/ deployable medical laboratory facility which you want to mention or do you have any comments?

→ If yes, please provide this information or comments using an attachment or use the space below:

ANNEX B – NATO HFM-177 DEPLOYABLE LAB SURVEY
Country: **Institution:** **Point of Contact:**

17. Which of the following agents can be detected in the laboratory and by which technology or method?

	Don't Know	Not Available	Molecular (PCR) Assay	Serological Assay	Microscopy (e.g. staining)	Culture	Other Methods
Abrin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Aflatoxins	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
B. pseudomallei	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Bacillus anthracis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Botulinum Toxine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Brucella spp.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Burkholderia mallei	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
CCHF virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Chikungunya virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Clostridium perfringens toxin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Coxiella burnetii	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Eastern-Equine-Encephalitis virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Ebola virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Escherichia coli	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Flaviviruses	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Francisella tularensis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Hantaviruses	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Influenza virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Junin virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Lassa virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Machupo virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Marburg virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Monkeypox virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Omsk virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Orientia tsutsugamushi	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Palytoxin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Ricin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Rickettsia rickettsii	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Rickettsia typhi	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Rift Valley fever virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Salmonella spp.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Salmonella Typhi	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Saxitoxins	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Shigella dysenteriae	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Staphylococcal enterotoxins	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Tetradotoxin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Tick-borne encephalitis (TBE) virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Trichothece	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Variola virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Venezuelan-Equine-Encephalitis virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Vibrio cholerae	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Western-Equine-Encephalitis virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Yellow fever virus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Yersinia pestis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Other (please list)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Country:**Institution:****Point of Contact:**

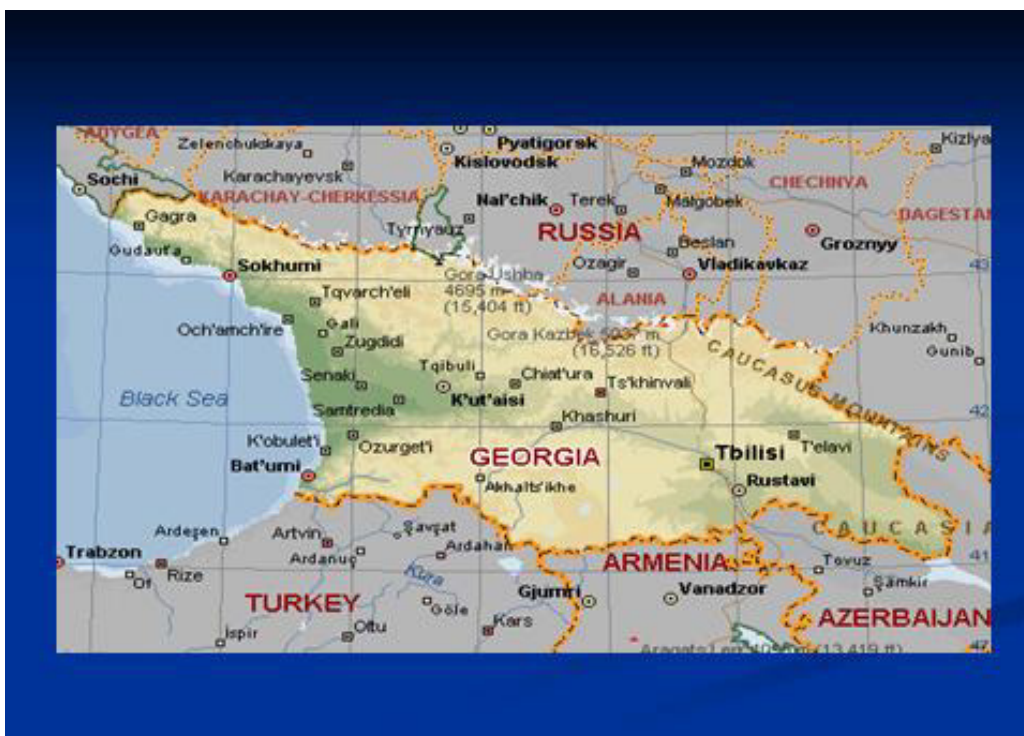
- | | | Yes | No | Don't Know |
|-----|--|--------------------------|--------------------------|--------------------------|
| 18. | Is the laboratory able to detect or identify Chemical Warfare Agents (CWAs)? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| | → If yes, which methods or technologies are used? | | | |
| | → Please identify which agents (Soman, Sarin, Tabun, VX, etc.) can be detected or identified: | | | |
| 19. | Does the laboratory have nuclear/radiological general or isotope specific survey detection systems and assays? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| | → If yes, which methods or technologies are used? | | | |
| | → Please identify which isotopes can be detected or identified. | | | |



Annex C – HFM-177 MEETING PRESENTATIONS

C.1 HFM-177 MEETING: 6-8 APRIL 2009, EDGEWOOD, MARYLAND, USA

C.1.1 Georgia Presentation – by Sergo Tabagari



CURRENT SITUATION

- The events that took place all over the world during last several years, have proved that the international terrorism is the biggest problem of our time.
- Bioterrorism is one of the cruelest and damaging types of terrorism.

CURRENT SITUATION

- Georgia has been in a very difficult situation since the last independence declaration more than 15 years ago.
- Georgia is located in one of the most unstable regions of the world. This causes the influx of the large numbers of refugees

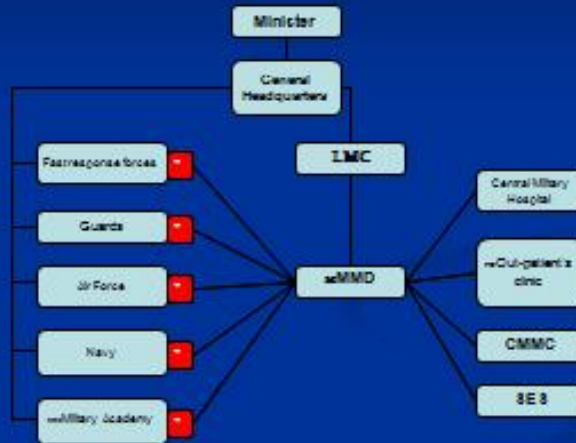
CURRENT SITUATION

- The borders are not protected with respect to EDP detection and isolation capabilities.
- The smuggling of goods and products is widespread
- The existing water reservoirs are not protected
- There are the Natural Nidus of the most dangerous infections: plague, tularemia, anthrax etc in Georgia

ORGANIZATIONAL CHART OF MEDICAL SERVICE OF MINISTRY OF DEFENSE



MEDICAL SERVICE ORGANIZATION CHART



LMC-Logistics Management Center
 MMD-Military Medicine Department
 CMMC-Central Military Medical Commission
 SES-Sanitary Epid. Service

SANITARY – EPIDEMIOLOGIC SERVICE



INFECTIOUS DISEASE DEPARTMENT LOCATIONS

1. Central Military Hospital*

2. Kutaisi Military Hospital*

3. Akhaltsikhe Military Hospital*

*No diagnostic kits available

PROPOSED EPIDEMIOLOGICAL MONITORING CENTER:

- Laboratory for pathogen isolation (microbiological, serological analysis)
- Epidemiological information system: electronic network with database, which will allow to communicate with remote sites and update the information regularly
- Training of the staff

PROPOSED EPIDEMIOLOGICAL MONITORING CENTER (CONTINUED)

Staff of the Sentinel Stations:

- a) Epidemiologist
- b) Bacteriologist
- c) 2 Paramedics
- d) Disinfectant
- e) Veterinarians
- f) Drivers

PROPOSED EPIDEMIOLOGICAL MONITORING CENTER (CONTINUED)

- Epidemiological Monitoring Center should be located in Tbilisi

- 3 Sentinel stations :

- Eastern Georgia Sentinel station –the information from 4 garrisons will go here- Tbilisi, Gori, Telavi and Vashli
- Western Georgia Sentinel station- the information from 3 garrisons will go here- Batumi, Poti, Kutaisi
- South Georgia Sentinel station- Akhaltsikhe garrison, location- Akhaltsikhe

THE PURPOSE OF SENTINEL STATIONS

- Epidemiological surveillance of appropriate garrisons
- In cases of disease outbreak taking all necessary actions for stopping the epidemics
- Creation of the database and the analysis of received data

Planning Epidemiological Monitoring System

- The 3 Epidemiological Monitoring Centers should be located in:
 - Tbilisi (Eastern Georgia)
 - Kutaisi (Western Georgia)
 - Akhaltsikhe (South Georgia)
- The 3 Mobile Groups working in nidus of Infections and on sites of bioterroristic attacks



BIOLOGICAL THREAT AGENT DETECTION & RESPONSE (TADR) IN GEORGIA

- Defence Threat Reduction Agency (US)
- Walter Reed Army Institute of Research (US)
- Ministry of Labor Health and Social Welfare (GEO)
- Ministry of Defence (GEO)
- Ministry of Agriculture (GEO)

Georgia

Threat Agent Detection & Response (TADR) Workshop
16 - 18 March 2004

- *Dr. Michael Balady (DTRA)*
- *Dr. Alicia Anderson, DVM, MPH, DACVPM*
Division of Preventive Medicine
Walter Reed Army Institute of Research
- *Roger Breeze, PhD*
- *Eric Casper, DTRA*
- *Timothy P. Endy MD, MPH*
Director, Communicable Diseases and Immunology WRAIR
- *Dr. R. Ross Graham (Bechtel National Inc.)*

INTEGRATED SYSTEM OF HUMAN DISEASE SURVEILLANCE AND RESPONSE IN GEORGIA

NCDC

- The National Center for Disease Control (NCDC) was founded on the basis of Georgian Station for Plague Control in 1996
- NCDC reports to the Georgian Ministry of Health
- Main office is located in Tbilisi. Branch office – in Batumi and two seasonal sentinel stations (Ninotsminda and Aspindza)
- NCDC has 258 employees, 20 of them are working in the Batumi branch office
- Approximately 50% of the staff are specialists with university education, and 30 of them have scientific degrees (candidates and doctors of sciences)
- Pathogens in use - Type 1-2 (Russian classification)

NCDC PARTICIPATED IN THE FOLLOWING PROJECTS:

- International Training and Research in Emerging Infectious Diseases ” (1997 – 2002) – Fogarthy Center, NIH
- “Establishing Epidemiological Network on the Territory of Georgia” (1997) - “Open Society Georgia” Foundation
- “Improvement of Epidemiological Network in Georgia” (1998) - “Open Society Georgia” Foundation
- Reproductive Health Survey (1999-2000) - UNFPA, UNICEF, USAID, UNHCR, AIHA, CDC
- Nutritional Status of Children Under Five Years of Age in Six Regions of Georgia (2000 – 2001) – USAID/Save the Children-US, Georgia Field Office
- Provision of Epidemiological Survey Services on Baku – Tbilisi – Ceyhan Pipeline Route – 2003, British Petroleum

ESTABLISH AN INTEGRATED, SECURE AND SUSTAINABLE DISEASE SURVEILLANCE SYSTEM IN GEORGIA

- Support human, environmental, and veterinary disease monitoring
- Ensure close cooperation among all relevant ministries and institutes and other international organizations
- Promote potential for integration into a regional disease surveillance system
- Ensure biosecurity and biosafety of biological facilities.

PROJECT GOALS

- **Laboratory**
 - Secure and safeguarded central reference laboratories
 - Safe, secure, and efficient pathogen transportation systems and capabilities
 - Verifiable training in biosafety/biosecurity, diagnostics
- **Epidemiology and Surveillance**
 - Standardized and repeatable human and animal disease monitoring systems
 - Mobile epidemiological response teams and secure transportation of disease elements
 - Verifiable epidemiology training
- **Communications and Information Technology**
 - Design, develop, and deploy and sustain a robust and secure electronic communicable disease reporting system
 - Create and sustain secure communications and data storage systems
- **Rules and Regulations**
 - Apply national regulations as they relate to BWPPP

BENEFITS TO GEORGIA

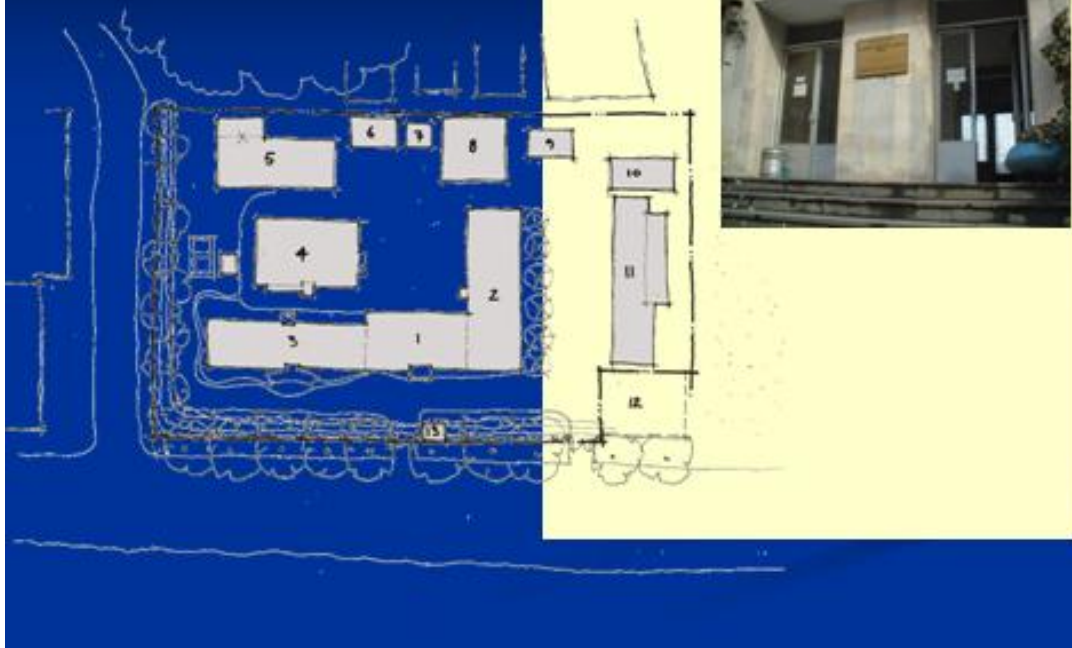
- Improved disease surveillance infrastructure and capabilities with state of the art technology
- A sustainable disease surveillance system that will continue to benefit Georgia
- Reduced disease proliferation risk
- Increased biosecurity and biosafety at biological facilities

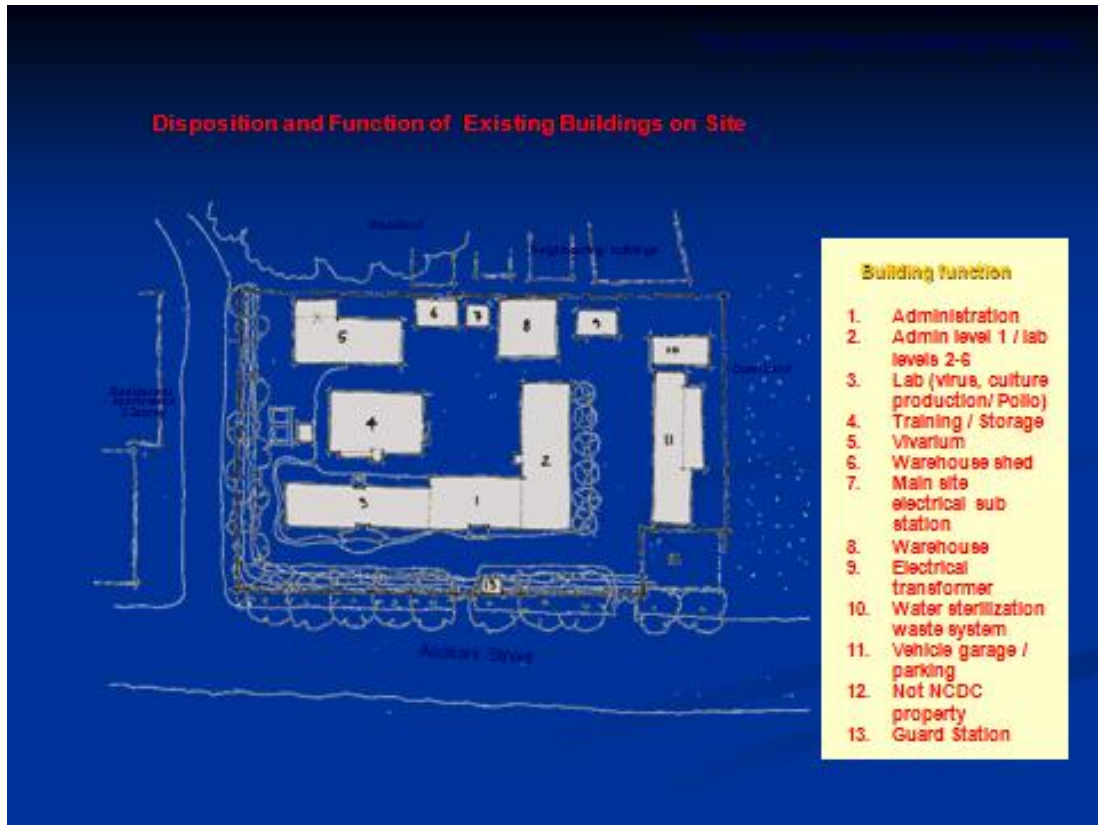
Georgia NCDC – Central Reference Laboratory & Repository

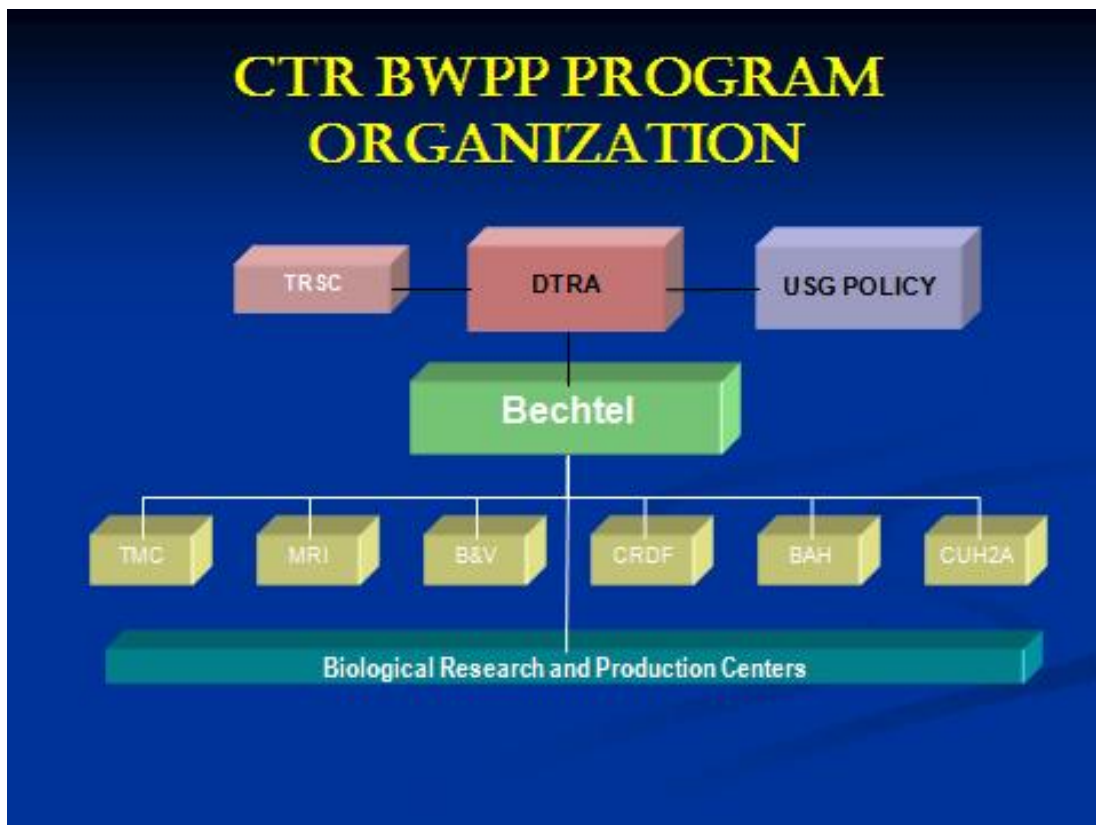
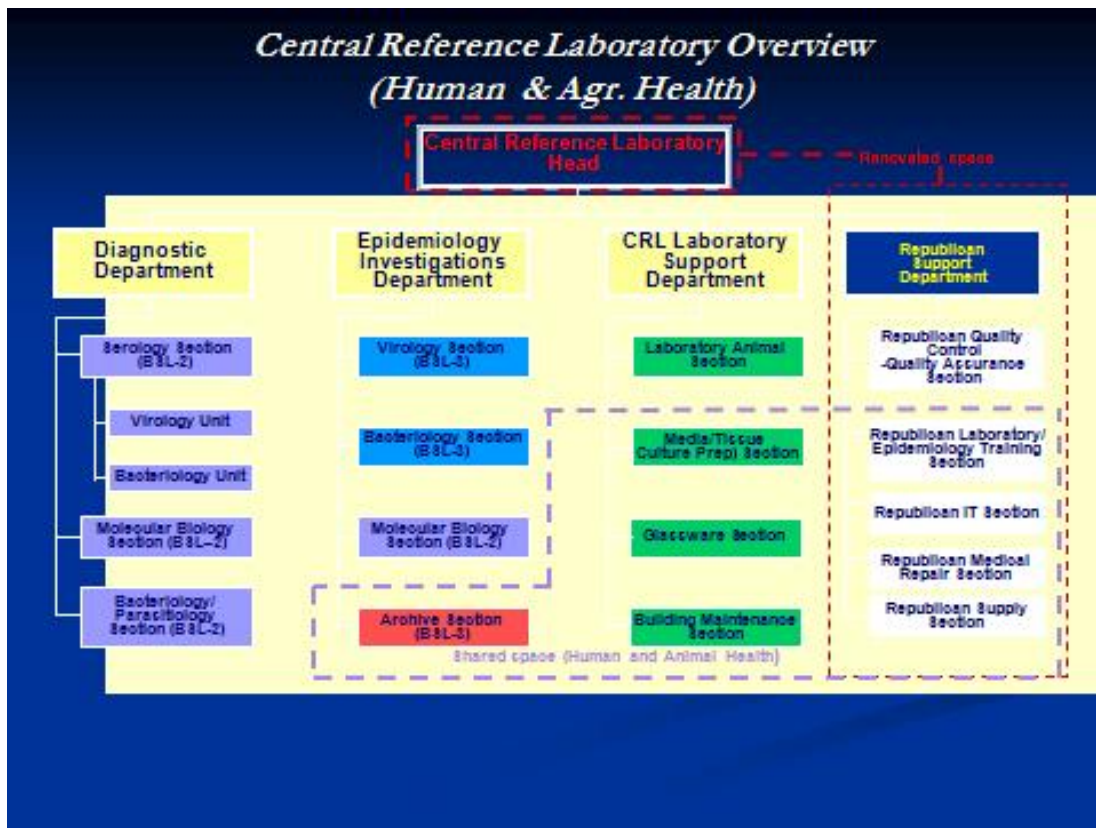


1

Site Opportunities & Constraints Overview

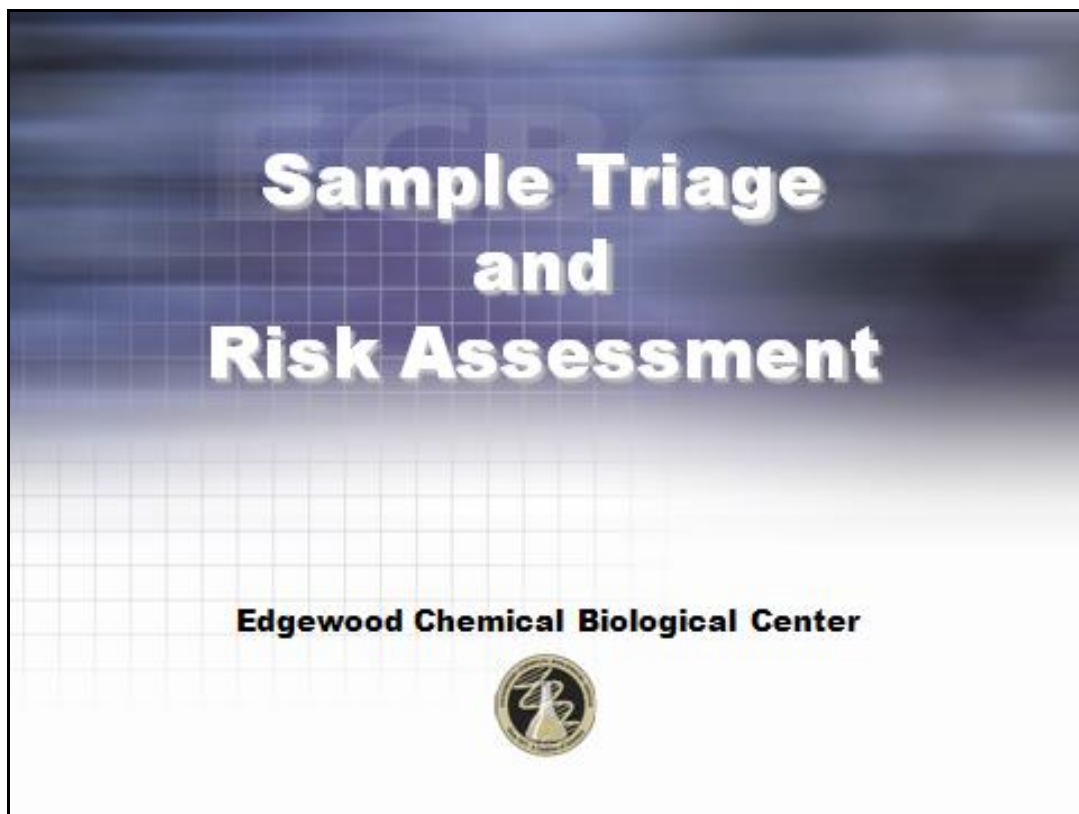








C.1.2 USA Presentation – by Raymond Mastnjak



“Unknowns” Triage Strategy

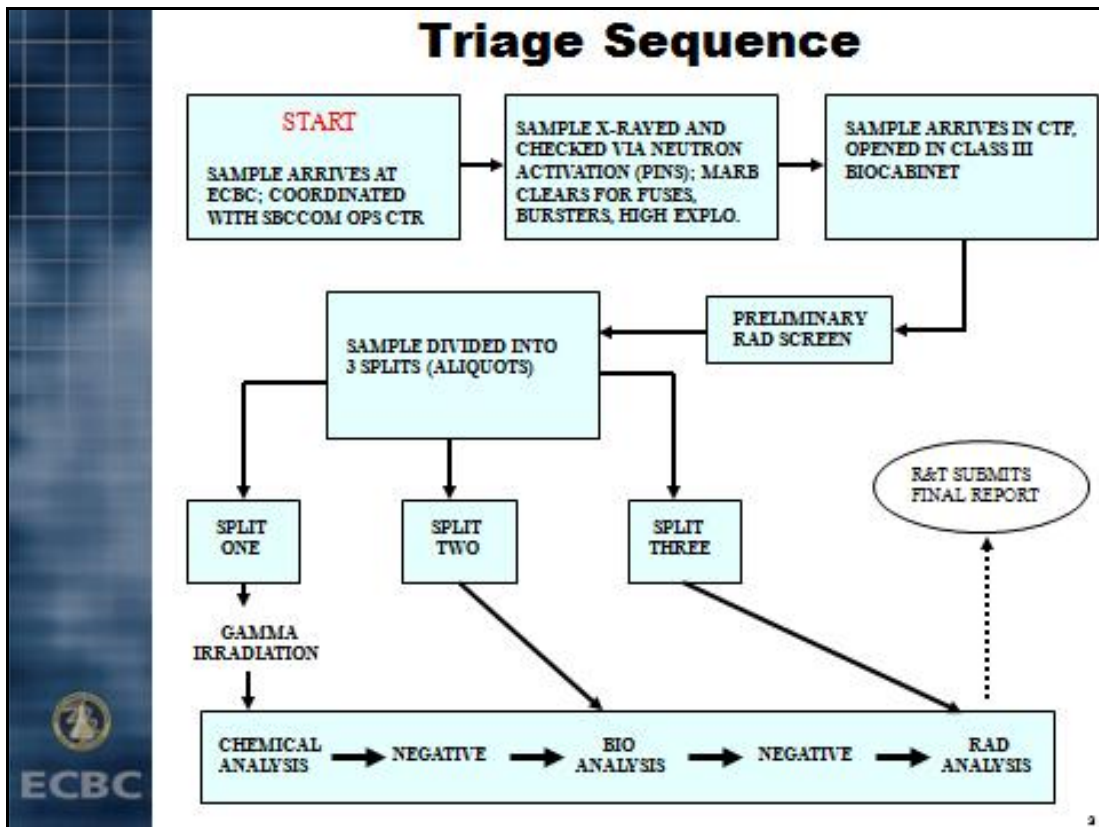
- Each Sample is Unique: Cookbook Protocols Do Not Work
- Key to Success: Desktop Risk Assessments
 - ✓ Must Include Experienced Chemists, Biologists, and Risk Management Personnel
 - ✓ Review All Available Data
- Special Concerns
 - ✓ Explosively Configured Devices / Munitions
 - ✓ Mixed Hazards (Dirty Bombs, etc)
 - ✓ Pressurized Containers
 - ✓ Protect Chemists from Biologicals, etc.







2



Special Requirements

- **Personnel:**
 - ✓ Chemists Experienced with Chemical Weapons / Related Compounds
 - ✓ Biologists Experienced with Bio Weapons / Select Agents / Toxins
 - ✓ Reliability Program (Chemical Surety / Biological Surety)
 - ✓ Vaccinations
 - ✓ Baseline Cholinesterase / Periodic Testing
- **Equipment:**
 - ✓ Class III Biosafety Cabinet
 - ✓ Remote Drilling Capability
 - ✓ Gamma Irradiator (26,000 Curie)
 - ✓ High Throughput Bio Screening (Robotics)
- **Infrastructure:**
 - ✓ Security Hardware and Guards 24 / 7
 - ✓ CW / BW Trained First Responders
 - ✓ Proficiency Testing Using Real Agents
 - ✓ Detoxification and Processing of Waste Products







4

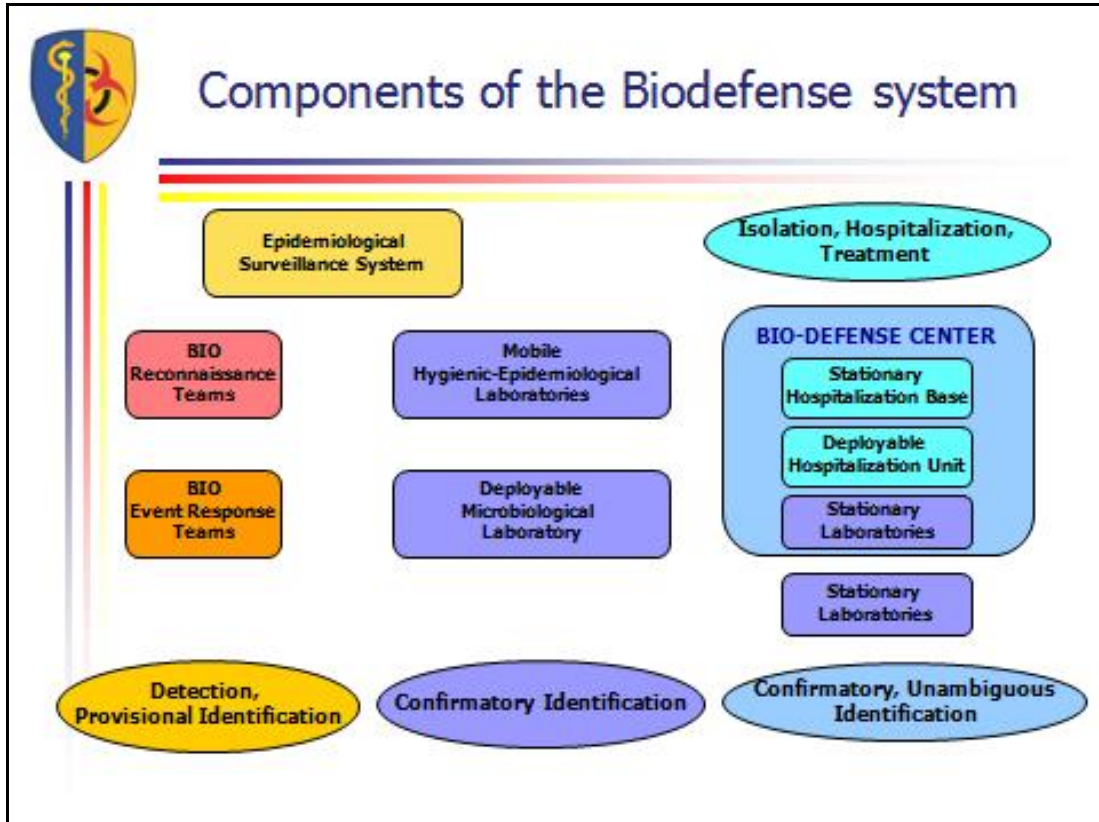
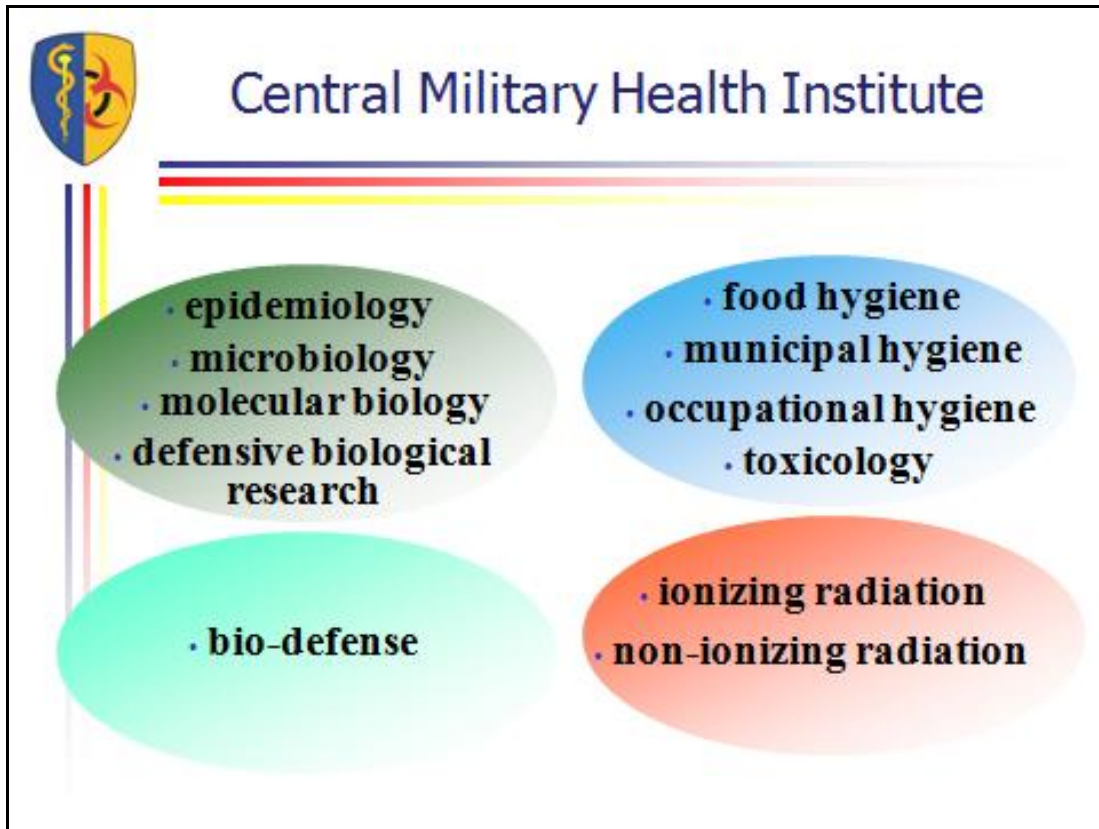
C.2 HFM-177 MEETING: 6-8 OCTOBER 2011, MUNICH, GERMANY

C.2.1 The Czech Republic Mobile Lab Presentation – by Libor Pisa



Deployable Biological Laboratory of the Armed Forces of the Czech Republic

LTC Libor Píša, M.D.
Central Military Health Institute






Biological Event Response Team




Mobile Hygienic and Epidemiological Laboratory






Deployable Biological Laboratory




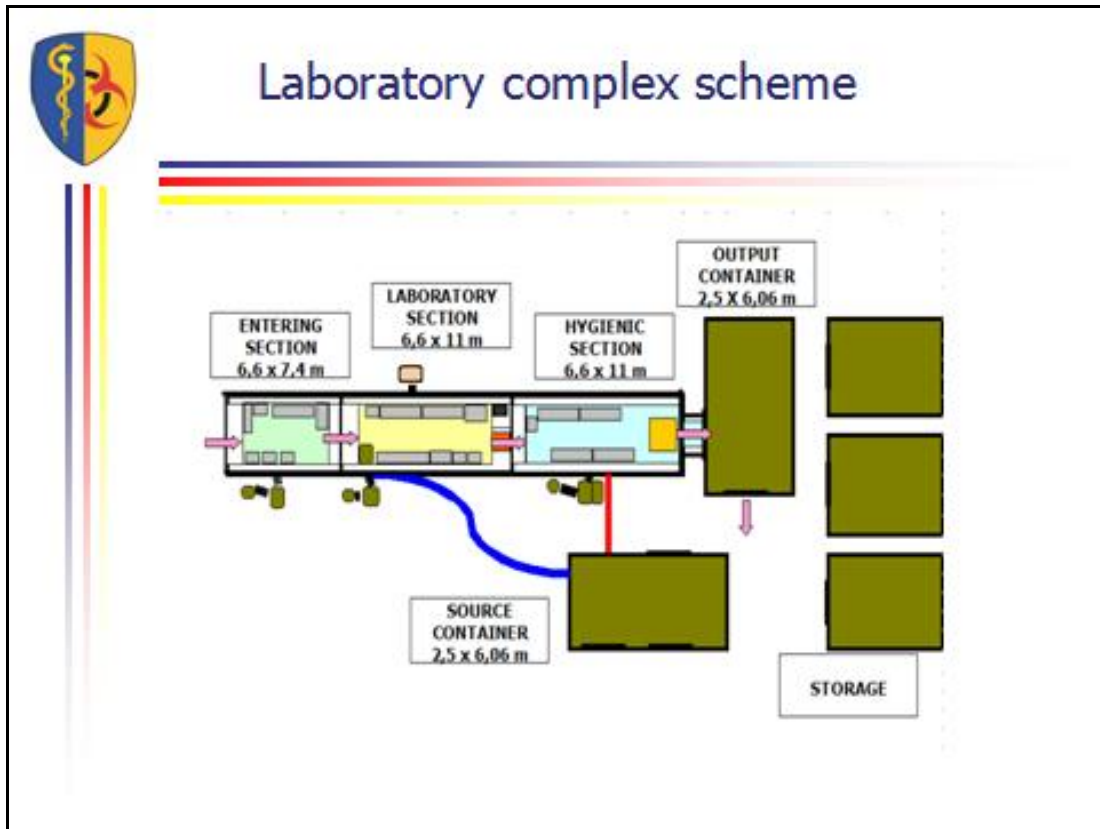
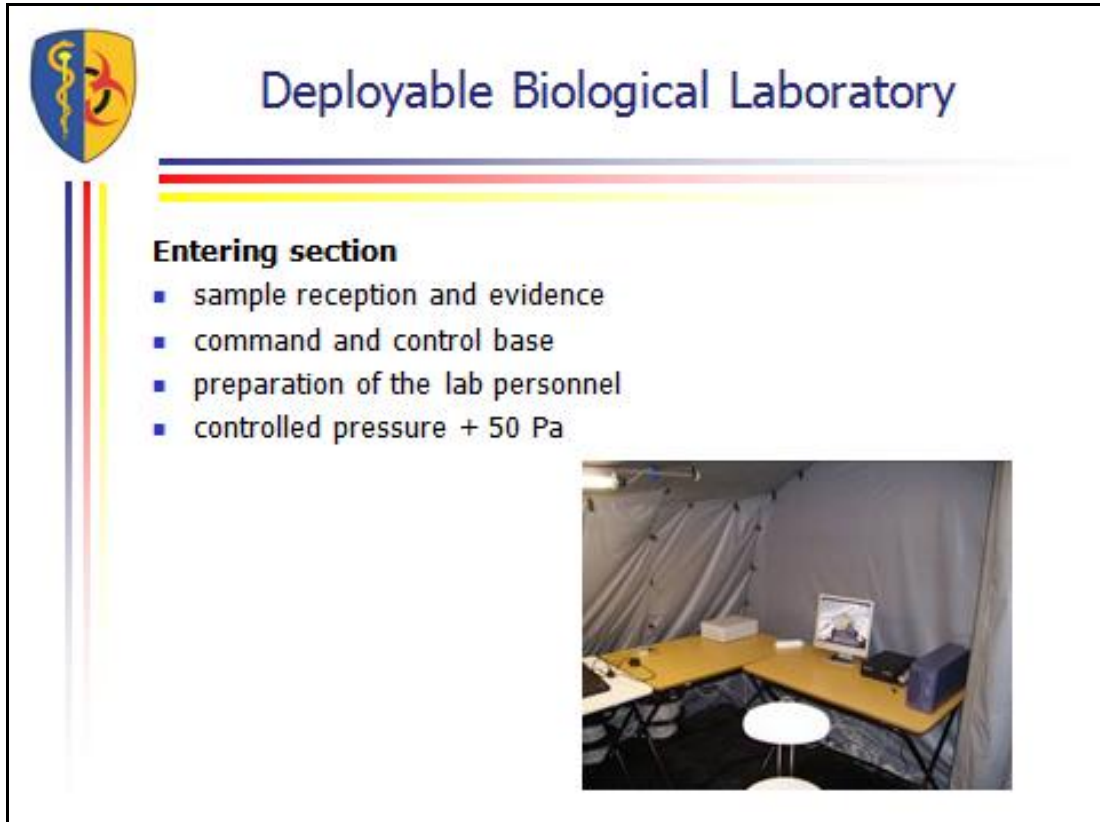
STANAG 4632
 Deployable NBC Analytical Laboratory



Deployable Biological Laboratory

- transportable by road, rail, air and ship
- required area for deployment: 50 x 25 meters
- preparatory time for examination: 72 hours
- three tents connected through tunnels
- operating without replenishment of consumables for 5 days
- own source of electricity and pressurized clean air but depends on the other logistic support
- interior is formed by three separate chambers ColPro




Deployable Biological Laboratory

Entering section

- sample reception and evidence
- command and control base
- preparation of the lab personnel
- controlled pressure + 50 Pa



The photograph shows the interior of a deployable biological laboratory. It features a yellow desk with a computer monitor, a keyboard, and other equipment. The room is enclosed by white fabric walls, and a white stool is visible in the foreground.



Deployable Biological Laboratory

Laboratory section

- identification of biological agents carried out according to authorized methods and SOP
- good and safe laboratory practices
- designed for at least 2 up to 4 workers
- lab security system provides an effective protection of the staff against the infection and against escape of pathogens to the outside



Deployable Biological Laboratory

Laboratory section - Bio Safety Precautions

- closed space of the lab section and transit of personnel only through chambers with air-locks
- monitoring of the lab work using camera system
- controlled under pressure -50 Pa
- filter ventilation units with NBC filter
- split air conditioning system with closed air circulation
- protective over pressurized suits with the clean air supply
- biohazard safety cabinet
- sterilizer of liquid waste (autoclave) and portable sterilizers of solid waste
- UV sterilizers of inner space




Deployable Biological Laboratory

Hygienic section

- decontamination of the workers
- waste water flows to the collector and to the sterilizer in autoclave
- drying of protective suits
- controlled over pressure +50 Pa







Deployable Biological Laboratory

„Source“ container

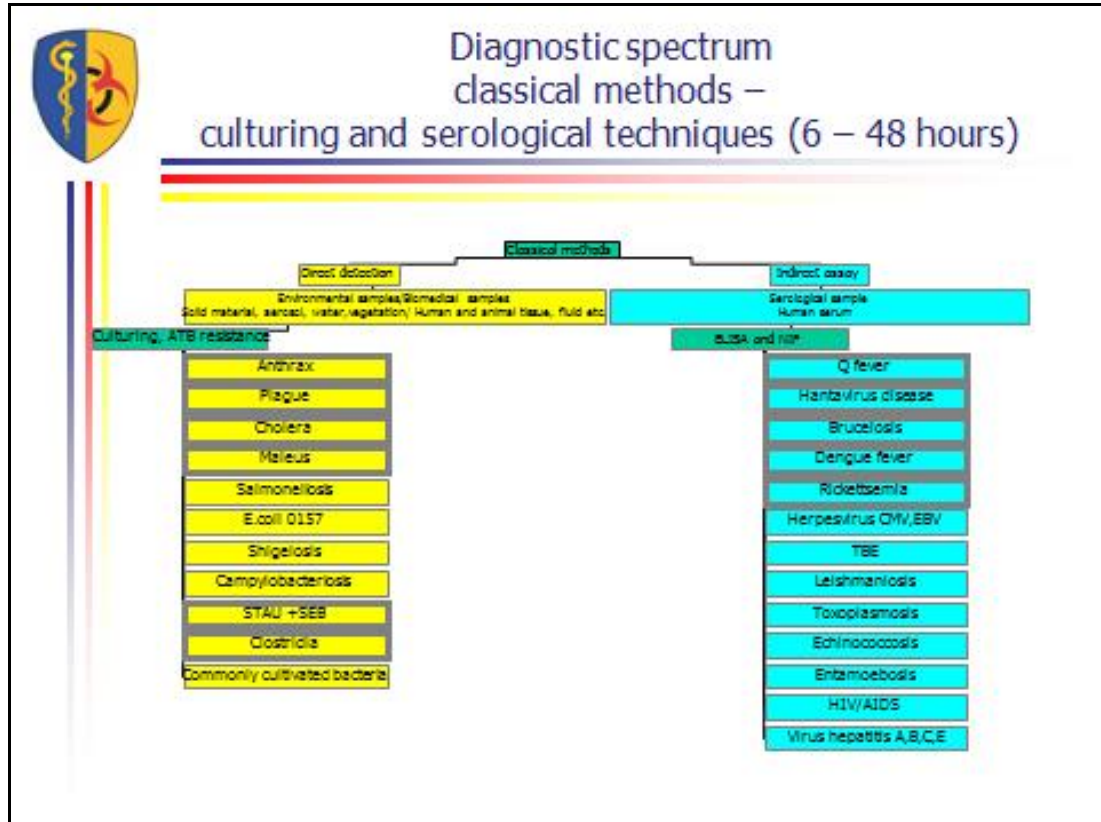
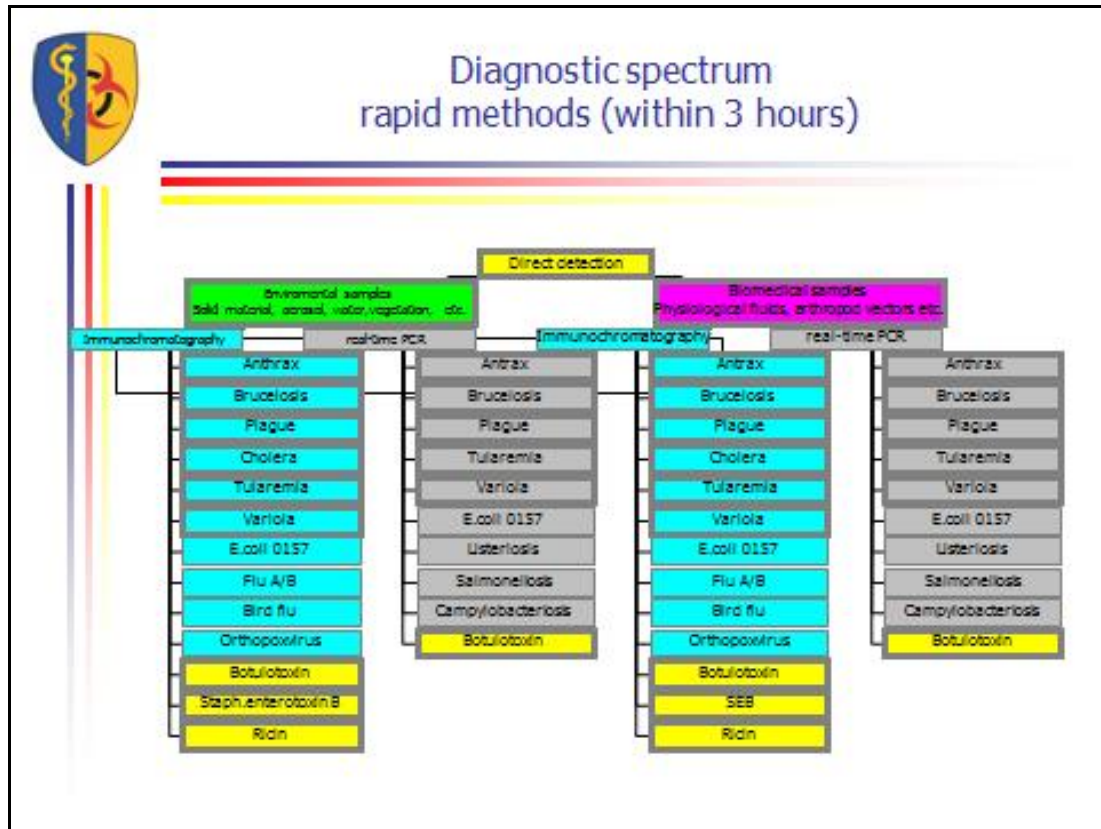
- electricity generator 60 kW
- fuel tank
- compressor





Deployable Biological Laboratory

	Post	Number
1.	Commander	1
2.	Medical/biological experts (microbiologist, epidemiologist, veterinarian, doctor of natural sciences)	4
3.	Laboratory technician	3
4.	Engineer	4
Total		12





Participation of the mobile components in NRF, NATO mission and summits

NRF and NATO missions:

- Enduring Freedom (Kuwait, Iraq) - 2002-2003
- NRF 3 – Mn. CBRN Bn. – 2004
- NRF 8 – Mn. CBRN Bn. – 2007
- NRF 12 – Mn. CBRN Bn. – 2009
- NRF 17/18 – Mn. CBRN Bn. - 2011-2012
- ISAF (Afghanistan) – since 2009

CBRN Defense support of summits:

- Summit NATO in the Czech Republic – 2002
- Summit of states of Latin America, Caribbean states and European Union – Peru, 2008
- Summit of Ministers of Foreign Affairs of NATO countries – Estonia, 2010



Thank you for your attention



C.2.2 Germany Mobile Lab Presentation – by Roman Wölfel

The Bundeswehr Rapidly Deployable Biolab

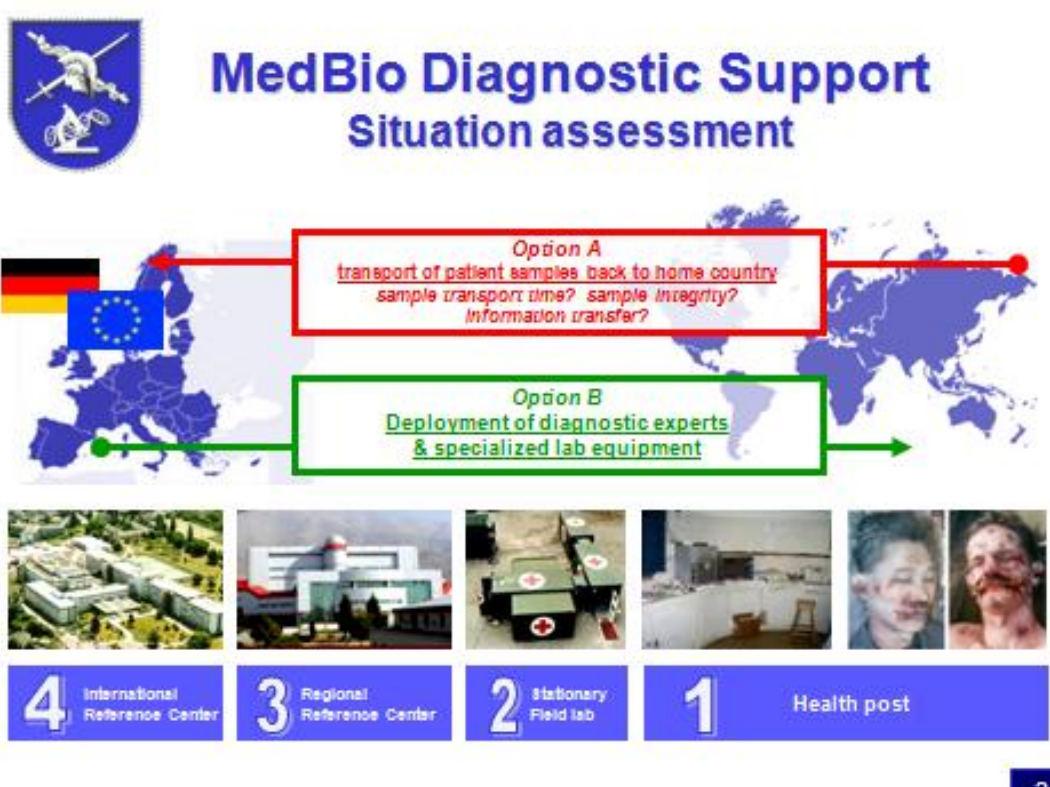
Microbiological High-Tech Diagnostics for Outbreak Investigations Abroad

Lieutenant-Colonel MC
Dr. med. Roman Wölfel
MD DTMH

Bundeswehr Institute of Microbiology
Department for Medical Bio Reconnaissance & Verification
Munich - Germany

Views expressed in this presentation are those of the author and do not necessarily reflect an official position of the German Ministry of Defence

MedBio Diagnostic Support Situation assessment



Option A
transport of patient samples back to home country
sample transport time? sample integrity?
information transfer?

Option B
Deployment of diagnostic experts
& specialized lab equipment

4 International Reference Center

3 Regional Reference Center

2 Stationary Field lab

1 Health post


2



Container-based Laboratory



3



Modular Operations Concept

4



Mission-tailoring

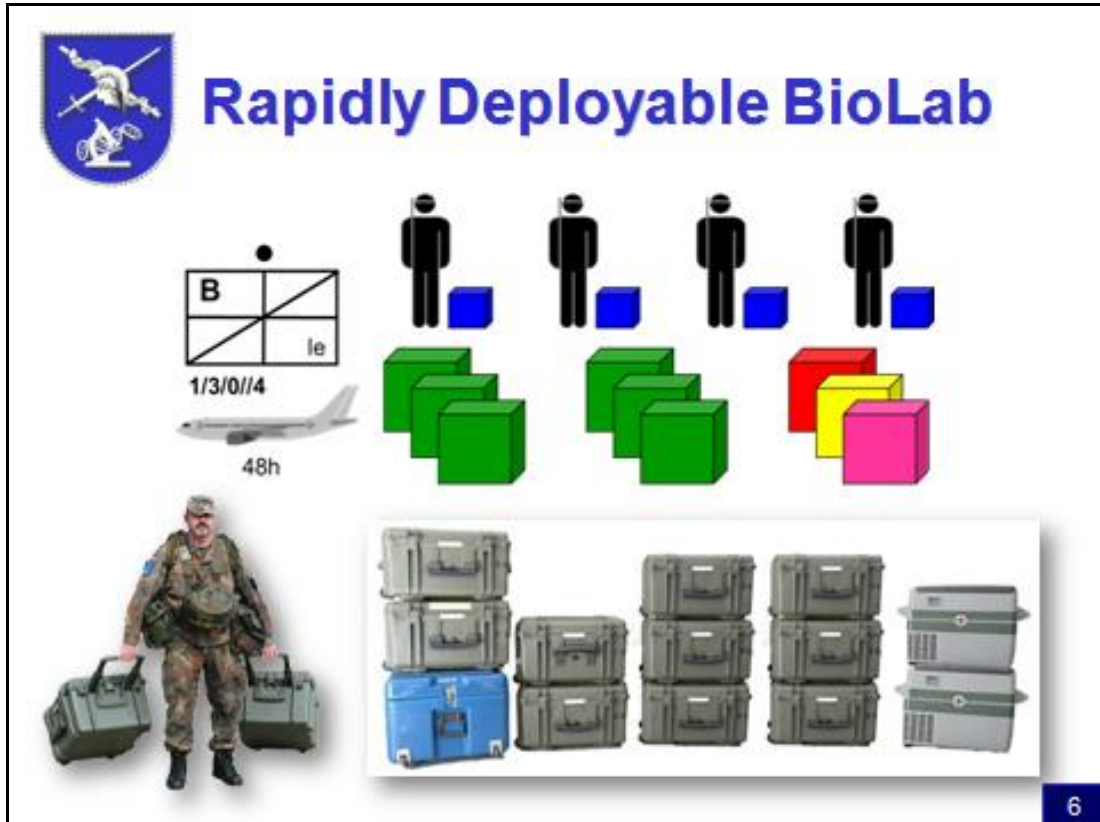
Equipment

- Personal protective equipment
- MedBio sampling
- Ultra-low-temperature transport
- Rapidly deployable BioLab
- Autonomus power supply
- Inflatable Biolab environment
- Vector I (rodents)
- Vector II (ticks & insects)

Mission requirements

- pathogen known/unknown
- available resources on-site
- need for sustainability
- transport resources
- available lead-time

5



Rapidly Deployable BioLab

B
le
1/3/0//4
48h

48h

6



Rapidly Deployable BioLab



7



Rapidly Deployable BioLab MECC Shelter



8



Rapidly Deployable BioLab Lab Setup



9



Rapidly Deployable BioLab Sample Acceptance



10




Rapidly Deployable BioLab


Inflatable BioLab Environment




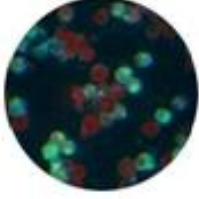
11




Rapidly Deployable BioLab

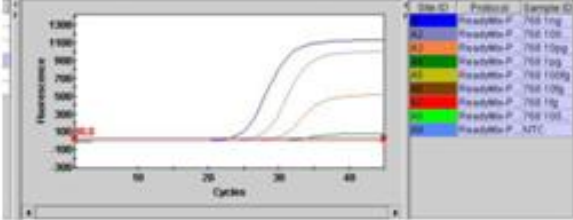








Site ID	Protocol	Sample ID	Sample Type	Notes
A1	ReadMe	760 1mg	Urn-H	
A2	ReadMe	760 100mg	Urn-H	
A3	ReadMe	760 100g	Urn-H	
A4	ReadMe	760 1g	Urn-H	
A5	ReadMe	760 100g	Urn-H	
A6	ReadMe	760 1g	Urn-H	
A8	ReadMe	760 100mg	Urn-H	
A9	ReadMe	NTC	Urn-H	



Site ID	Protocol	Sample ID
A1	ReadMe P	760 1mg
A2	ReadMe P	760 100
A3	ReadMe P	760 100g
A4	ReadMe P	760 1g
A5	ReadMe P	760 100g
A6	ReadMe P	760 1g
A8	ReadMe P	760 100
A9	ReadMe P	NTC

12



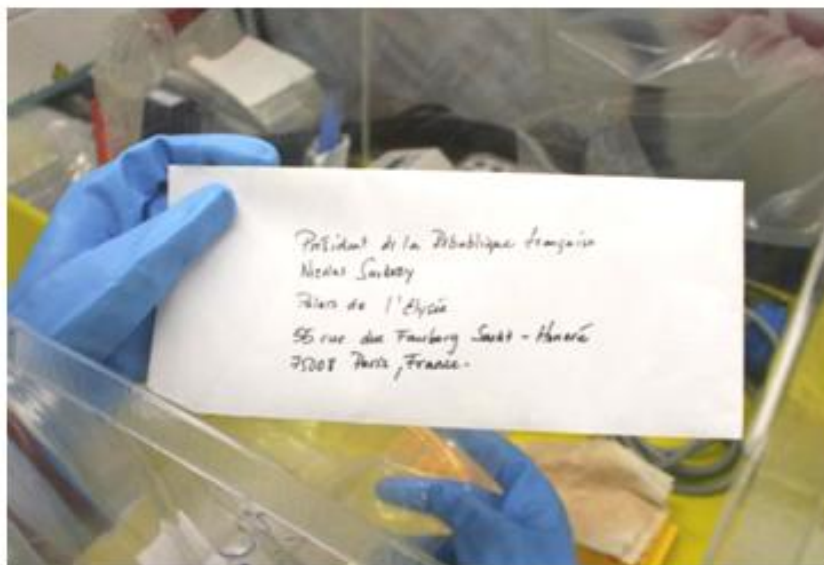
Rapidly Deployable BioLab Sample Preparation



13



Rapidly Deployable BioLab Sample Documentation





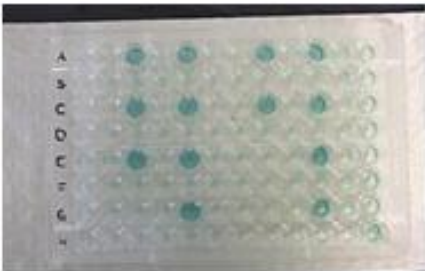


14

 **Rapidly Deployable BioLab
Sample Documentation**



15

 **Rapidly Deployable BioLab
Testing Methods**



16



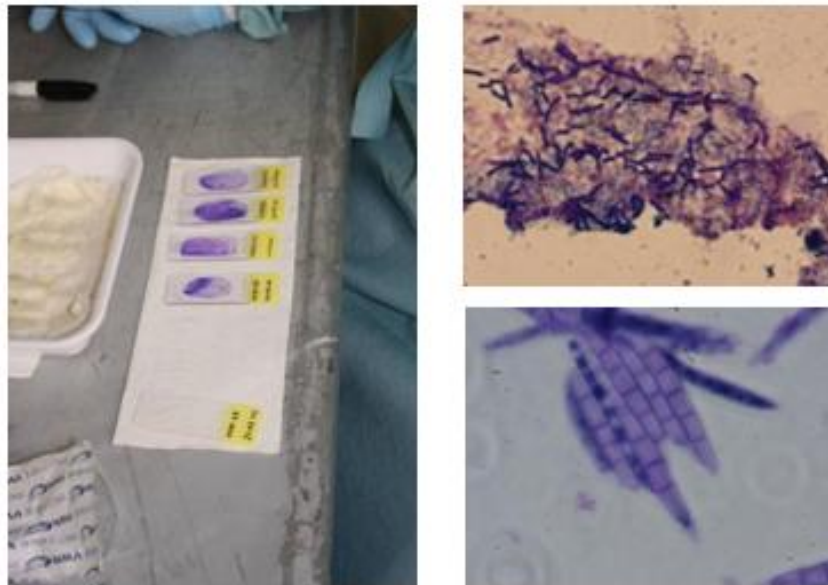
Rapidly Deployable BioLab Flash Gel Electrophoresis




17



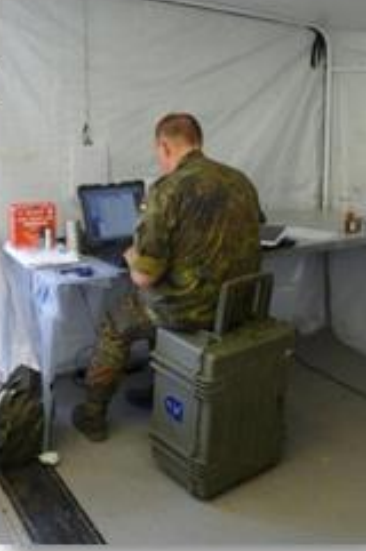
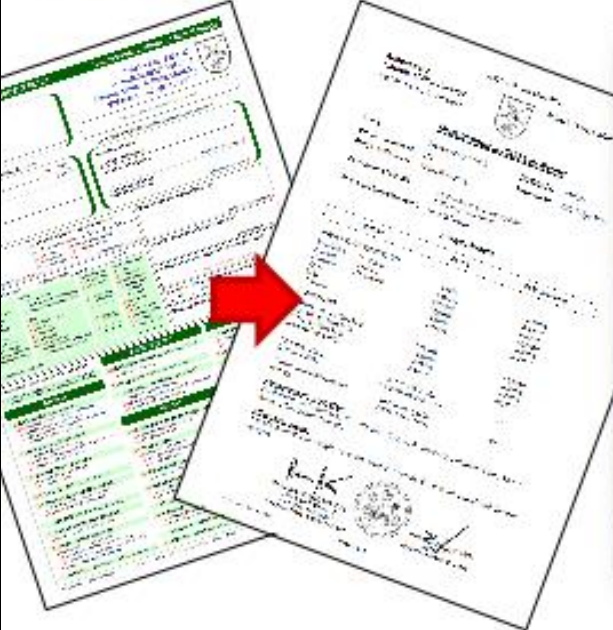
Rapidly Deployable BioLab Staining Methods



13



Rapidly Deployable BioLab Individual Lab Reports



19



NATO Mission Support Operations

Kosovo 2007 & 2008

20

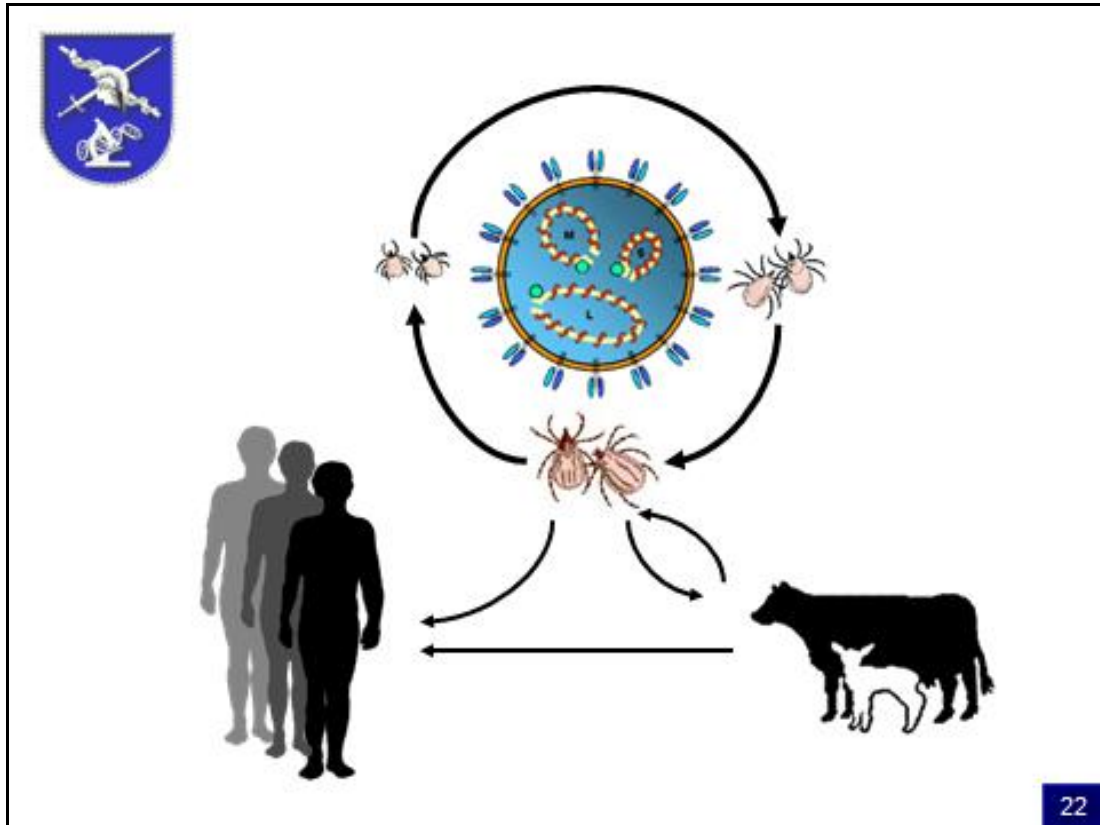


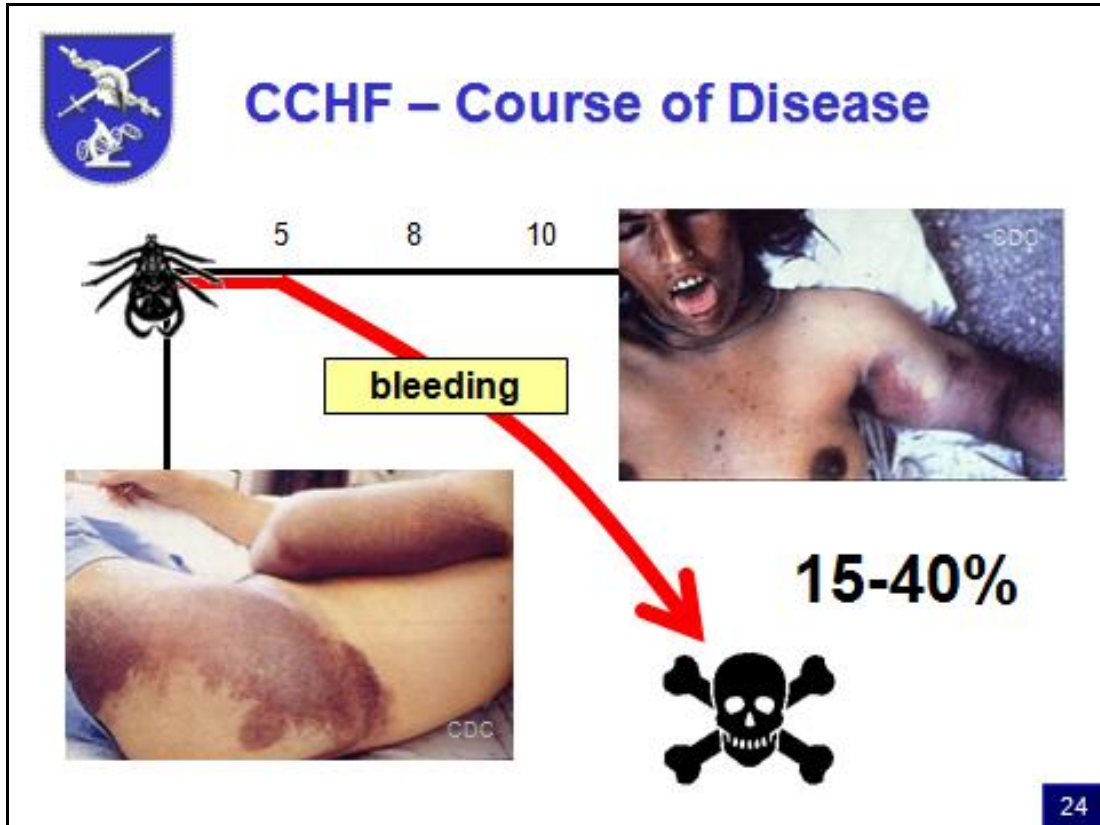
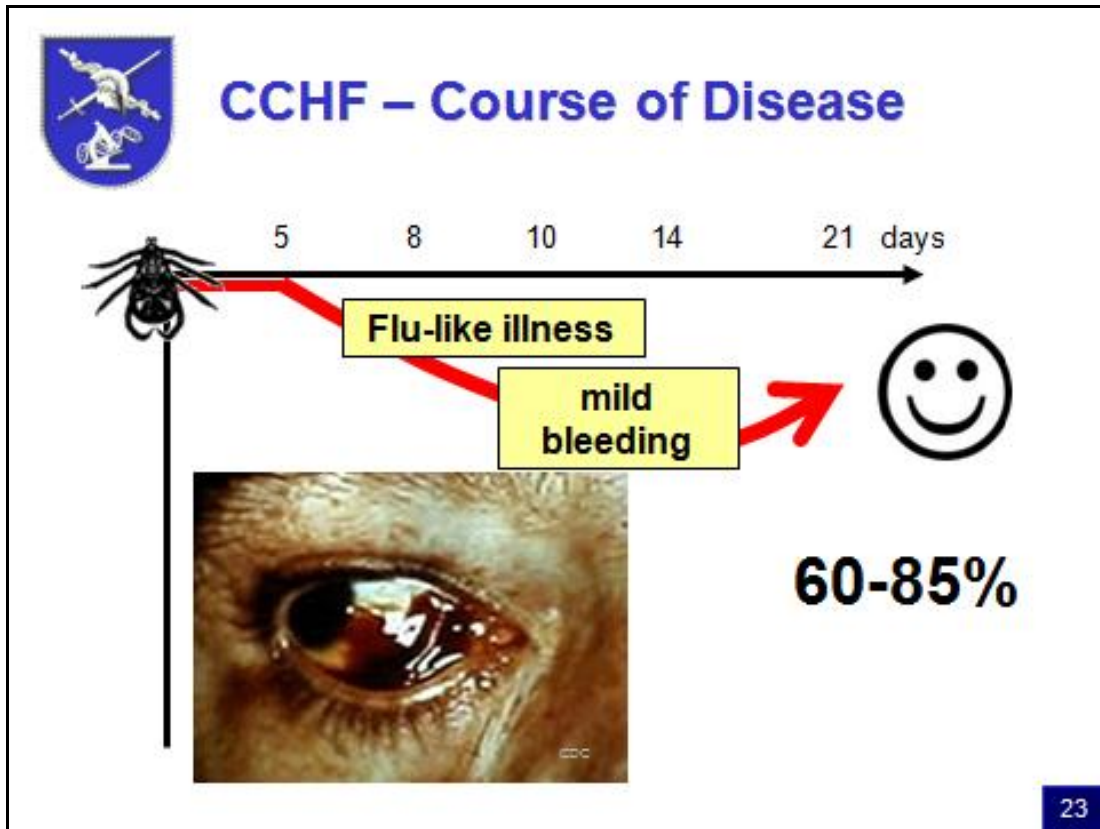
Bundeswehr missions worldwide



Crimean-Congo Hemorrhagic Fever

21







CCHF Diagnostics in Kosovo



25



CCHF Diagnostics in Kosovo



26



Epizootological survey




27













CCHF Diagnostics in Kosovo

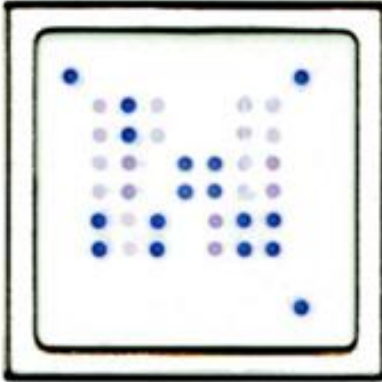


28



CCHF Diagnostics in Kosovo

 IbAr 10200	 ArD 39554
 ArB 604	 ArMg 951
 SPU 128/81	 UG 3010
 SPU 246/02	 SPU 9/00-5
 Baghdad-12, BT-958	 7803, 4348/02



KOSOVO

29



CCHF in Kosovo May 2008 & June 2009





30



Med. Biological Reconnaissance & Verification Key Skills & Capabilities

- mobilizes military medical expertise**
 - provides scientific advise and risk analysis**
 - collects infectiological and microbiological data**
 - conducts biomedical sampling**
 - provides deployable diagnostics**
 - improves safety and confidence**
- on-site
 - abroad
 - in the field
 - in an outbreak

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romanwoelfel@bundeswehr.org

Bundeswehr Institute of Microbiology
Department for Medical Biological
Reconnaissance & Verification
Munich – Germany

C.2.3 United States Lab Construction Presentation – by Raymond Mastnjak



Edgewood Chemical Biological Center



TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

**HFM-177: Construction of Deployable Laboratories
During Times of Reduced Funding**
29, 30 October 2011





**Construction of Deployable Laboratories
During Times of Reduced Funding**



- Safety/Health versus cost considerations.
- Use of CONEX type containers for mobile analytical platforms.
- Use of existing military vehicles for mobile analytical platforms .
- Dual use scenarios: Mobile laboratories as back up facilities to fixed site labs





TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

Safety/Health Versus Cost Considerations

- Design should be based on actual samples anticipated, avoid over-designing.
- Biological safety level 2 (BSL-2) containment should be sufficient for most scenarios.
- Consider contributing factors such as level of screening before samples come to the deployable laboratory.
- If true unknowns are anticipated, start with a Class III biological safety cabinet or consider 100% exhaust Class II, Type B cabinet.
- Consider higher level of personal protective equipment for scenarios exceeding BSL-2.
- Consider separate portable shower out facility for scenarios exceeding BSL-2.
- Keep sample size to smallest amount needed for each assay (PCR / ECL, etc).

TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.




Use of CONEX Type Containers for Mobile Analytical Platforms.

- Standard shipping containers can be used for many deployable laboratory situations.
- Containers can be handled at any marine port or airfield/airport and can easily be shipped by rail or road.
- Containers can include slide outs to accommodate larger work areas.
- Containers can be fitted with temporary wheel sets for deployment to military theatres of operation.





TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

U.S. ARMY RDECOM **Use of CONEX Type Containers for Mobile Analytical Platforms.**



TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

U.S. ARMY RDECOM **Use of CONEX Type Containers for Mobile Analytical Platforms.**



TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

Use of Existing Military Vehicles for Mobile Analytical Platforms

- Use of existing fleet of military trucks, containers, trailers and generators can save considerable funds.
- Design should include hardened shipping containers for analytical instrumentation.
- Integration of analytical equipment can be challenging.
- Requires ongoing training for military field technicians.
- Reachback to civilian scientists / engineers is vital.




TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

Use of Existing Military Vehicles for Mobile Analytical Platforms





GAS —
POWER —
HVAC —
FUEL —



TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

U.S. ARMY RDECOM **Dual Use Scenarios: Mobile Laboratories As Back Up Facilities to Fixed Site Labs**

- Popular choice for decision makers. A solution to the complaint that deployable labs are used infrequently.
- A deployable BSL-2 laboratory parked near a fixed facility can be used for routine sample analysis; then transported quickly to an incident site.
- A deployable lab can be used when the fixed site laboratory is undergoing maintenance /fumigation.
- Requires safety/health approval for dual use.
- Keeps the deployable laboratory in a constant state of readiness.

TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

C.2.4 United States Sample Triage Presentation – by Raymond Mastnjak

US ARMY RDECOM

Edgewood Chemical Biological Center



TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

HFM-177: The Role of Triage in Sample Analysis
29, 30 October 2011



The Role of Triage in Sample Analysis



- Rapid risk assessment for theatre commanders / first responders.
- Sample flow in a deployable laboratory.
- Special circumstances.
- Using a triage plan to develop a deployable laboratory design.





TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.



Rapid Risk Assessment for Theatre Commanders / First Responders



- What is a rapid risk assessment?
- Rapid risk assessments should include experienced chemists, biologists and risk management personnel.
- The assessment should consider field screening, intelligence reports, experience of operators, engineering controls, etc.
- The assessment should sequentially notify each person in the analysis chain of actions completed and hazards.
- Special concerns include:
 - Protecting personnel from hazards they are not familiar with (such as biologists working with samples contaminated with highly toxic chemicals).
 - Explosively configured devices / samples with energetic material.
 - Mixed hazards (dirty bomb scenario).
 - Pressurized containers.
 - Regulatory requirements for field operations.










TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

U.S. ARMY RDECOM Sample Flow in a Deployable Laboratory




- Field screening: What is known about the sample before it comes to the deployable lab?
- Is a pass through needed? Is there a need for a sterilization station using vaporous hydrogen peroxide or 5% Sodium hypochlorite?
- Can the sample container fit the opening of the pass through or the Class III biological safety cabinet?
- Balance the safety benefits of a Class III biological safety cabinet against the difficulties of sample manipulation.
- Will a sample aliquot be transferred to a Class II biological safety cabinet?
- Movement of samples to cell culture (incubator) or to analytical equipment (PCR, ECL, sample prep robotics).
- Limitations of a deployable laboratory.

TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

U.S. ARMY RDECOM Special Circumstances

- Samples requiring invasive techniques.
- Use of portable X-ray devices, neutron activation devices and other special equipment for field screening.
- Gamma irradiation of "true" unknowns.
- Use of ancillary structures such as negative pressure tents to augment the deployable laboratory.

TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.



Using a Triage Plan to Develop a Deployable Laboratory Design



- From the triage plan, determine minimum engineering controls needed.
- Determine if analytical instruments need to be in engineering controls.
- Determine if majority of operations can be performed at Biological Safety Level 2 / Risk Group 2.
- Determine if ancillary equipment can be used for Biological safety Level 3 / risk Group 3 scenarios (PAPR respirators / portable shower out facility).
- Determine if field screening can identify other potential hazards such as toxic chemicals, radionuclides and energetic materials.





TECHNOLOGY DRIVEN. WARFIGHTER FOCUSED.

C.2.5 Israel Nano-Technology – by Robert S. Marks

Robert S. Marks

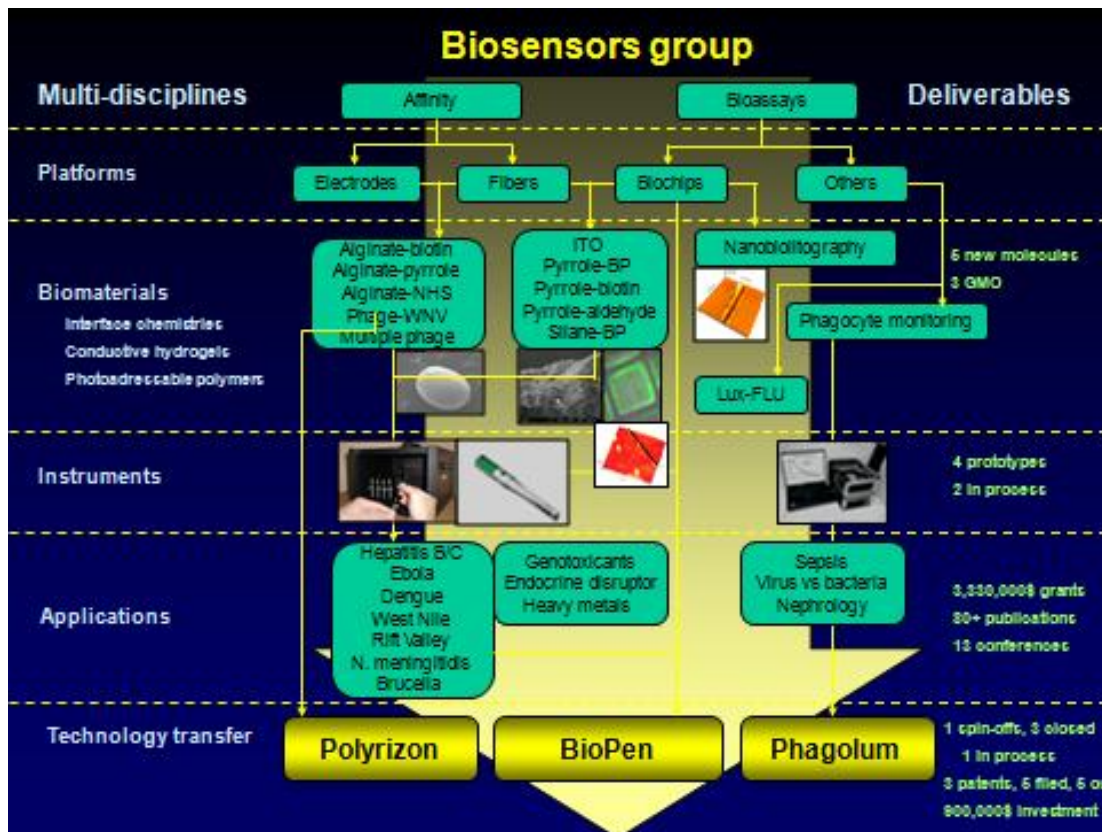
Department of Biotechnology Engineering
 &
 National Institute for Biotechnology in the Negev
 &
 Ilse Kats Institute for Meso and Nano science
 @
 The Ben-Gurion University of the Negev

Adjunct



Nanyang Technological University

University of Maryland



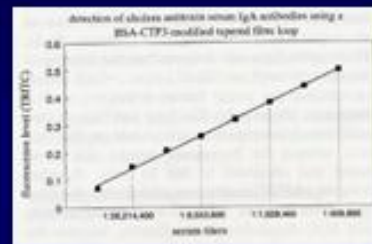
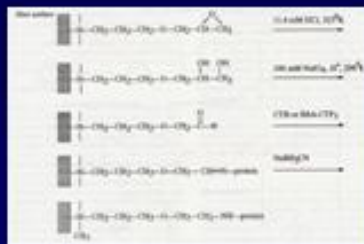
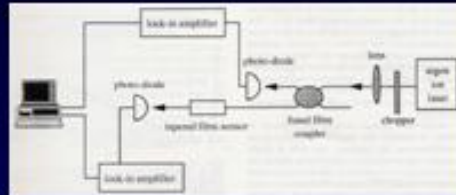
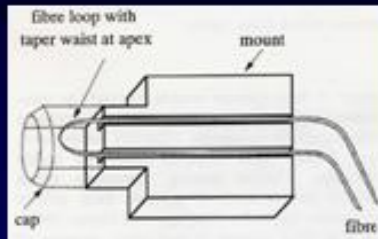
Fluorescence

DOCTOR FUN

Mighty Small Dots

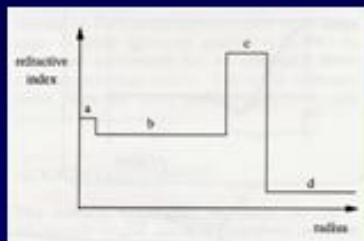
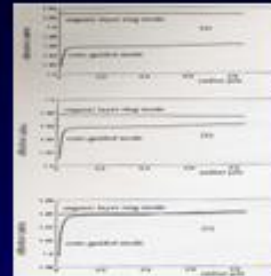
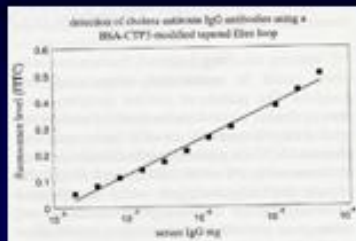
Single-mode tapered optical fiber loop immunosensor. II. Assay of cholera antitoxin

Marks, R.S., Z.M. Hale, M.M. Levine, C.R. Lowe and F.P. Payne (1994). *SPIE*. 2131: 495-503

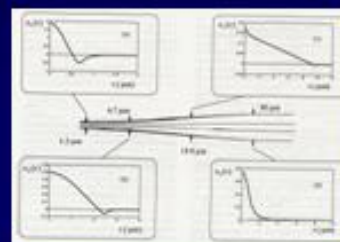


The single mode tapered optical fibre loop immunosensor

Hale, Z.M., F.P. Payne, R.S. Marks, M.M. Levine, C.R. Lowe (1996). *Biosensors and Bioelectronics*. 11: 137-148

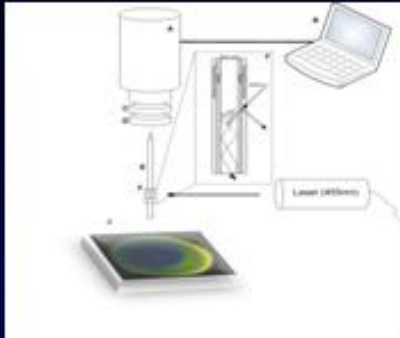


[a] core (1.469); [b] clad (1.458); [c] organic layer (1.6 est.); [d] buffer (1.32)

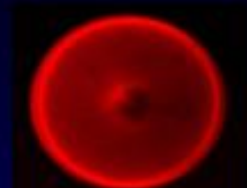


Metal-enhanced fluorescence on fibers

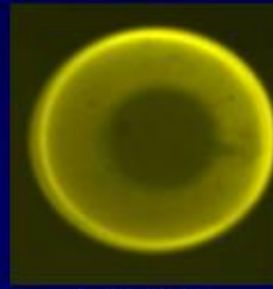
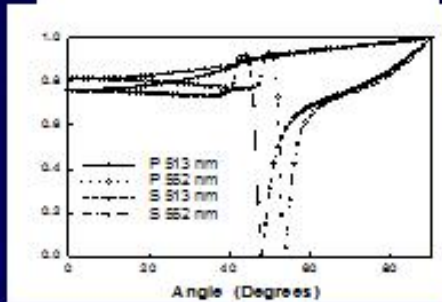
Daria Prilutsky, Evgeni Eltzov, Robert S. Marks, Leslie Lobel and Chris D. Geddes 2009
in prep



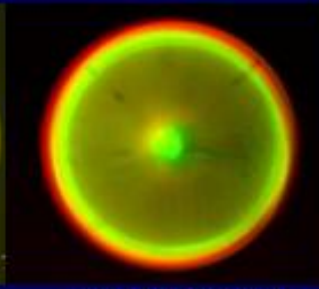
FITC non-silvered fiber,
500 nm LP filter.



Rhodamine 6G non-silvered
fiber, 700 nm LP filter

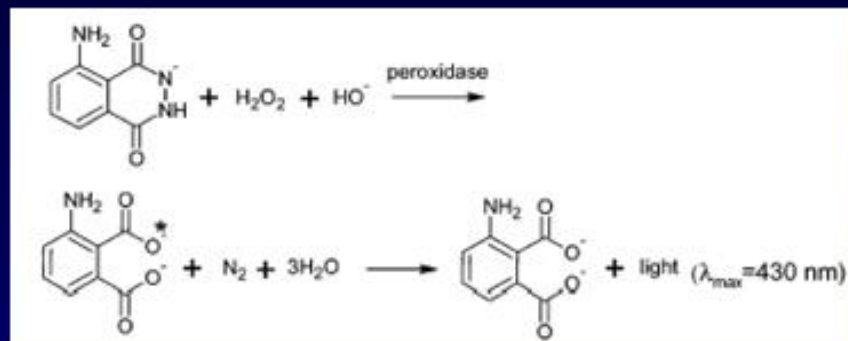


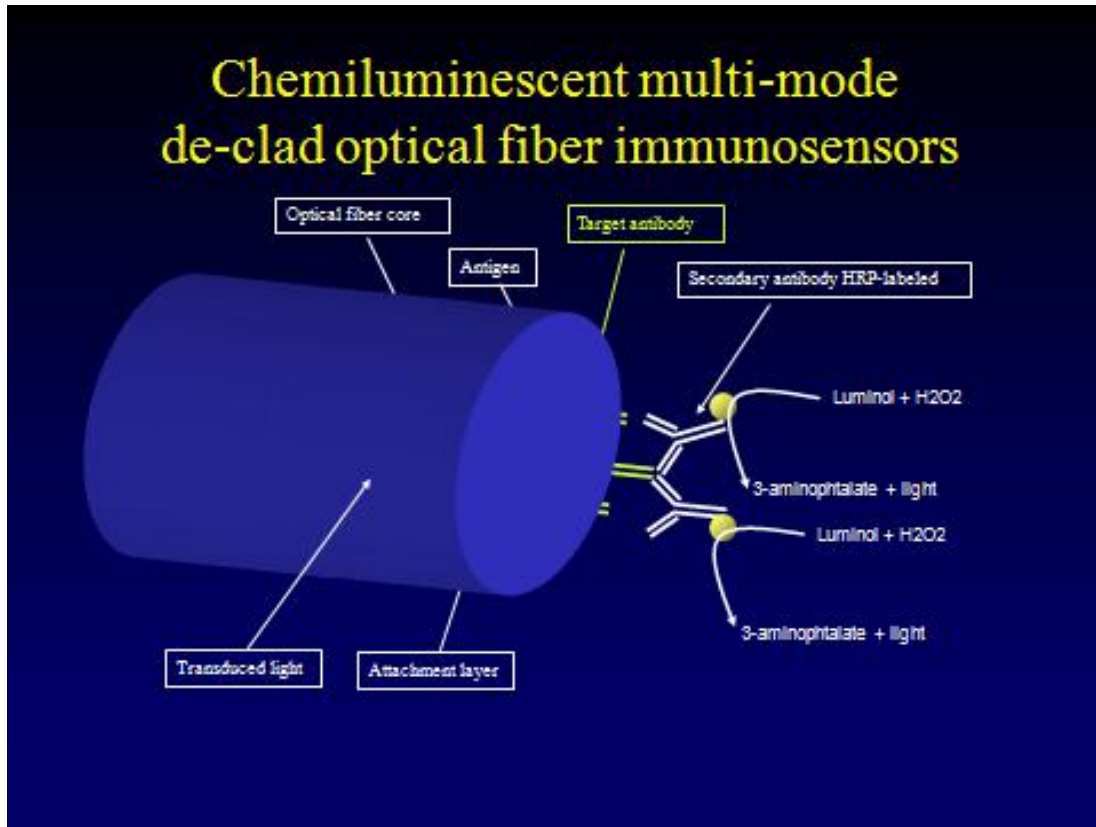
Rhodamine
non-silvered fiber, 500 nm
and 700 nm LP filters



Rhodamine 6G on
silvered fiber, 500 nm
and 700 nm LP filters

Chemiluminescence





Chemiluminescent optical fiber immunosensor for detecting cholera antitoxin

Marks, R.S., E. Basis, A. Bychenko and M.M. Levine (1997). *Optical Engineering*, 36 (12) 3258-3264

Chemical synthesis steps:

- Step 1: $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-CH}_2$ (11.8 mM HCl, 10%)
- Step 2: $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-CH}_2$ (OH) (500 mM NaOH, 80%, 200°C)
- Step 3: $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CHO}$ (CTB or BSA-CTP)
- Step 4: $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CHO}$ (NH₂CH₃)
- Step 5: $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-NH}_2$ (NH₂CH₃)

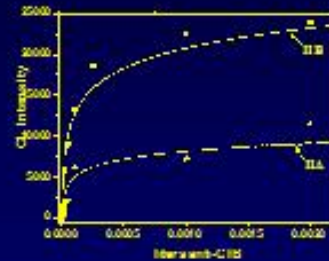
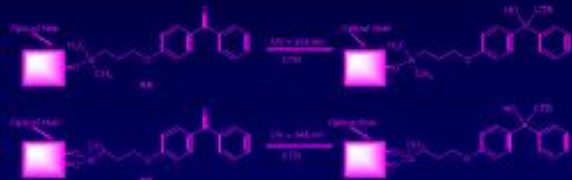
Antibody structure:

- Heat-labile enterotoxin (LT) and cholera toxin (CT)
- CTB or BSA-CTP
- CTP3: 50-64

[a] buffer; [b] air

Silane-benzophenone for photochemical attachment of bio-Molecules

Leshem, B., G. Sarfati, A. Novoa, I. Breslav and R.S. Marks (2004) Photochemical attachment of biomolecules onto fiber-optics for construction of a chemiluminescence immunosensor. *Luminescence*, 19: 69-77

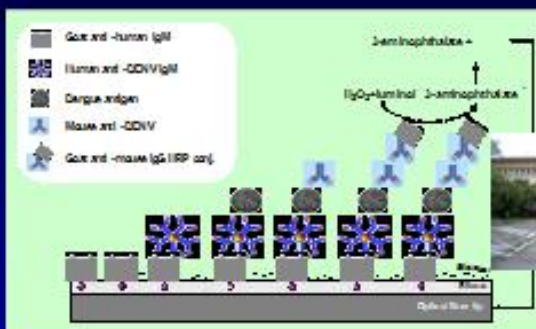


Increased bio-receptor coverage with 4-(3'-dichloromethylsilyl)propyl-oxybenzophenone

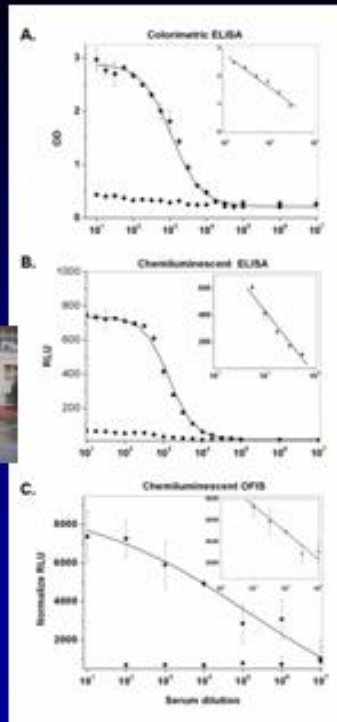


French Guiana dengue 1, 2, 3 virus immunosensor

Danit Atias, Yaël Lieber, Vered Chalifa-Caspid, Laetitia Brémand, Leïla Lobela, Robert S. Marks, Philippe Dussart *Sensors & Actuators* 2009 in press



OFIS: lower detection limit: 100 x MacELISA, 10 x CL-ELISA; correlations between methods over 0.97
OFIS Specificity (87.0%) & Sensitivity (98.1%)
CL MAC ELISA Specificity (95.6%) & Sensitivity (100%)



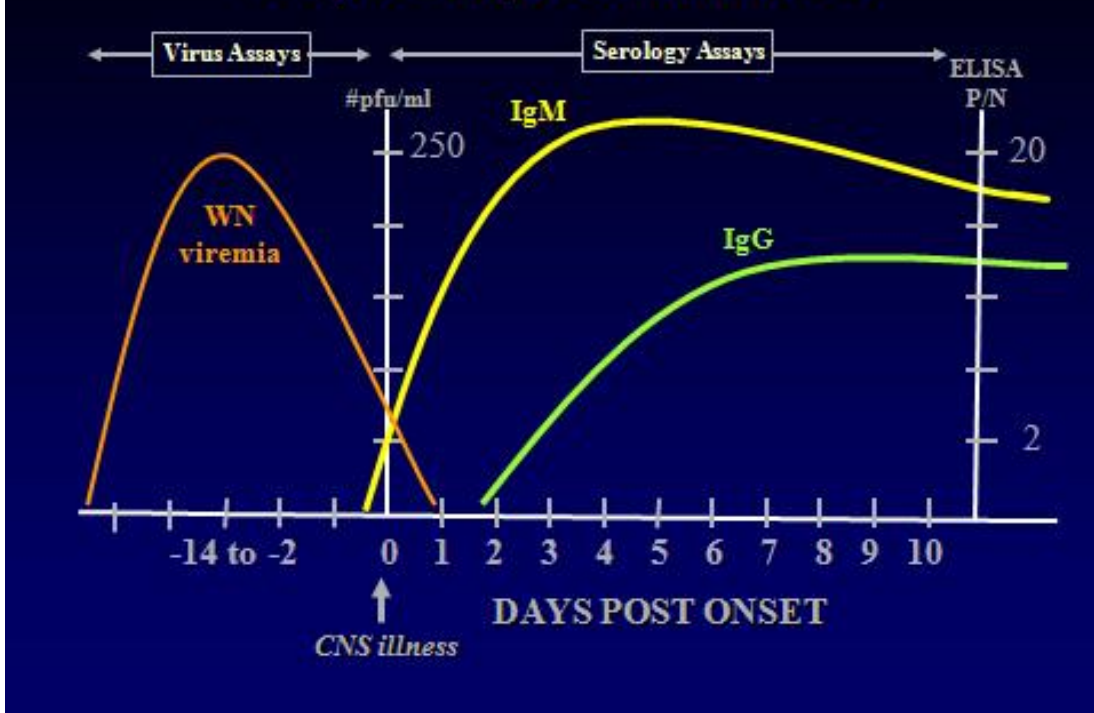
Limits of actual diagnostic assays

	Focus technology				Luminex		Biomerieux		M. A. S.	
Name	ELISA	PRNT	IFA	Microsphere	NASBA	RTF-PCR	VeebTest	Isolation		
Sensitivity	+	++	++	++	+++	+++	-	+++		
Specificity	-	++	++	-	+++	+++	++	+++		
Speed	+	--	--	+	--	--	+++	--		
Staffing	+	--	---	+	--	--	+++	---		
Safety	++	--	---	++	+++	+++	++	---		
Portability	-	--	--	-	-	-	++	--		
Cost	++	+	+	+	+	+	++	+		

Serological Tests
Virological Tests

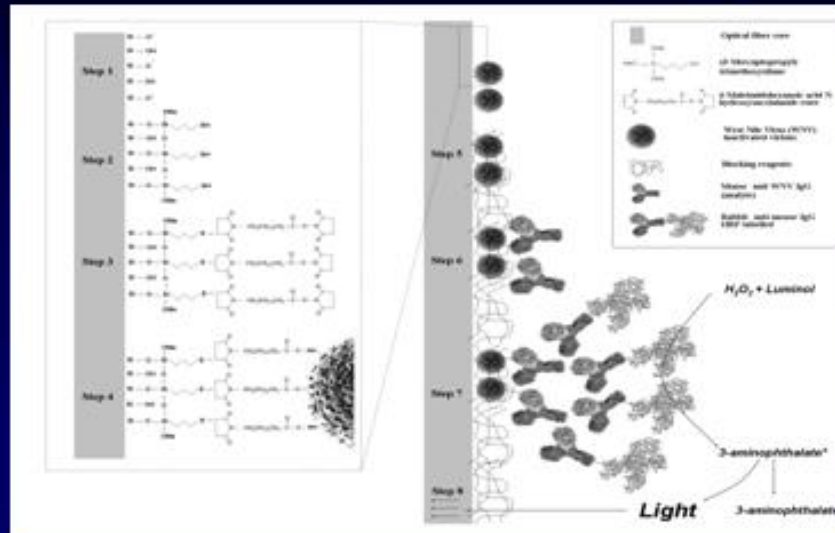
Need a test enabling both high sensitivity/specificity and speed, safety and portability

Physiological markers

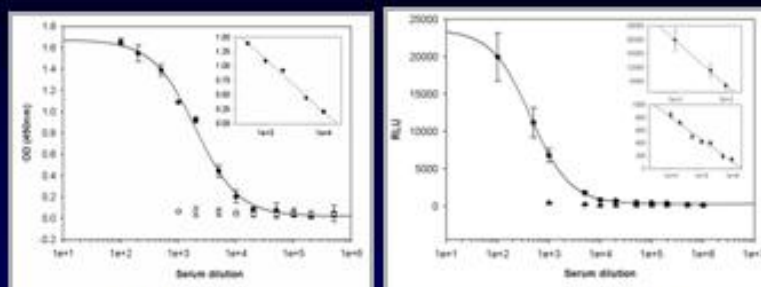


Chemiluminescent optical fiber immunosensor for the detection of anti-West Nile virus IgG

Herrmann, S. B. Leshem, S. Landes, B. Rager-Zisman and R.S. Marks (2004) *Talanta* 66: 6-14



The anti-WNV IgG immunosensor is more sensitive than that of ELISA

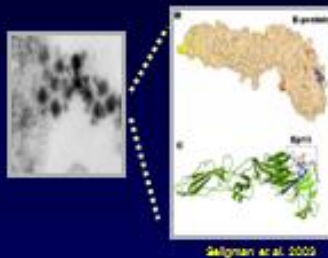


ELISA	Speed	OFIS
3h	Lower detection limit	1h
1:10,000	Linear range	1:1,000,000
500-10,000	Temperature	100-2,000 10,000-1,000,000
37° C		RT

Chemically neutralized viruses should not enter a kit

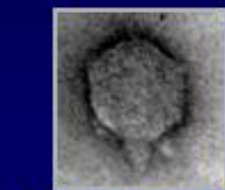
T7 phage display of Ep15 peptide for the detection of WNV IgG

Herrmann, S., B. Leshem, L. Lobel, H. Bin, E. Mendelson, D. Ben-Nathan, P. Dussart, A. Porgador, B. Rager-Zisman, R.S. Marks (2007). *Journal of Virological Methods* 141: 133-140



- The WNV E glycoprotein is a highly immunogenic flaviviral antigen
- Bioinformatics of conserved regions gave highly rated B-cell linear epitopes

p10B-GGG-Ep15-GGG-Ep15
415 copies/phage



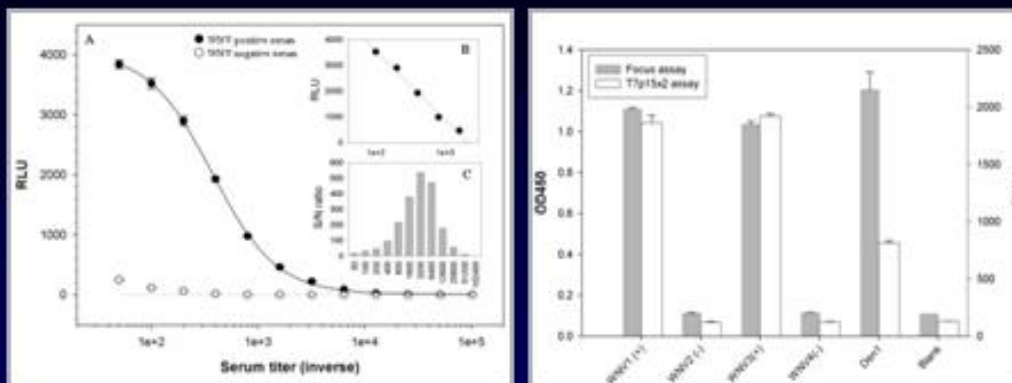
T7 phage particles displaying ~415 copies



Checking the ligation by PCR/electrophoresis

Phage ELISA based on T7-Ep15x2

Herrmann, S., B. Leshem, L. Lobel, H. Bin, E. Mendelson, D. Ben-Nathan, P. Dussart, A. Porgador, B. Rager-Zisman, R.S. Marks (2007) T7 phage display of Ep15 peptide for the detection of WNV IgG. *Journal of Virological Methods*. 141: 133-140

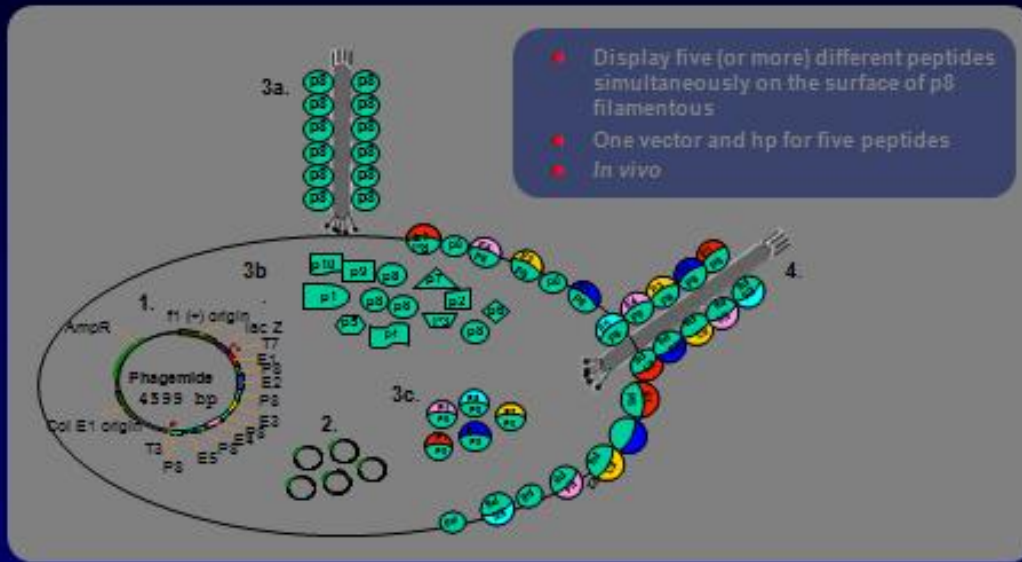


- Improved specificity as it does not cross react with Dengue virus unlike the FDA approved Focus Diagnostics kit
- The T7-Ep15x2 ELISA shows a lower detection limit of 1:51,200, a linear range from 1:100 to 1:2,000 and the best S/N ratio at 1:3,000
- Very good correlation when testing 4 reference human sera (WNV1-4)

Lower sensitivity

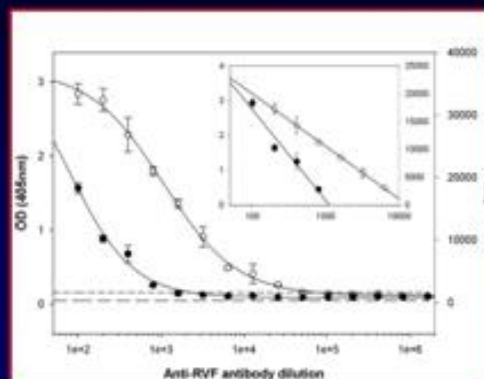
M13 Phage displayed multiple epitopes

Atias, D., L. Lobel, M. Virta and R.S. Marks (2007). Marks, R.S., D. Cullen, C. Lowe, H.H. Weetall and I. Karube (eds). *Handbook of Biosensors and Biochips*. John Wiley & Sons Ltd Publishers



Optical fiber immunosensor for the detection of IgG antibody to Rift Valley fever virus in humans

Sobarzo, A., J.T. Paweska, S. Herrmann, T. Amir, R.S. Marks and L. Lobel (2007) *Journal of Virological Methods* 146 (1-2) 327-334

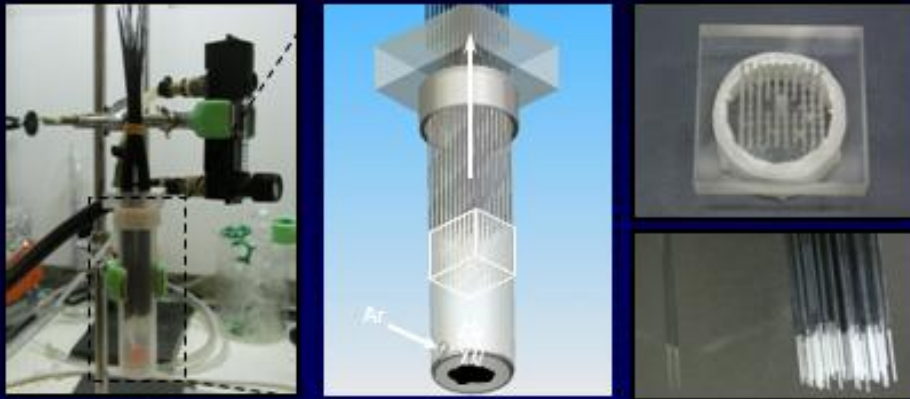


1:51,200
Vs.
1:1,638,400

On the left Titration curves for high-positive (—) and negative control serum (--) generated by OFIS (●) and colorimetric ELISA (○). The result of the linear regression analysis of the middle part of the calibration curves for high positive control is shown upper right corner of the graph. On the right signal to noise ratio between ELISA and OFIS.

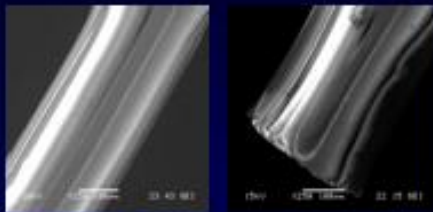
Surface modification of fiber core

Argon phase silanization of fused silica

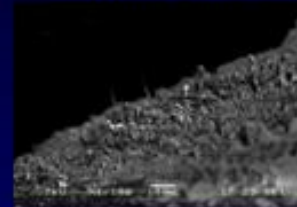


Argon vaporization of thiol-silane

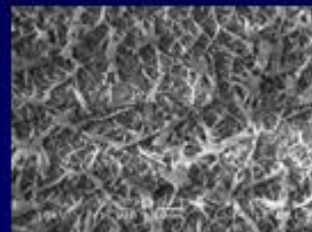
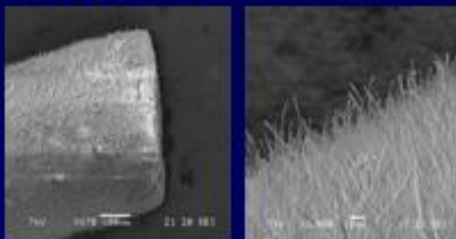
The Fiber Tip After Cleaning

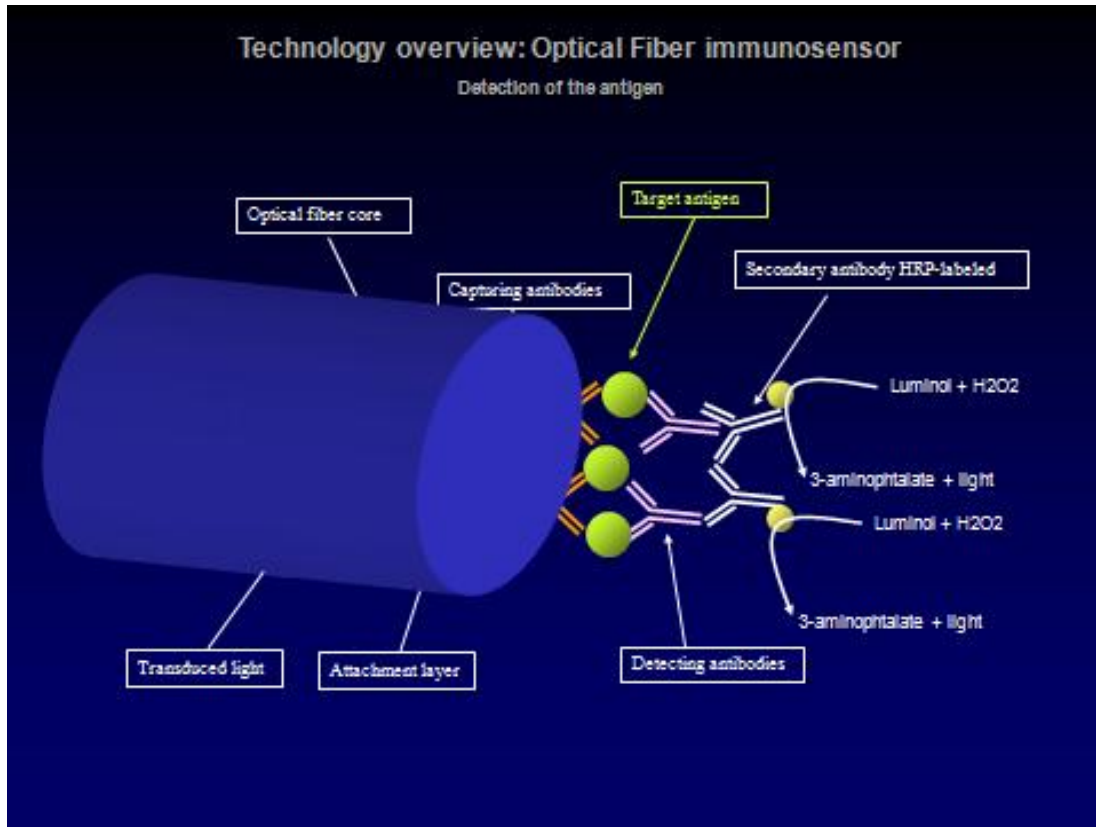


Fiber Tip After EMCS And Rift Valley Fever Antigen Binding


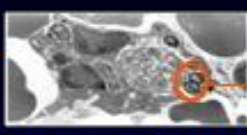
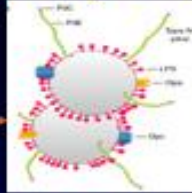


Fiber Tip After Chemical modification




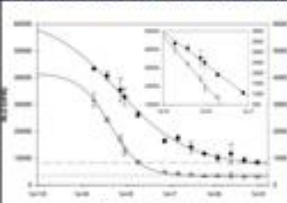


Neisseria meningitidis: 25% mortality < 72hrs

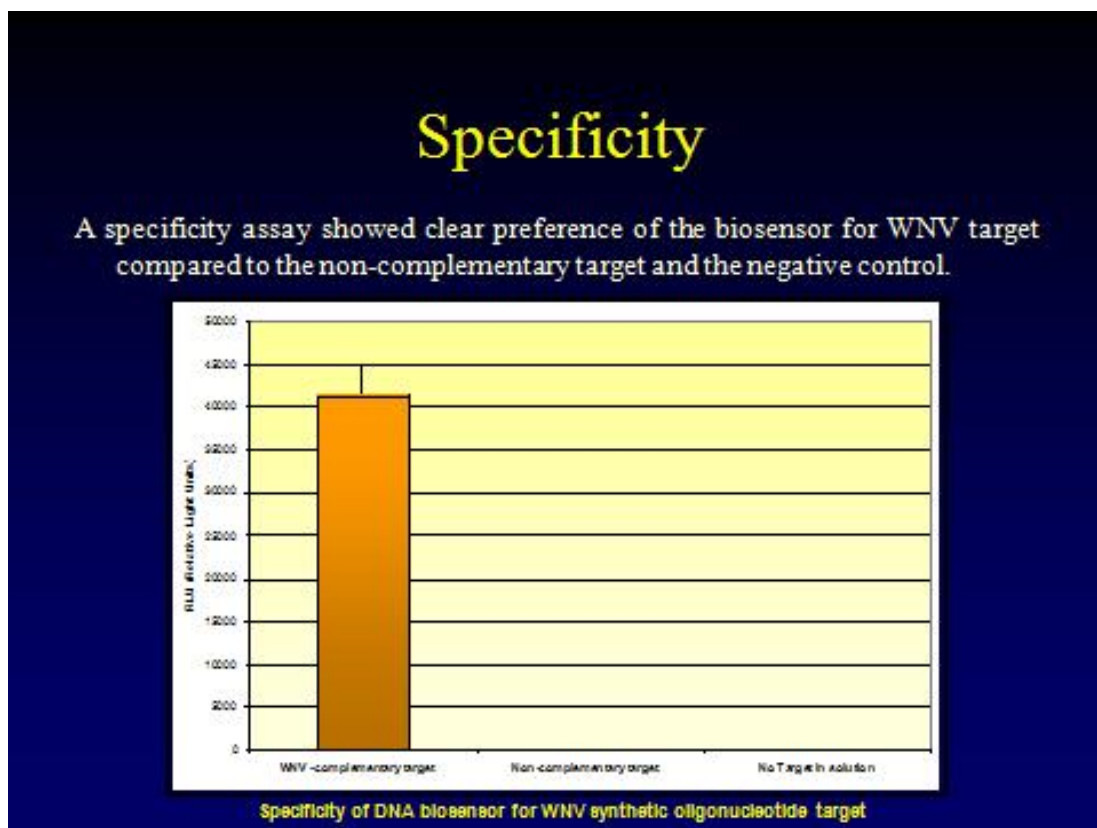
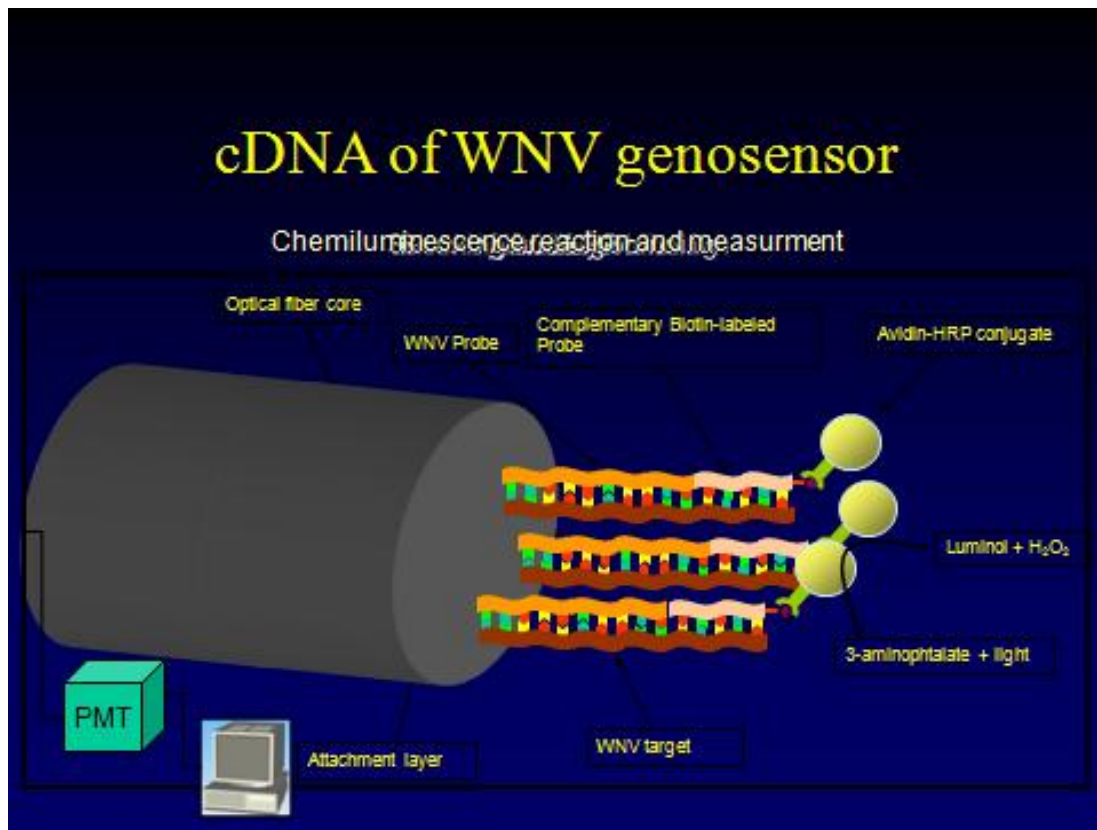




Calibration curves - ELISA & OFIS

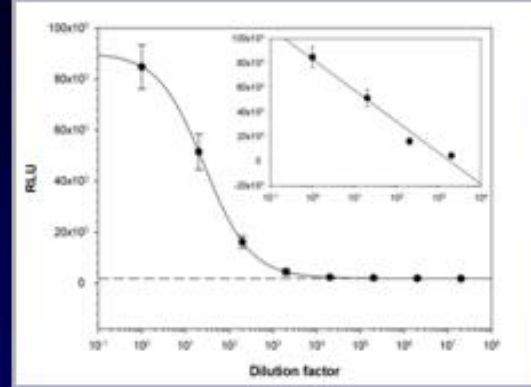
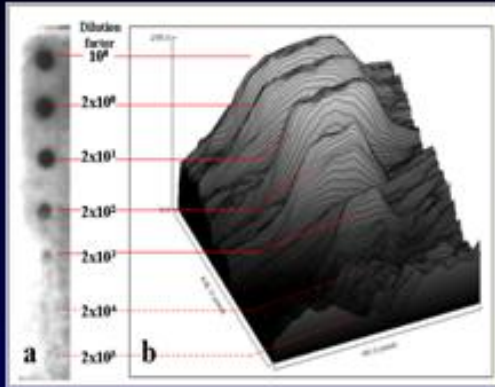
The positive samples are spiked buffered samples at serial dilutions

	ELISA	OFIS	
R² (curve, linear)	0.99, 0.98	0.99, 0.99	Gain
Linear range	1 order: 1E9-1E8	2 orders: 1E9-1E7	1 order
Overall assay time	180 min	60 min	/ 3
LLD	3.28E6 bac/ml	5.13E4 bac/ml	X100
Sensitivity	2383 RLU/log	17549 RLU/log	x6



Results of the sensor



Dot Blot

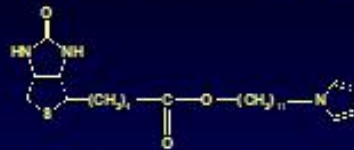
OFDS

0.5 ng	Lower detection limit	0.5 pg
0.5 μg-0.5 ng	Linear range	1 μg-0.5 ng

An innovative strategy for immobilization of receptor proteins on to an optical fiber by use of poly(pyrrole-biotin)

Marks, R.S., A. Novoa, D. Thomassey and S. Cosnier (2002) *Analytical and Bioanalytical Chemistry*, 374: 1056-1063

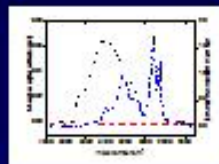
Pyrrole-biotin



FeCl₃ was selected as oxidizer since the potential of the polymerization threshold (0.67 V) is under the Fe(III)/Fe(II) reduction potential (0.77 V)

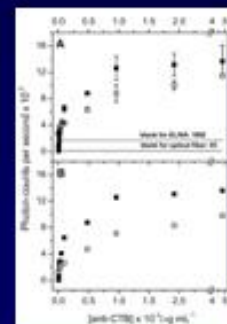


Avidin-TRICT conjugated to poly(pyrrole-biotin)



FT-IR Spectra

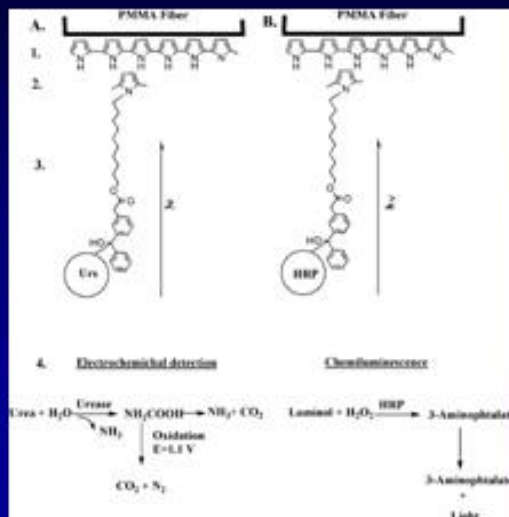
Pp-biotin fiber optic
Pyrrole-biotin
Bare fiber-optic



Optical-fibers (■) and classical ELISA (□)

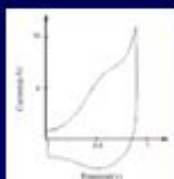
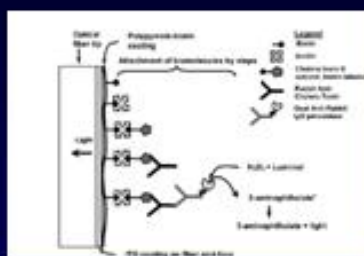
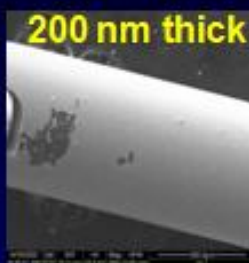
Development of Poly (methyl metacrylate) optic-conductive fiber transducers as dual biosensor platforms

D. Atlas, K. Abu-Rabeah b, S. Herrmann, J.Frenkel, D. Tavor, S.Cosnier and R.S. Marks Biosensors & Bioelectronics (2009) 24: 3683-87

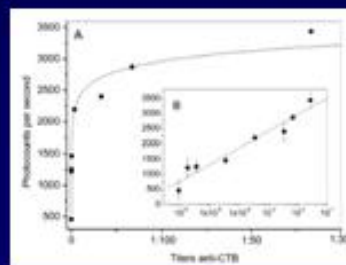


Indium tin oxide-coated optical fiber tips for one step electro-polymerization of robust films on complex geometries

Marks, R.S., A. Novoa, T. Konry, R. Kraus and S. Cosnier (2002) *Materials Science and Engineering C*, 21 (1-2) 189-194



Cyclic voltammogram of the electro-polymerized conducting film on the ITO surface



Physico-Chemical studies of an ITO-coated fiber-optic biosensor

Konry, T. and R.S. Marks (2005). *Thin Solid Films*, 492: 313-321

- ITO is highly transmissive
- ITO has low resistivity
- ITO is a tin oxide-doped indium oxide

Element	Wt %
SiO ₂	25.96
In ₂ O ₃	73.63
SnO ₂	0.41
Total	100.00

Thickness	260 nm
Resistance	$4.7 \times 10^{-2} \Omega \cdot \text{cm}$
Lattice constant	10.12 Å
Average grain size <D>	11.5 nm
Optical transmittance	85%
Refraction index	2.136

Optical immunosensor based on a poly(pyrrole-benzophenone) film for the detection of antibodies to viral antigen

Konry, T., A. Novoa, Y. Shemer-Avni, N. Hanuka, S. Cosnier, A. Lepellec and R.S. Marks (2005). *Analytical Chemistry*, 77 (6) 1771-1779



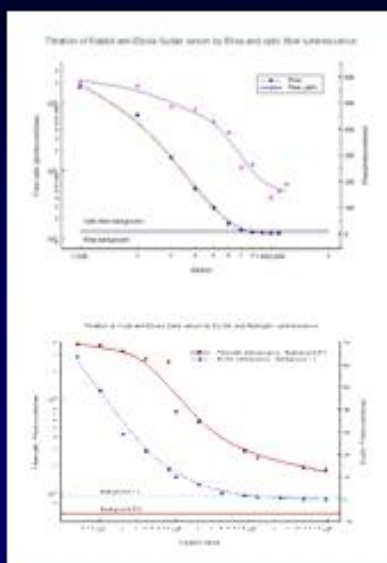
Screening of patients with HCV infection

Serological state of patients	Total tested	Anti-E2+ Western Blot	Anti-E2+ Immuno sensor	Western blot Detection percentage	Immuno-sensor Detection percentage
Anti HCV+ RNA+	13	9	13	69	100
Anti HCV- RNA+	8	2	4	25	50
Anti HCV- RNA-	7	0	0	0	0

*Anti HCV: Anti Core, NS5 & NS3

Indium tin oxide-coated fiber optic immunosensor for the detection of antibodies to Ebola virus

Petrosova, A., T. Konry, S. Cosnier, I. Thrakt, J. Lutwama, E. Rwaguma, A. Chepurinov, E. M. Mühlberger, L. Lobel R.S. Marks. (2006) *Sensors & Actuators. B Chemical* B 122:578-586



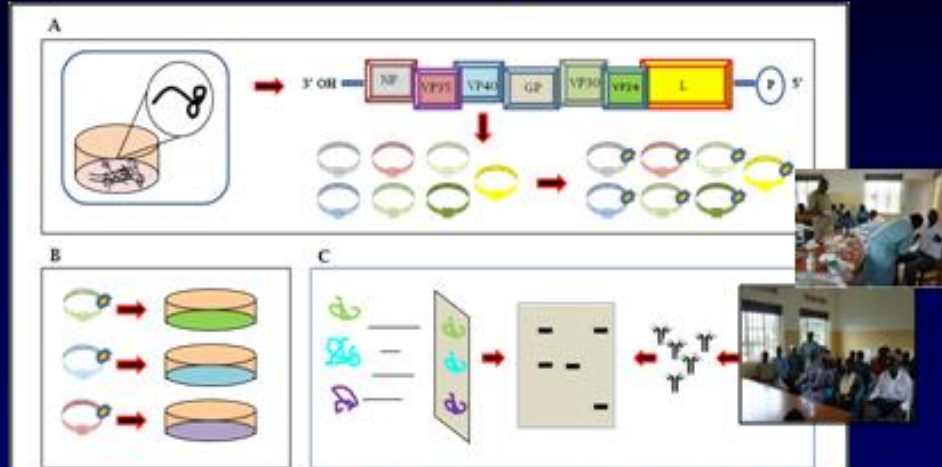
Ebola virus immunosensor vs ELISA for the detection of antibodies from Sudan and Zaire subtype strains

Calibration curve



	Elisa	Fiber optic immunosensor
Linear range	1:500 – 1:10,000	1:2,000 – 1:80,000
Lowest detection limit	1:20,000	1:960,000

Use human immune response profile to find epitope candidates



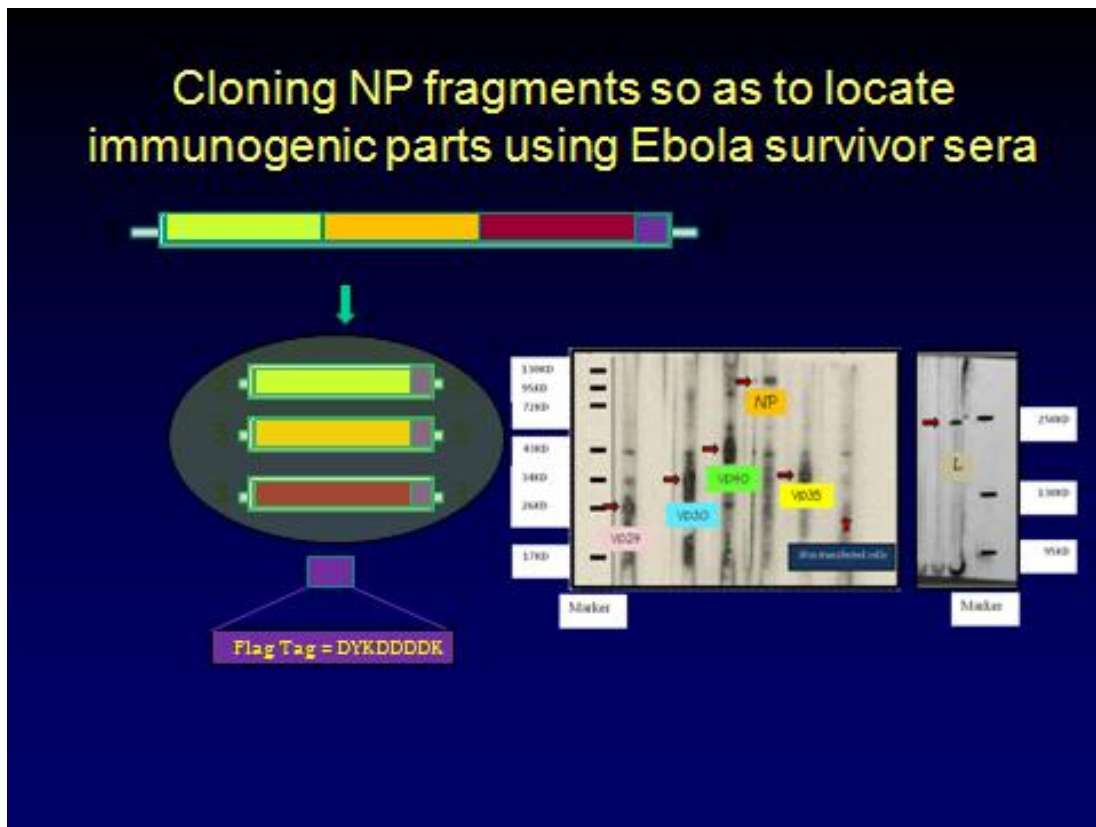
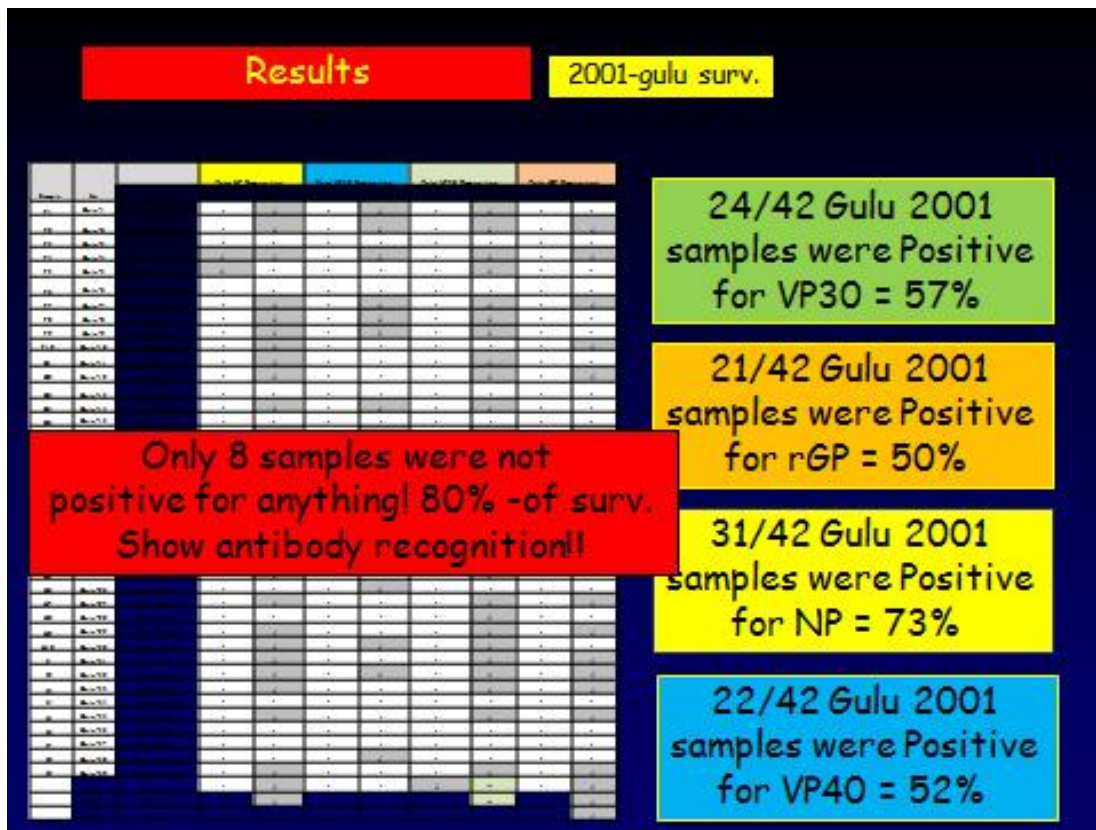
From 21 human samples with positive recognition to the NP, 20 were observed in individual survivors whereas only one in a fatal case. All .VP40 positive recognition samples were linked to survival


Cloned Ebola-S proteins screening Ebola-S survivor sera

Sample	Ebola-virus Sudan (Guinea) Recombinant			
	VP30	VP40	NP	rGP
Infected	1/78	6/78	21/78	1/78
Non-Infected	1/100	0/100	2/100	2/100
Total	2/178	6/178	23/178	3/178



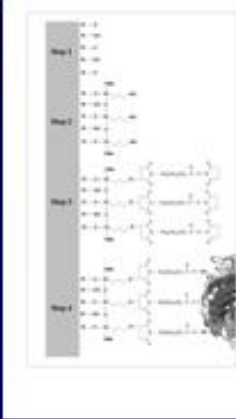
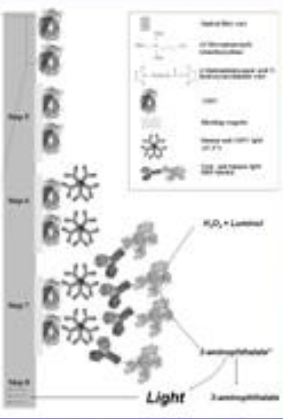
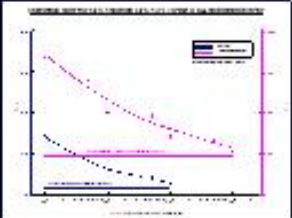
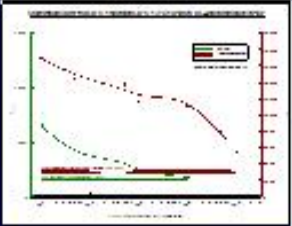
Sample Group	Ebola-virus Sudan (Guinea) Recombinant Protein				Ebola-virus Sudan (Guinea) Complex antigen
	VP30	VP40	NP	rGP	
Infected	7/78	11/78	33/78	10/78	40/78
Non-infected	1/100	2/100	5/100	1/100	3/40
Total	8/178	13/178	38/178	12/178	42/118





Greater sensitivity may enable earlier cancer detection

using 27.B1 and 27.F7 anti-GIPC-1
Biosensors & Bioelectronics 22: 1508

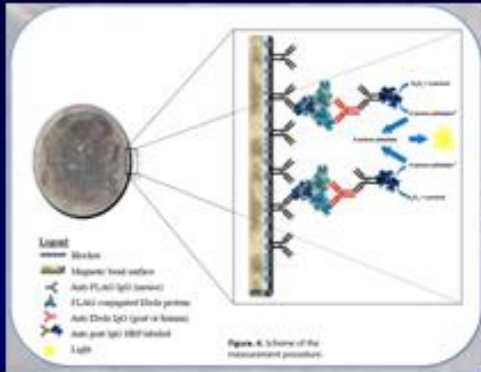





GIPC – tumor associated antigen
Human IgM monoclonal antibodies originally from ovarian cancer patients

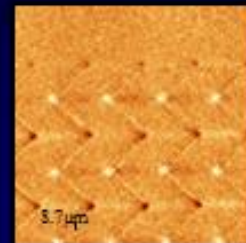
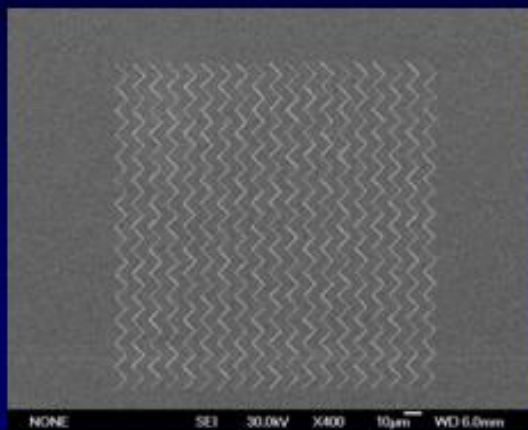
Identification of elevated IgM anti-GIPC-1 specific auto-antibodies in ovarian and breast cancer patients

	CL- ELISA	Immunosensor		CL- ELISA	Immunosensor
Total Samples	11	11			
-	9	5			
+	1	4	Total Samples	22	22
++	0	1	-	16	5
+++	1	1	+	2	2
Sensitivity	18% (2/11)	54% (6/11)	++	3	11
			+++	1	4
			Sensitivity	27% (6/22)	77% (17/22)

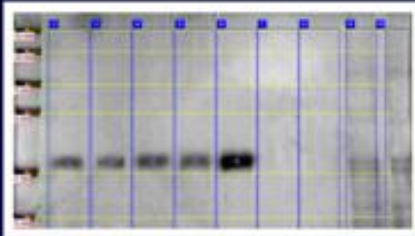
Liquid light guide magnetic immunosensor



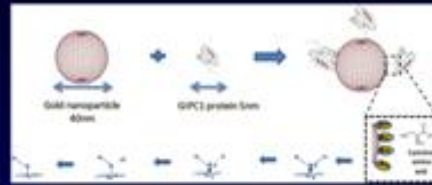
Magnetic nanostructures for magnetic bead capture of target immunoreagents



Lateral flow immunosensor



Purify the bioreceptor



Conjugation of gold nanoparticles

Combine with transducer technology



Viralcheck

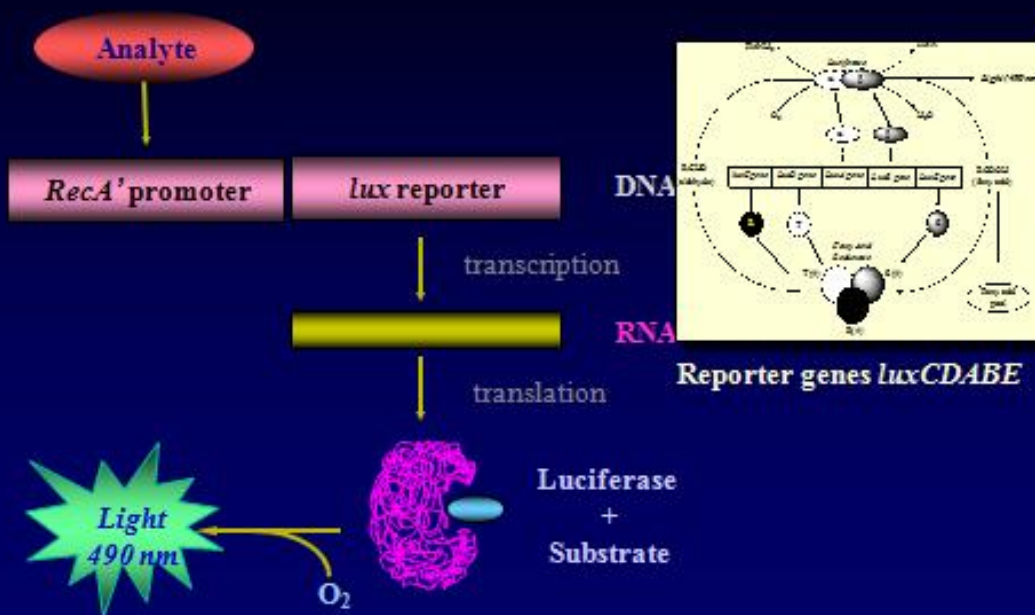
June 21-27, 2008 - Dakar, Senegal

- **Funding:**
 - US Army Research Labs
 - US State Department
- **Content**
 - Tutorial
 - Hands-on workshop with blind viral samples
 - Mock outbreak
 - Symposium
- **African Research Network: inauguration**
- **Book: Advanced diagnostics for the detection of viral pathogens**

Bioassays



- Natural whole organisms
 - Microbial cell cultures
- Natural sub-organisms
 - Mammalian cell cultures
 - Blood sample
- Engineered organisms
 - Microbial cell cultures
 - Mammalian cell cultures

DNA damage sensing

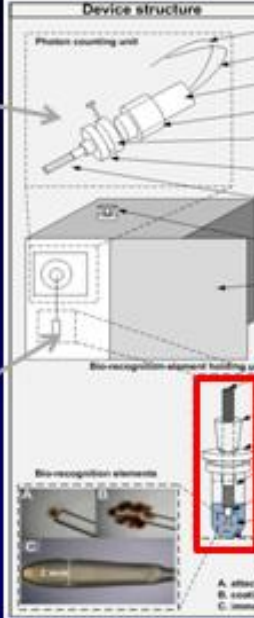


FIBER OPTIC BIOSENSOR

Eltsov, E. et al. (2009). "Parameters to Consider in the Construction of Fiber-Optic Biosensors as Alternative Bioanalytical Tools." *IEEE Instrumentation & Measurement Magazine* 12(5): 10-16.

Device structure


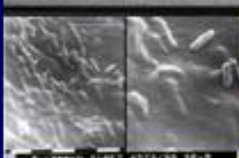



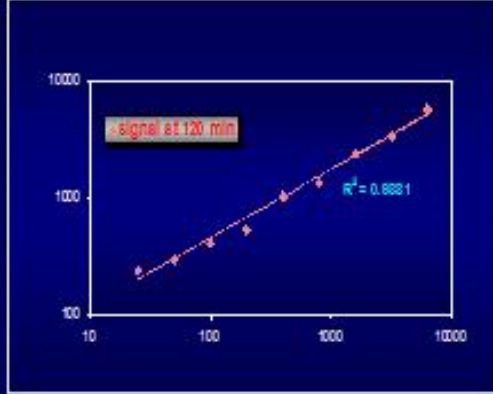
Part name	Purpose
Electric cable	Supply electricity to the sensor
Connection wire of PMT to computer	Transfer signal to the computer
PMT fixation ring	Prevent PMT movement
PMT sensor module	Collect light photons from the bio-recognition elements
Manual shutter	Prevent damaging PMT from the light
Fiber holder	Prevent fiber optic movements
Fiber optic	Transmission of the light from the bio-recognition element to the PMT
Outside handle of manual shutter	Open and close manual shutter from outside, in order, to prevent light entrance to the PMT when door is opened
Door	To seal the PMT for preventing background light entrance
Fiber optic	Transmission of the light from the bio-recognition element to the PMT
100µl syringe	Prevent movements of the fiber optic
Conical tube cap	Prevent movements of the fiber optic
Point of fixation of fiber	Point of fixation of fiber
Optic fiber core	Point of fixation of bio-recognition elements on the fiber
Bio-recognition elements	Produce light in presence of the specific pollutants (analyte)
Test samples	Samples

A. attachment of a lens bead to the end of the fiber
B. coating of the fiber with a number of microcapsules
C. immobilized bacterial adherers on optical fiber tip

Optical fiber bioluminescent whole-cell microbial biosensors to genotoxicants

Polyak, B., E. Bassis, A. Novodvoretz, S. Belkin and R.S. Marks (2000). *Water Science and Technology*. 42 (1-2) 305-311

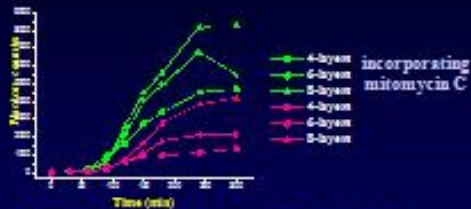






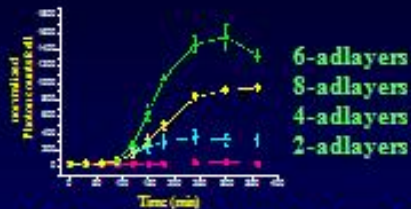
log(Mytomycin C concentration)
25-6,400 ppb

Bioluminescent whole-cell optical fiber sensor to genotoxicants: system optimization

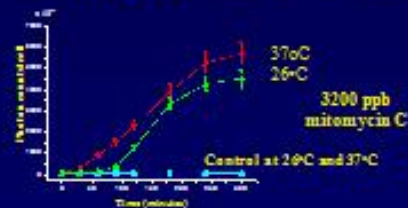
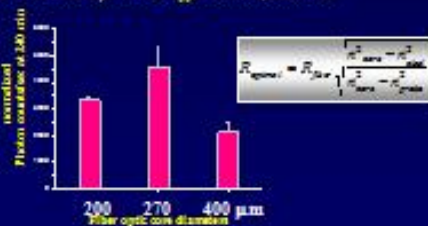
Polyak, B., E. Bassis, A. Novodvoretz, S. Belkin and R.S. Marks (2000). *Sensors and Actuators*, B 3656: 1-9



Optrode adlayers is diffusion dependent



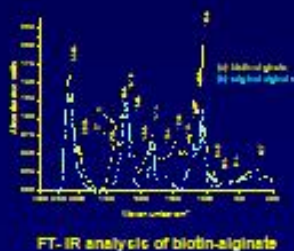
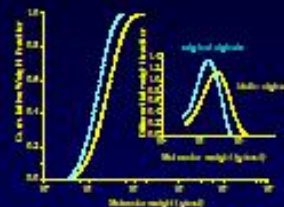
Optimized for ray optics and cell numbers



E. coli DPD 1718 works best at 37°C

Synthesis and characterization of a biotin-alginate conjugate and its application in a biosensor construction

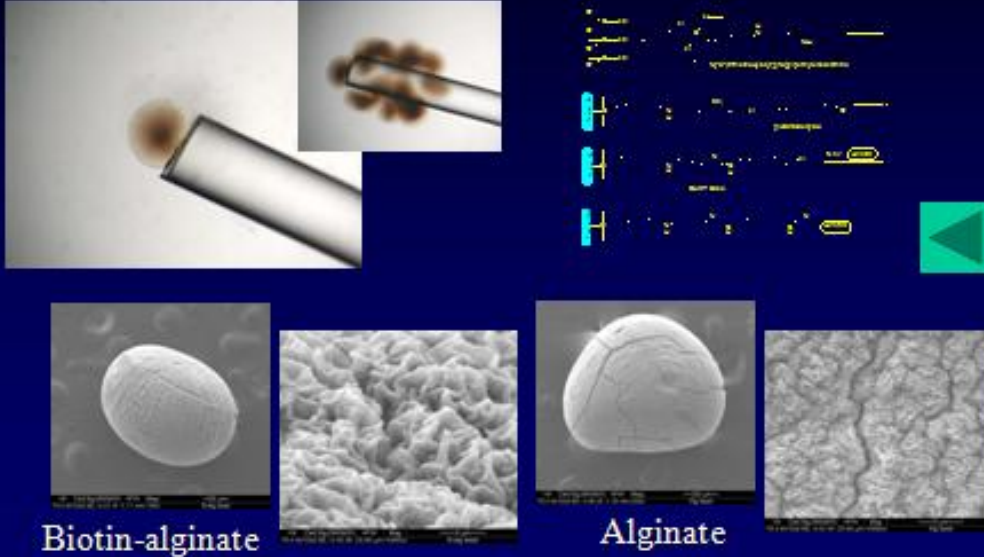
Polyak, B., S. Geresch and R.S. Marks (2004). *Biomacromolecules*, 5: 389-396



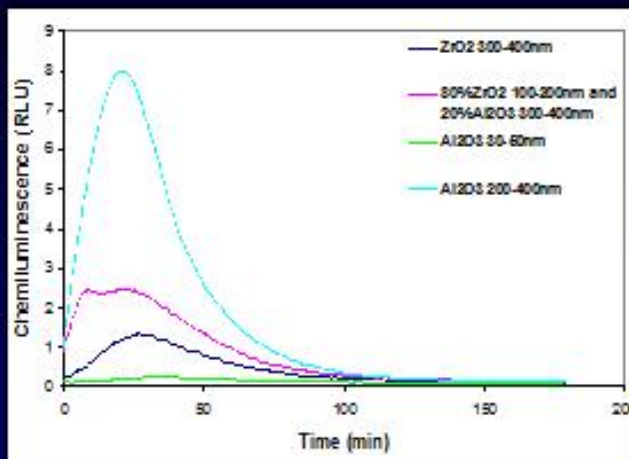
polymer concentration (% w/v)	biotin-alginate (10%) (cP@1c)	original alginate (cP@1c)
1.5	88	128
2.0	139	278
2.5	262	482
3.0	414	822
3.5	721	1230

Viscosity measurements at a shear rate of 100 s⁻¹

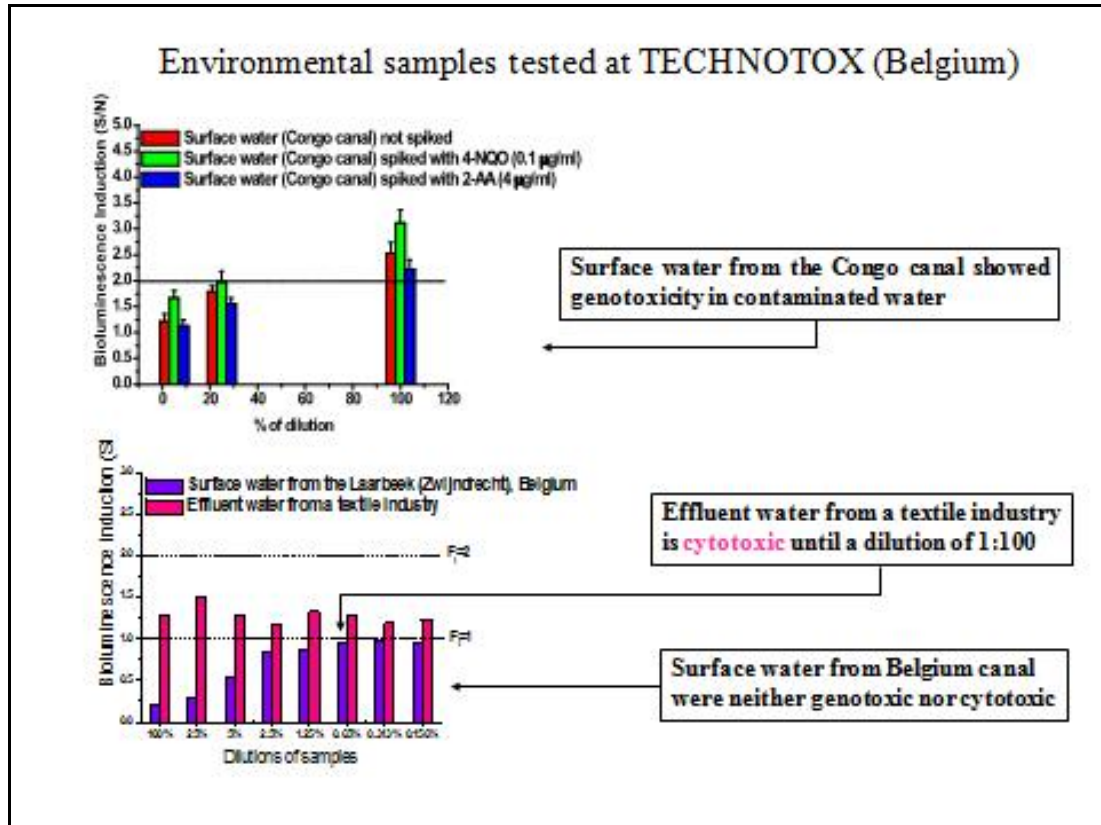
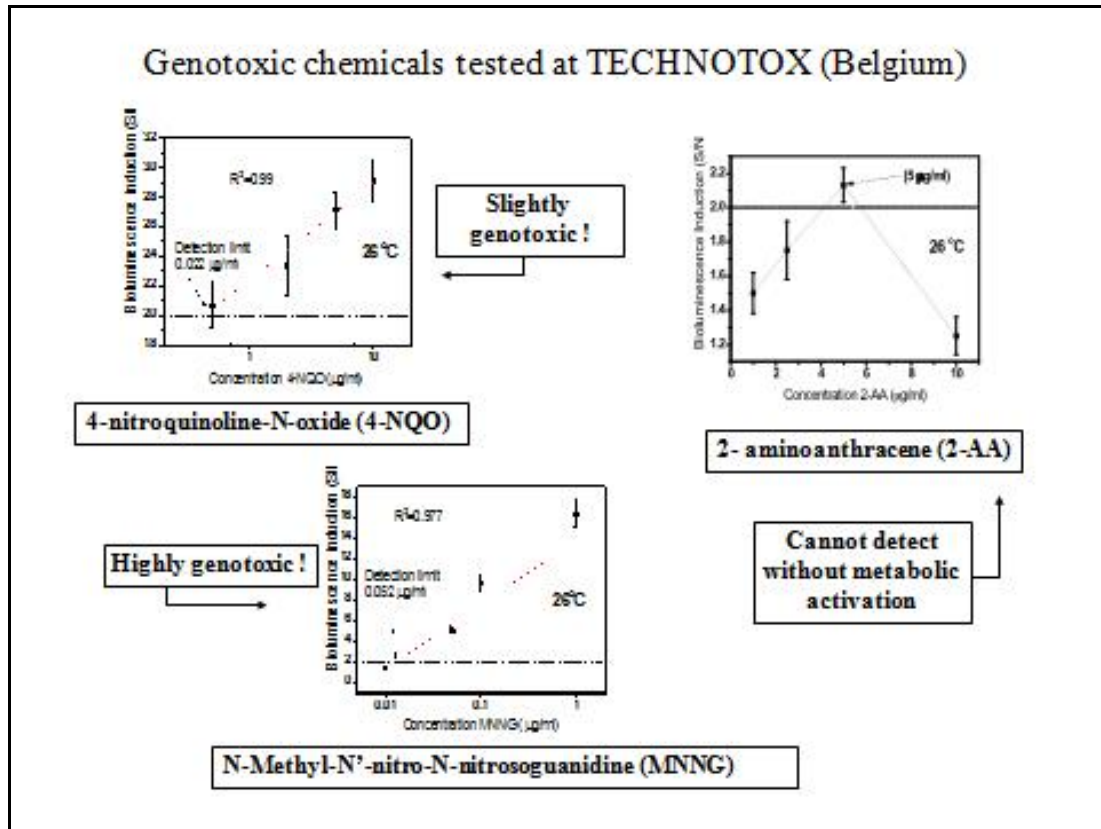
Biotinylated microsphere attached to an avidinylated fiber-optic endface






Phagocyte luminescence-based biotoxicity assay





Decision tree designed with WEKA, J 48 algorithm, 60 points per graph



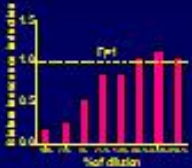
The HMDC/MERI project





**“Leachate” indicated
cytotoxic
contamination !**


Results




EILATox-Corvallis Quorum of biosensors




Biofilm-sensors
USA




FluoroTox
USA



CheckLite, Israel




Latex-bioreporters
USA




Chromatophore sensors
USA




Neuron cytosensor
USA




Fish soldiers
USA




CytoPro & Vitotox, Finland




Fiber-optic biosensors
Israel



Luminescent & Flash bioreporters
Finland, Israel



Crustaceans biomonitors
Hungary



Fish nucleoli, Ukraine



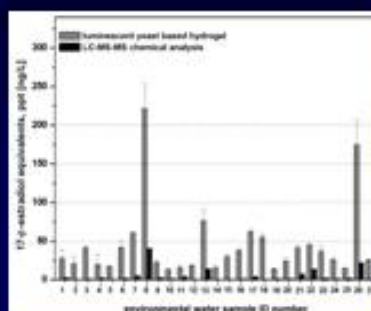
Luminescent yeast based hydrogels for Endocrine Disrupting Compound biodetection

Fine, T., F. Cedroni, T. Gotoh, H. Shiroishi, M. Morita, R.S. Marks and M. Yano (2002) Luminescent yeast with embedded in hydrogels for estrogen endocrine

disrupting chemical biomarkers. *Biotechnology & Bioengineering* 77: 2102-2109

Estrogenic compound	EC50 (ppb)	Relative potency ER ₁	ER ₂	Detection limit (ppb) (ug/L)
17- β -estradiol (E2)	0.6	1	1	0.05
Diethylstilbestrol (DES)	0.1	5.6	15.2	5.0x10 ⁻⁴
Ethynylestradiol (EE2)	0.6	1.8	na ^a	6x10 ⁻⁴
Estron (E1)	2.1	0.2	0.02	0.05
Coumestrol	27	0.016	0.02	0.2
Genistein	259	0.0012	0.0025	15.9
Biochanin A ^b	252	0.0014	0.0025	22.6

^ana, not available

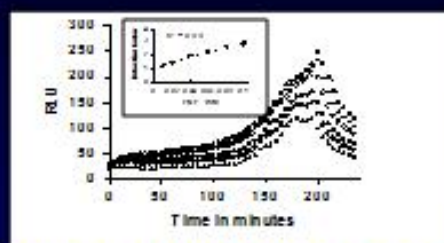
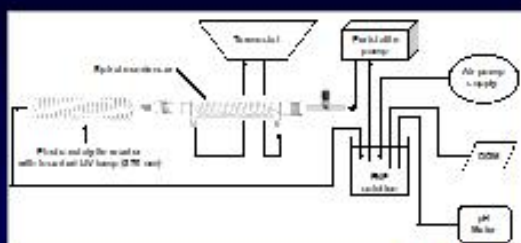


17- β -estradiol EEQs [ug/L] measured in environmental water samples from Tokyo bay

- Samples from 27 different locations in Tokyo bay metropolitan area: 8 effluents from sewage treatment plants; 19 river waters (Dr. Isobe Tomohiko, National Institute for Environmental Studies, Tadokura 205-8506, Tsukuba, Japan)
- Most estrogenic samples are similar with both measurements
- Overestimation of the luminescent hydrogels

Monitoring genotoxicity during the photocatalytic degradation of *p*-nitrophenol

Shani Sekler, M. Y. Levi, B. Polyak, A. Novoa, PSM Dunlop, JA Byrne and RS Marks (2004). *Journal of Applied Toxicology*, 24: 395-400

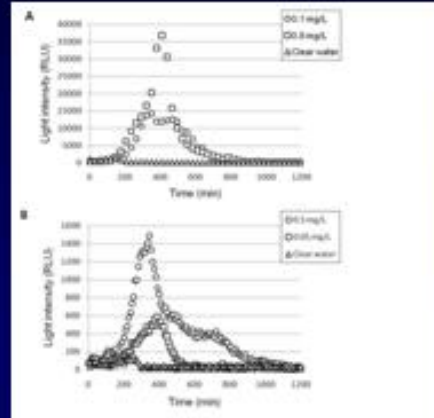
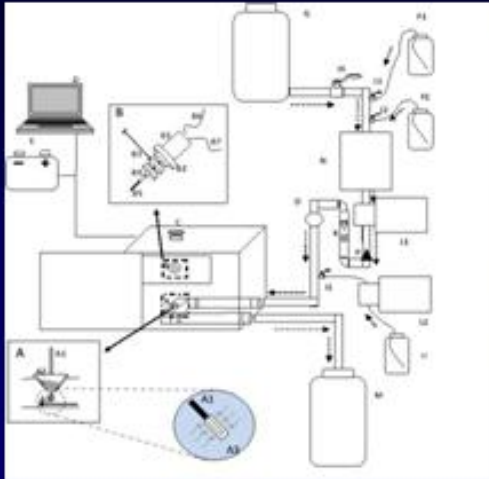


Inset: Induction factor values of each PNP concentration

- Titanium dioxide (TiO₂) is a semiconductor metal oxide that when irradiated with UV light radiation, it produces an electron/hole pair generating hydroxyl radicals at the surface of the particle that will oxidize pollutants.
- TiO₂ can be immobilized so that post treatment removal would not be necessary
- Water treatment would require monitoring its toxicity level

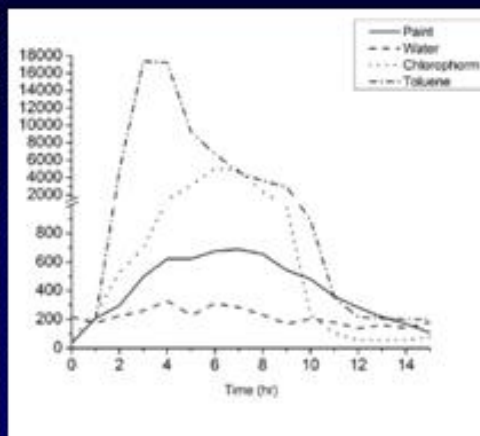
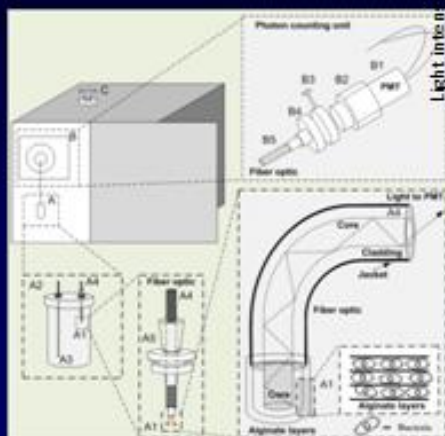
Flow-through real-time bacterial biosensor for toxicants in drinking water

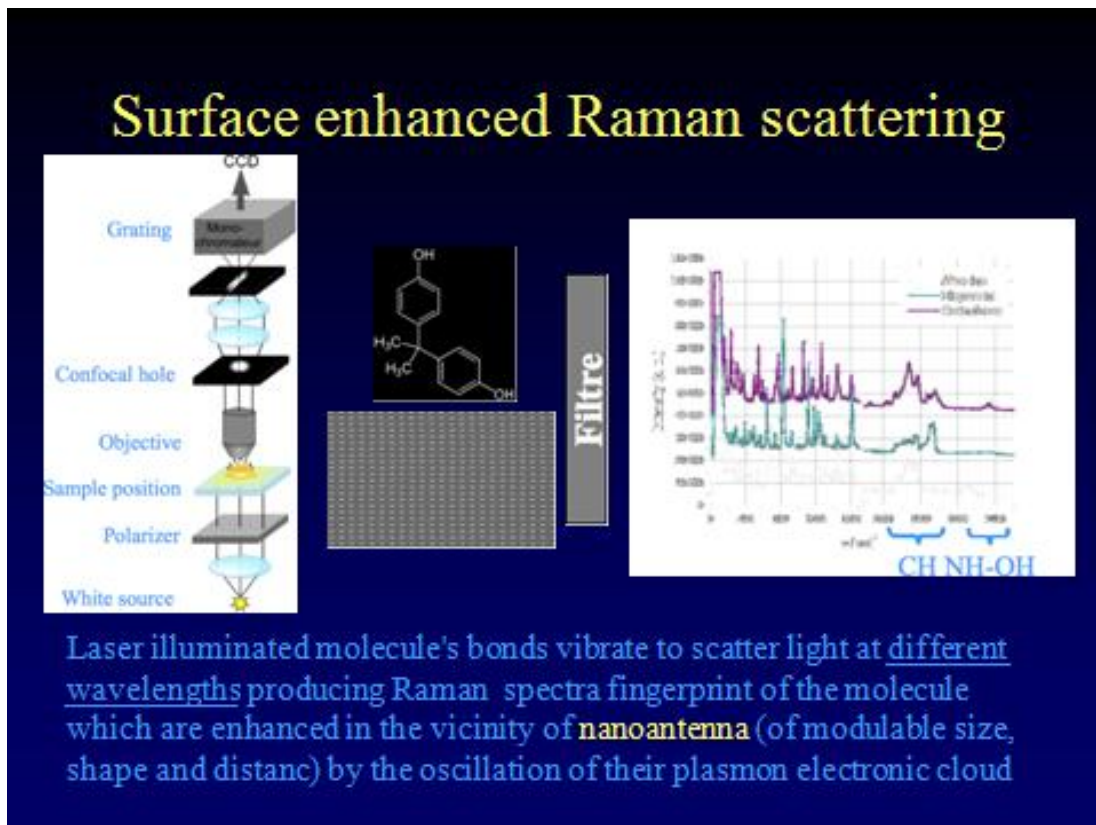
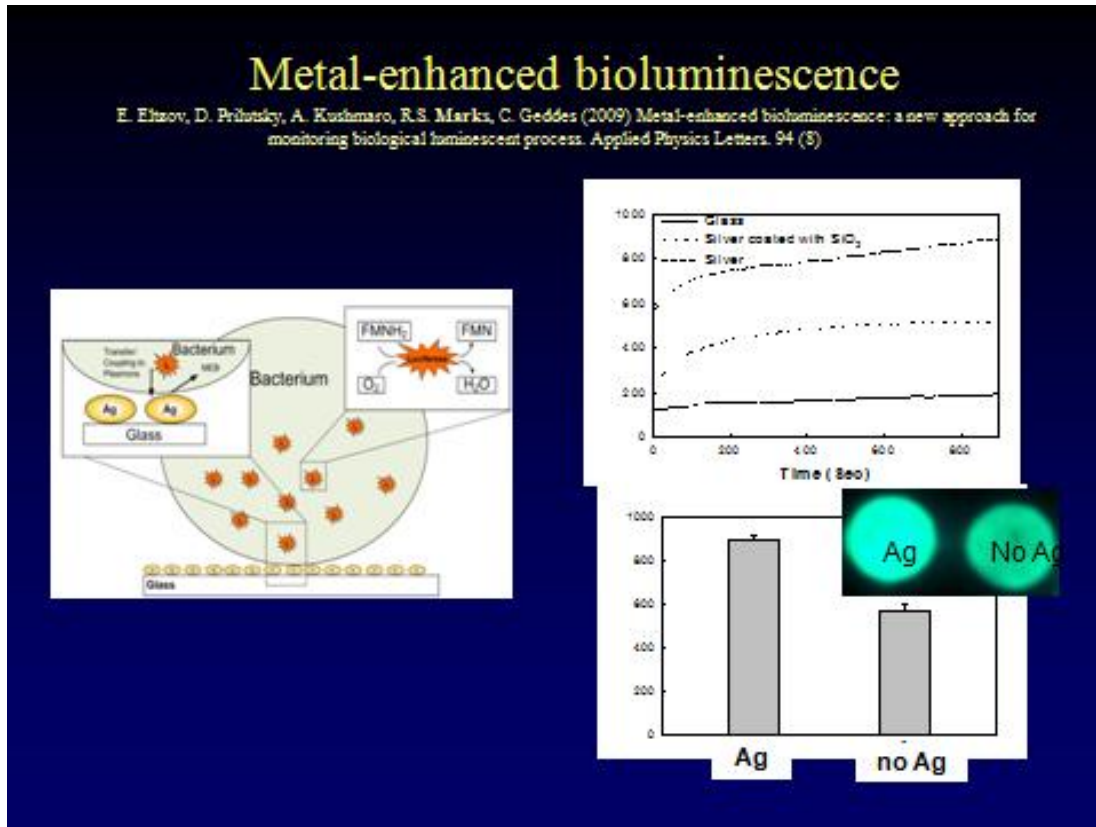
Eltzov, E. et al. (2009). "Flow-through real time bacterial biosensor for toxic compounds in water." *Sensors and Actuators B-Chemical* **142**(1): 11-18.



FIBER OPTIC BIOSENSOR FOR AIR TOXICITY MONITORING

Eltzov, E. et al. (2010). "Creation fiber optic based biosensor for air toxicity monitoring." *Sensors and Actuators B-Chemical*, **proofs**.





Surface-enhanced fluorescence from metallic nano-sculptured thin films

Abdulhalim, I., A. Kumburavsky, C. Patzig, B. Roschkebeck, B. Fuhrmann, E. Elzev, R. Markel, J. Xu, F. Zhang, and A. Likhachev (2009)
 Surface-enhanced fluorescence from metal nano-sculptured thin films with application to bio-sensing in water. *Applied Physics Letters*, 94 (6)

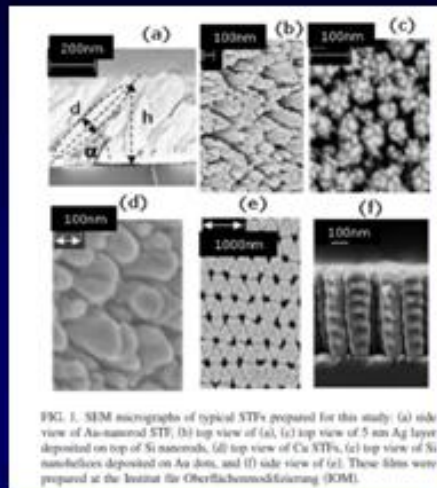
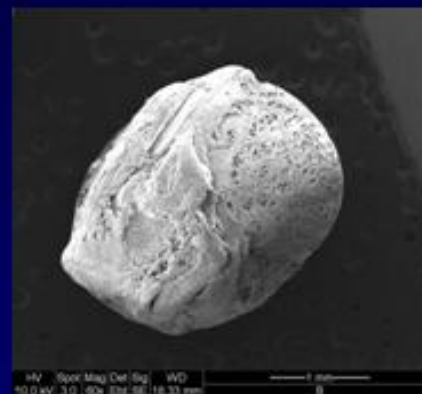
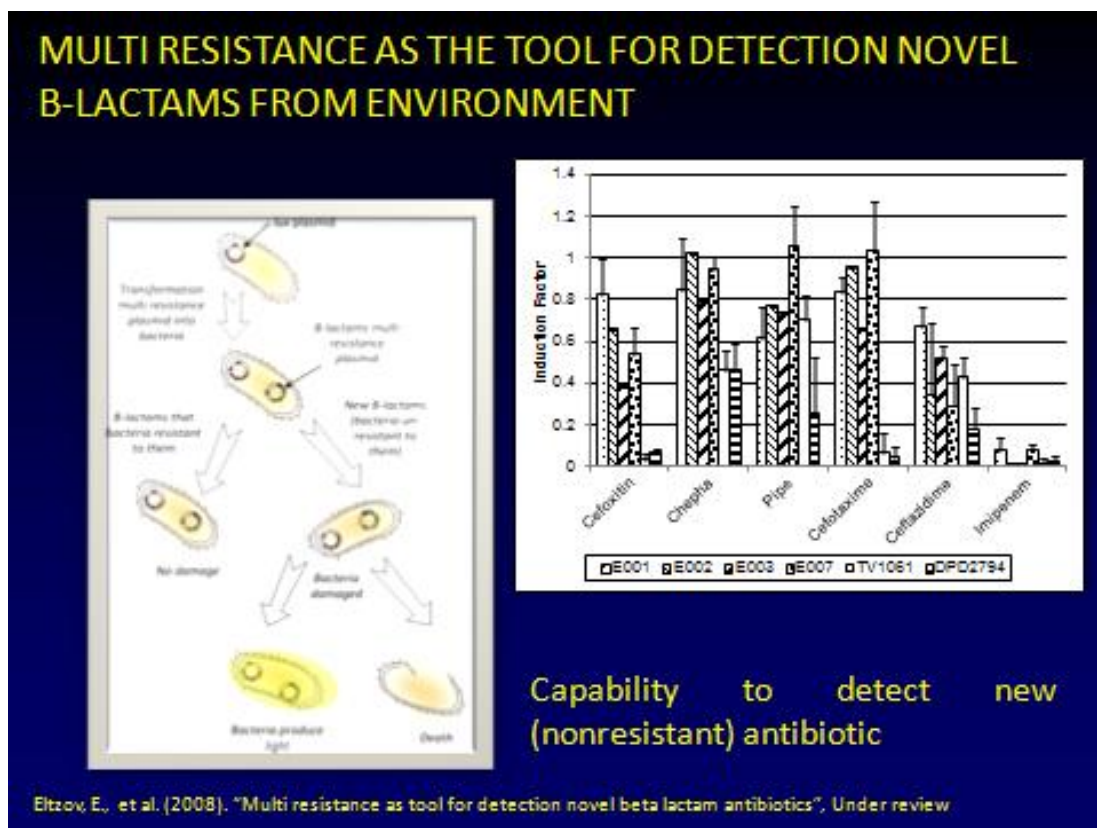
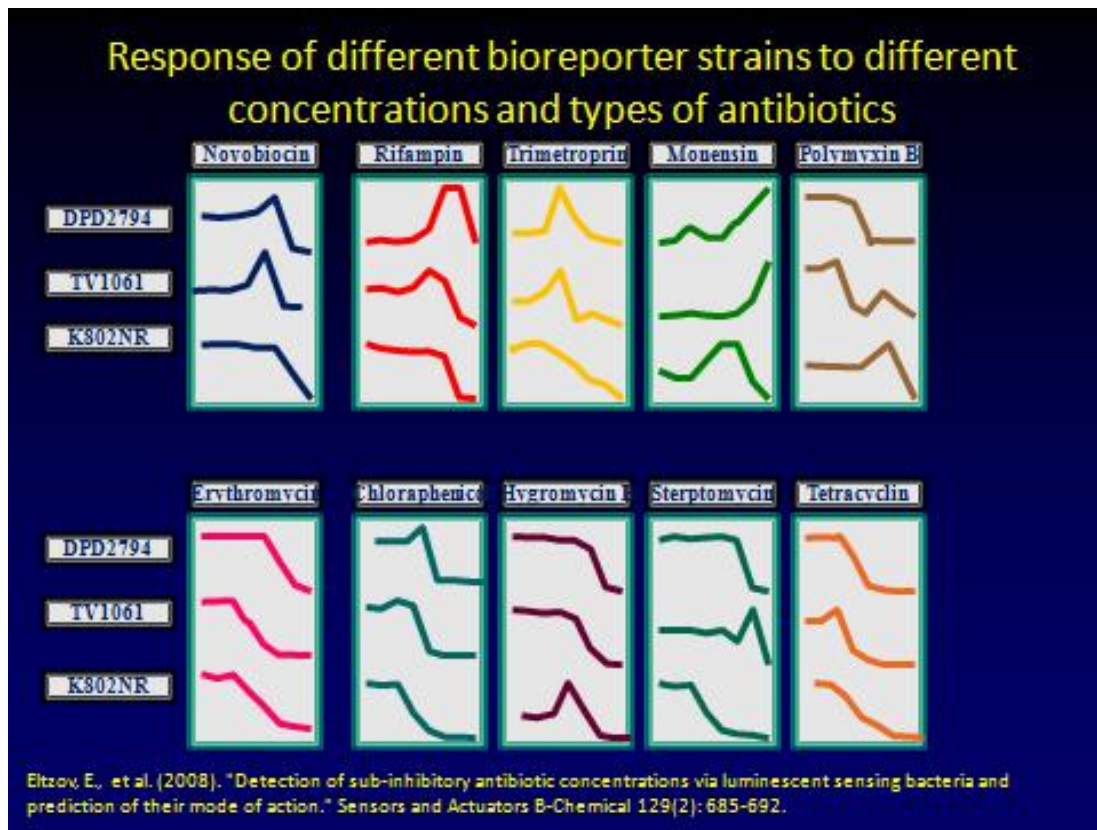


FIG. 1. SEM micrographs of typical STFs prepared for this study: (a) side view of Au-nanostructured STF, (b) top view of (a), (c) top view of 5 nm Ag layer deposited on top of Si nanorods, (d) top view of Cu STFs, (e) top view of Si nanobelts deposited on Au dots, and (f) side view of (e). These films were prepared at the Institut für Oberflächenmodifizierung (IFOM).



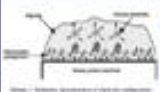

Growing ‘uncultivable’ microorganisms : Agar Sphere Polymeric Encapsulation Technology Platform

- Discovery of new antibiotics and new degraders of recalcitrant anthropogenic pollutants will lead to wealth as well as novel and economic treatment processes.





Electrochemical Biosensors Developed

Transducer	Analyte	Receptor	Immobilization Procedure
Platinum disk electrode	Glucose <i>(in aqueous solution)</i>	Glucose oxidase	Micro-encapsulation in latex films 
Platinum disk electrode	Glucose <i>(in aqueous solution)</i>	Glucose oxidase biotin labeled	Biotinylated Alginate matrix 
Glassy carbon rotating disk electrode	Catechol <i>(in organic solvent)</i>	Polyphenol oxidase biotin labeled	Poly-pyrrol-biotin electro-polymerized film 
0.9 mm HB drawing leads	Paraoxon	Molecular imprinted polymer	Imprinted template 

- Cosnier, S.; S. Szmerits, R.S. Marks, A. Nova, L. Puech, E. Perez, I. Rico-Lattes. *Electrochemistry Communications* 2 (2000) 851-855.
- Cosnier, S.; S. Szmerits, R.S. Marks, A. Nova, L. Puech, E. Perez, I. Rico-Lattes. *Talanta* 55 (2001) 889-897.
- Cosnier, S., A. Nova, C. Mousty and R.S. marks (2002) *Analytica Chimica Acta* 453: 71-79
- Mousty, C., A. Leppelec, S. cosnier, A. Nova and R.S. Marks (2001) *Electrochemistry Communications*. 3: 727-732

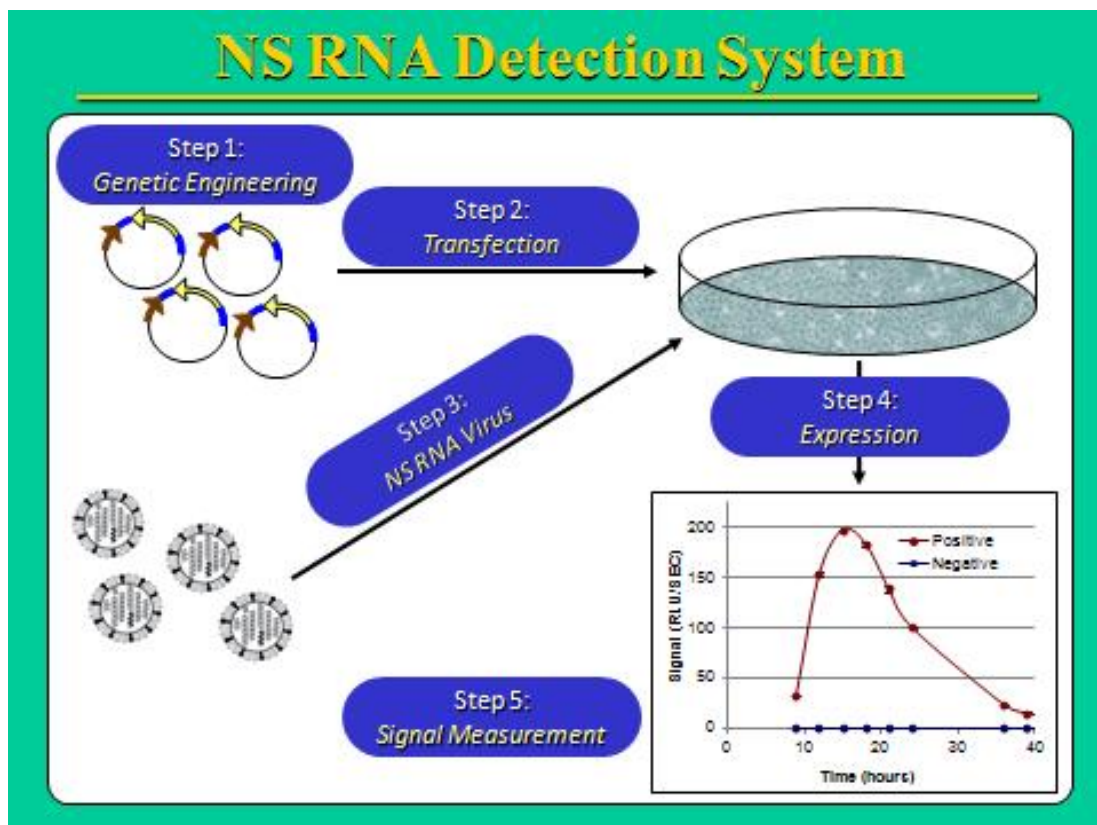
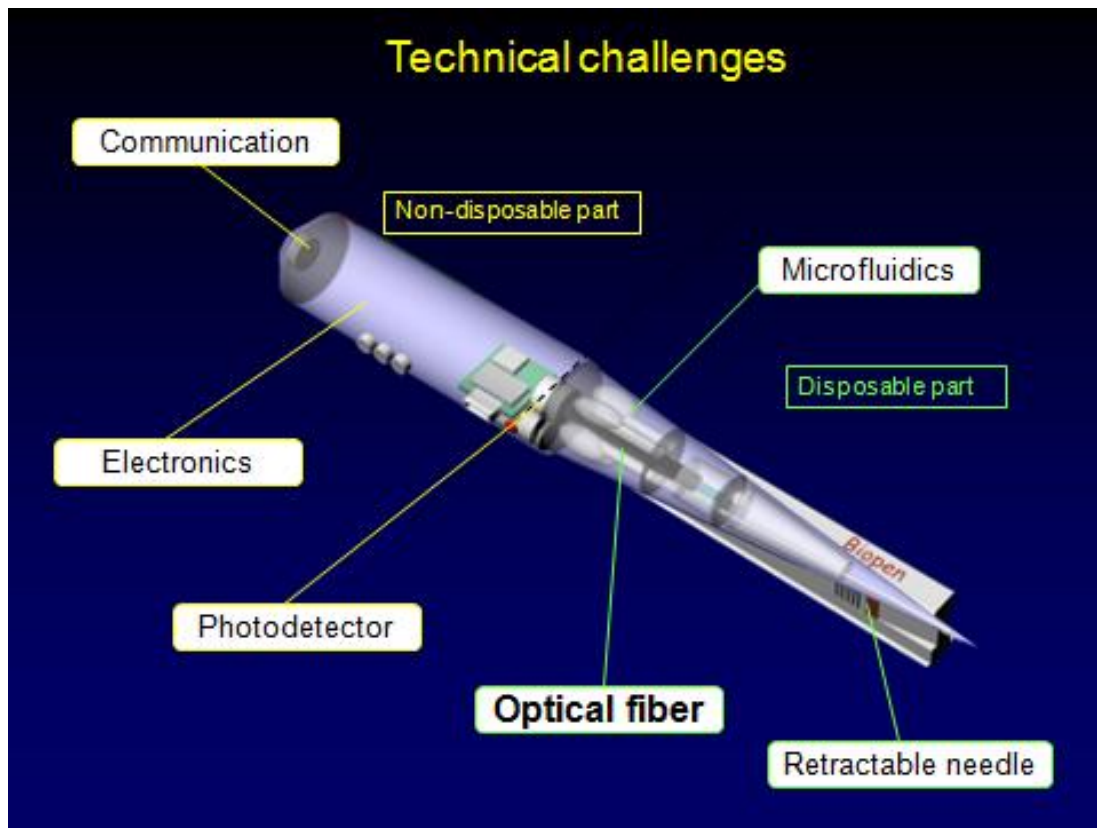
Project Biopen: a vision

A portable device
for monitoring pollutants, biotoxins and pathogens
in drinking water and biological fluids

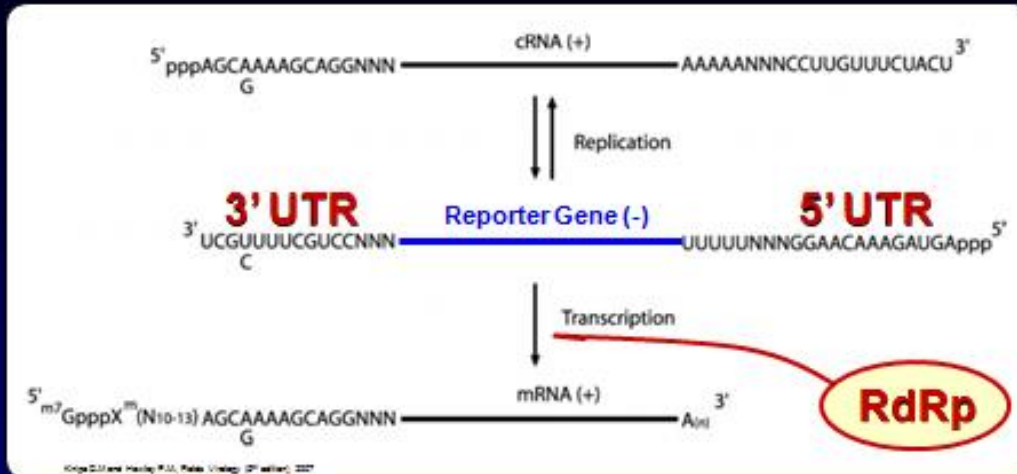
The first
"Lab-in-a-pen"



National Institute for Biotechnology in the Negev
Ben-Gurion University of the Negev

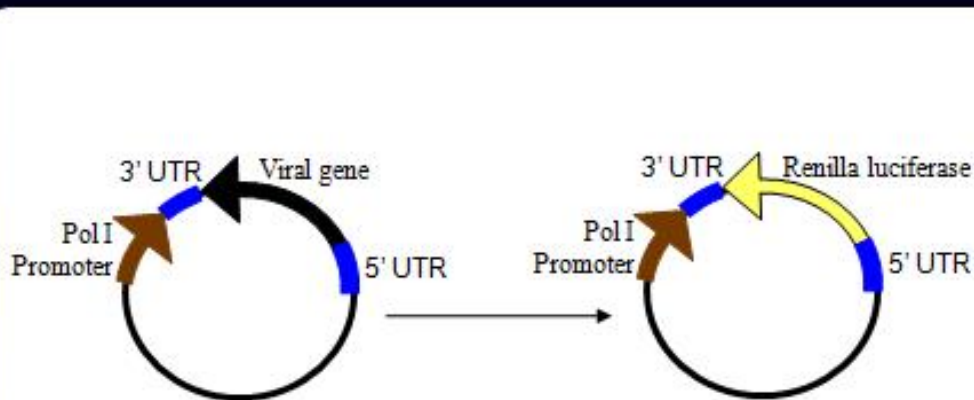


Negative Stranded RNA Viruses



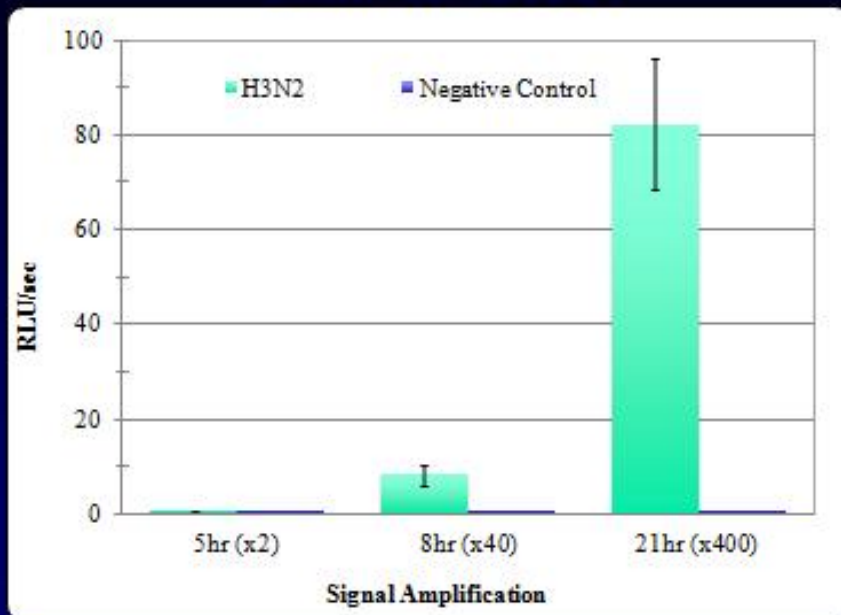
- RdRp – RNA dependent RNA polymerase
- UTRs – UnTranslated Regions

We replace the NP viral gene with a *Luc* gene



Real Time Detection

Our transfected cells report on the presence of influenza virus



Clinical problem

1. Clinical diagnostics are usually incomplete
2. Identification of the etiological agent ordered
3. Therapies could be directed quasi blind
4. The patient's immune reaction to the infection may be crucial to therapy

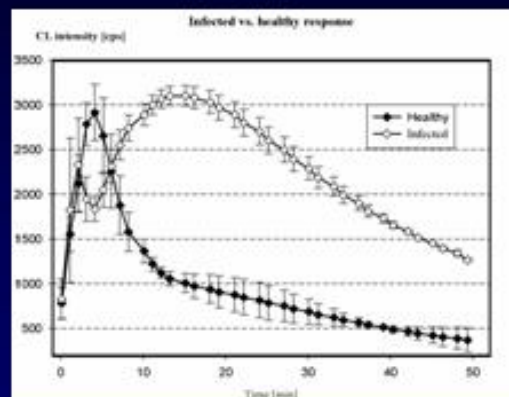
There is no diagnostic test today providing physicians with a reflection of the status of the insulted innate system as well as its potential course

‘Primed’ neutrophils ‘mirror’ the clinical status of the patient and may provide diagnostics and prognosis

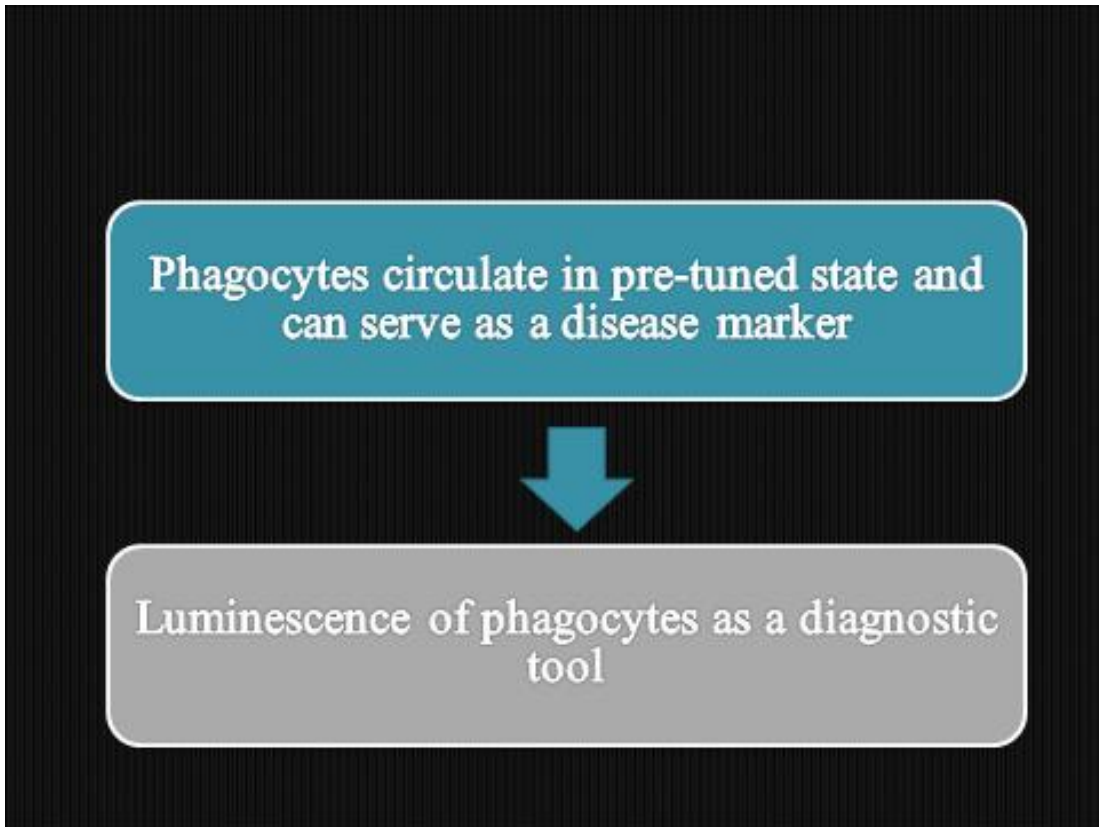
- The respiratory burst is complex due to a variety of mechanisms and localizations
- Neutrophils report on the innate immune status
 - Huge numbers, so cannot miss them
 - Permanently ‘broadcast’ the status patient
 - First enlisted against infection
 - Neutrophil glow depends on their activation status
- The phenotypic luminescent imprints of neutrophils is modulated by:
 - the insult
 - the genetic make-up of the host
 - the environmental memory

Fiber-optic biosensor to assess circulating phagocyte activity in whole blood by chemiluminescence


Magnano, M., O. Ertan, G. Pich, A. Novodromov, G. Poca-Avraham, F. Schaeffer and R. S. Marks (2005). *Sensors & Bioelectronics* 21: 1210-1218



Simultaneously recorded CL responses of healthy and infected patient blood



Patient blood samples processed




Collection of whole blood in heparinized tubes

Opsonization of zymosan (stimulant)

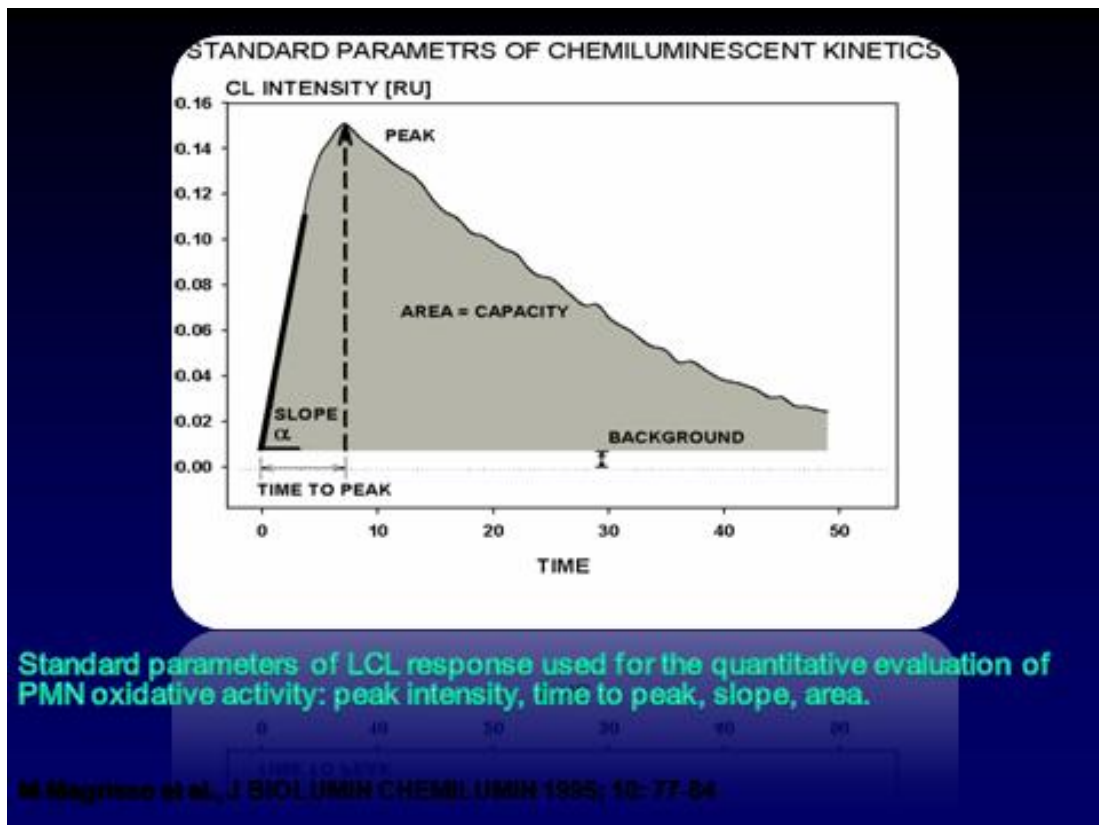
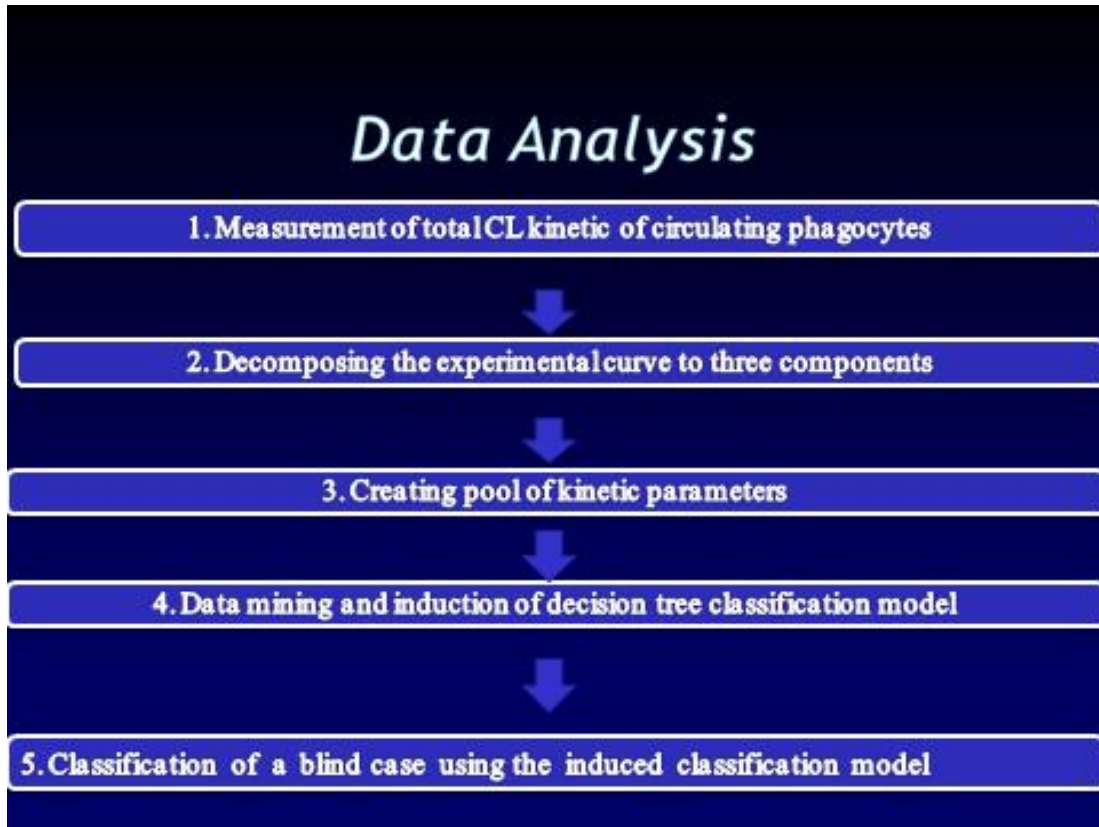
Preparation of the plate

Stimulation with zymosan and measurement

Analysis



- 1
- 2
- 3

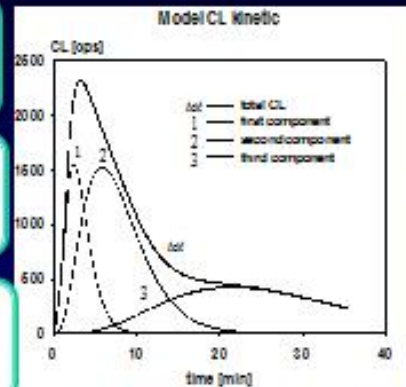


Parameters driven from the CL sub-kinetics: functional states of PMNs

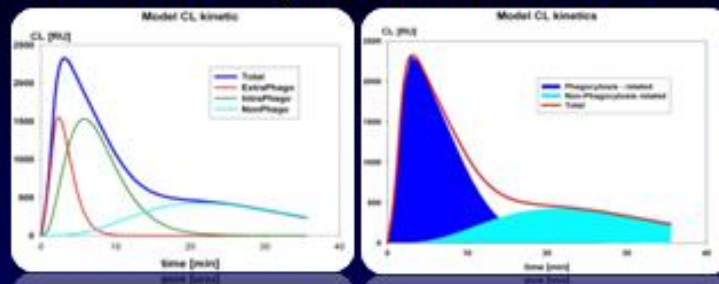
Capacity (C):
the total CL capacity of unit cells, reflecting their capability to generate ROS.

$$Effectiveness = \frac{Capacity\ of\ intracellular\ component}{Capacity\ of\ extracellular\ component}$$

$$Velocity = \frac{intra+extra\ components}{third\ component}$$



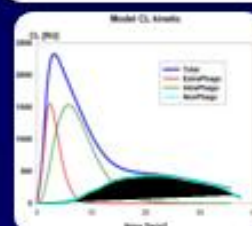
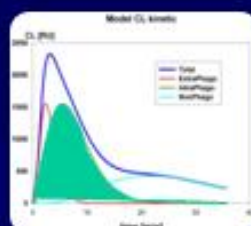
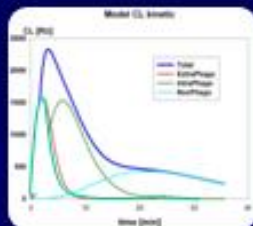
Parallel CL imprints of intracellular & extracellular production of ROS

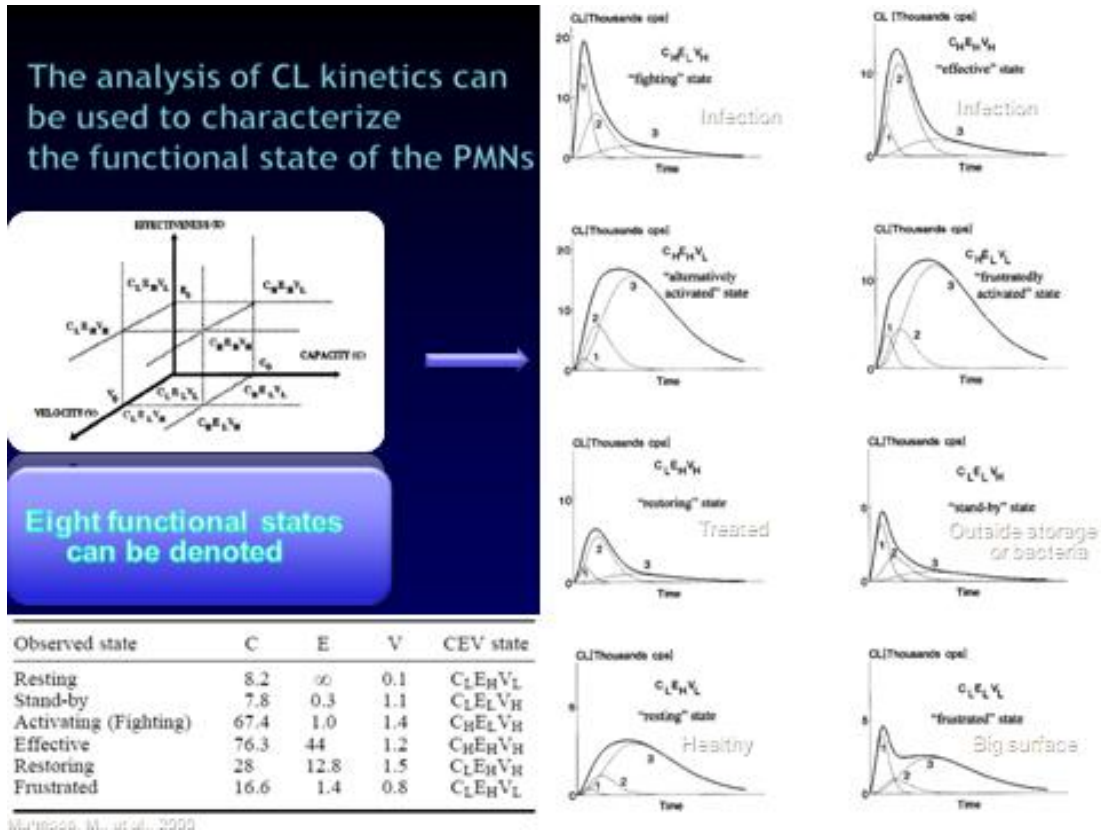


Extracellular component

Intracellular component

Intra cellular not connected to phagocytosis





Phagolum. 60/656,926 (2004); 20092-WO-05; 20346-WO-06

Each patient has 82 parameters!

Parameter	Definition
PtimeSP	Peak time of primed sample
Extra_SP	Extra-cellular phagocytosis-related emission of primed sample
CapS	Capacity of standard sample
RelTimeInPh_SA	Time of intracellular phagocytosis of aged sample divided by time of intracellular phagocytosis of standard sample
S-bkg	Background CL of standard sample
nonPhago_SA	Non-phago-related CL of aged sample
nonPhago_S	Non-phago-related CL of standard sample
RelCapInPh_SP	Intracellular phagocytosis capacity of primed sample divided by intracellular phagocytosis capacity of standard sample
RelTimeEx_SA	Time of extra-cellular phagocytosis-related emission of aged sample divided by time of extra-cellular phagocytosis-related emission of standard sample
RelIntranonPhago_SP	Intracellular non-phagocytosis capacity of primed sample divided by intracellular non-phagocytosis capacity of standard sample
RelPhago_SA	Phagocytosis capacity of aged sample divided by total capacity of aged sample
RelTimeInPh_SP	Time of intra-cellular phagocytosis-related emission of primed sample divided by time of intra-cellular phagocytosis-related emission of standard sample
CapSP	Capacity of primed sample
SP_vel	Velocity of primed sample
RelPhago_S	Phagocytosis capacity of standard sample divided by total capacity of standard sample

Application of J48 (C4.5) data-mining algorithm for induction of the decision tree classification model

Decision tree classification model

Classifier output

Time taken to build model: 0.09 seconds

=== Evaluation on training set ===

=== Summary ===

Correctly Classified Instances	30	100	%
Incorrectly Classified Instances	0	0	%
Kappa statistic	1		
Mean absolute error	0		
Root mean squared error	0		
Relative absolute error	0	%	
Root relative squared error	0	%	
Total Number of Instances	30		

=== Detailed Accuracy By Class ===

TP Rate	FP Rate	Precision	Recall	F-Measure	ROC Area	Class
1	0	1	1	1	1	1
1	0	1	1	1	1	2
1	0	1	1	1	1	3
1	0	1	1	1	1	4

=== Confusion Matrix ===

```

# # # # <--> CLASSIFIED AS
12 0 0 0 | a=1
0 20 0 0 | b=2
0 0 22 0 | c=3
0 0 0 31 | d=4
    
```

You can discriminate nephrology conditions using neutrophil chemiluminescence


Prilutsky, D., B. Rogachev, M. Vorobiov, M. Zlotnik, M. Last, L. Lobel, and R. S. Marks (2008)
Dynamic component chemiluminescent sensor for assessing circulating morphonuclear leukocyte activity of peritoneal dialysis patients. Analytical Chemistry. 80: 5131-5138

Established classification model for diagnostics of intra-abdominal pathological processes afflicting peritoneal dialysis patients

Training set: 100% accuracy
Testing set: 84.6% accuracy

We can differentiate between acute viral and bacterial infections

Prilutsky, D., Shneider, E., Shefer, A., Rogachev, B., Lobel, L., Last, M., Marks, R.




Algorithms used:
C4.5, Support vector Machines, Naïve Bayes

Accuracy:
Training set: 94.7%
Testing set: 88.9%

Anal. Chem., 2011, 83: 4258-65

Feature sets and classification models for an identification of several infectious diseases were discovered

Prilutsky, D., Rogachev, B., Lobel, L., Last, M., Marks, R.



Feature selection: wrapper and filter methods

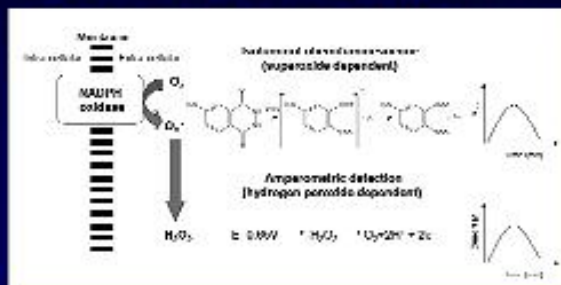
Algorithms used:
C4.5, Support vector Machines, Naïve Bayes

Artificial Intelligence in Medicine, 2011, 52: 153-63

Reactive Oxygen Species production in neutrophil-like PLB 985 & HL 60 cells detected by electrochemistry and chemiluminescence

Ashkenazi, A. and R.S. Marks () Luminol dependent chemiluminescence of human phagocyte cell lines:

comparison between DMSO differentiated PLB 985 and HL60 cells. Luminescence. 24 (3) 171-7



Electrochemistry		Luminol CL		Response time (sec)	Limit of detection
DMSO induced PLB 985	Human neutrophils	DMSO induced PLB 985	Human neutrophils		
52 ± 12	17 ± 6	32 ± 3	8 ± 2		
<500 cells		<500 cells			

why biochips? ... go sub-micron



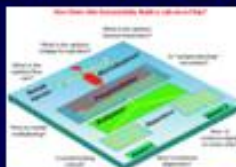
Diagnostic tests are mostly done in laboratories



... nanotechnology packs more!



... are usually sophisticated



... can we pack all in a biochip?



... are sometimes too complicated to run

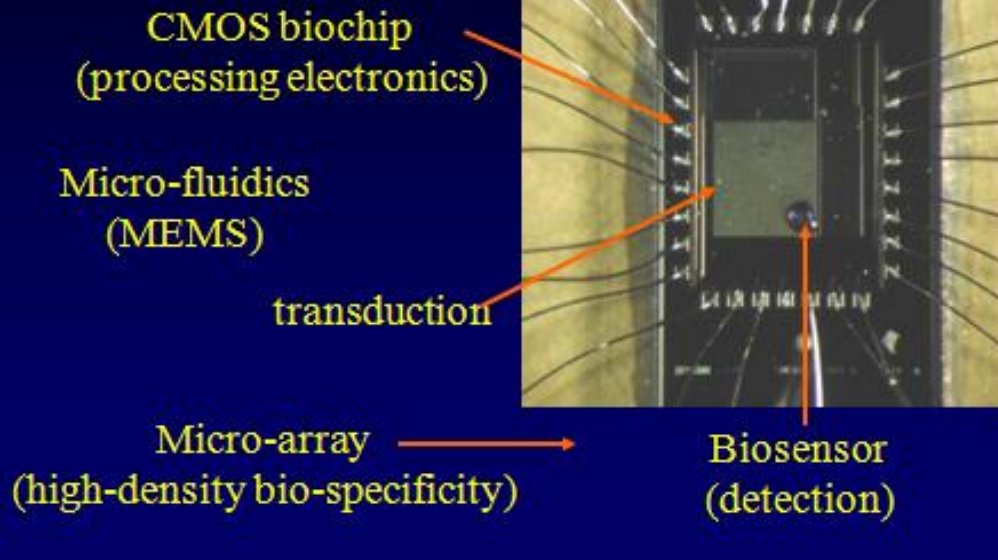


... what we wish to replace

Small provides ...

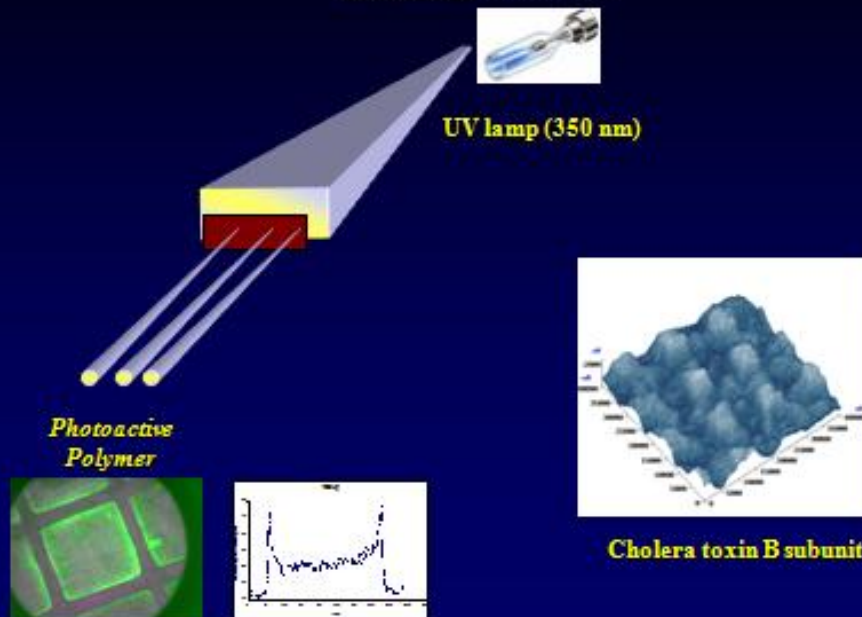
- ... high density of probes
- ... rapid reaction kinetics
- ... large number of analyses on a single chip
- ... miniaturization
- ... we will need sub-micron features
- ... but is small good?
- ... you may miss your sample!

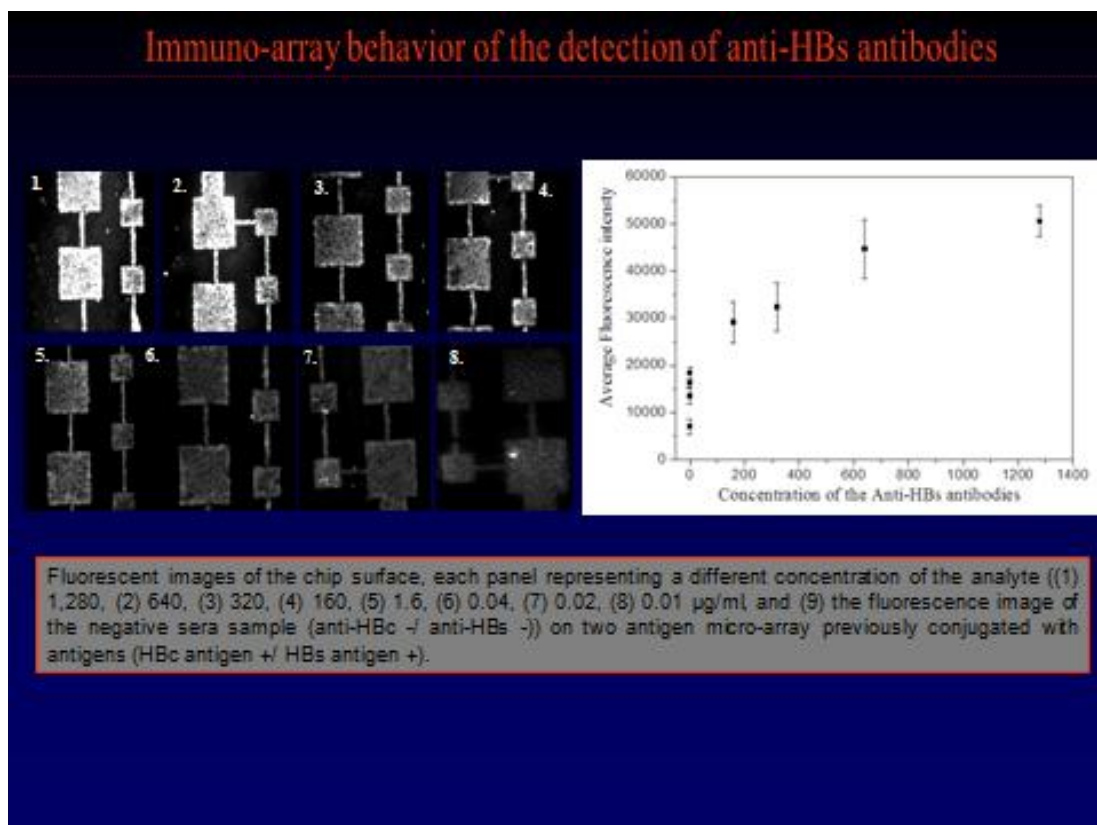
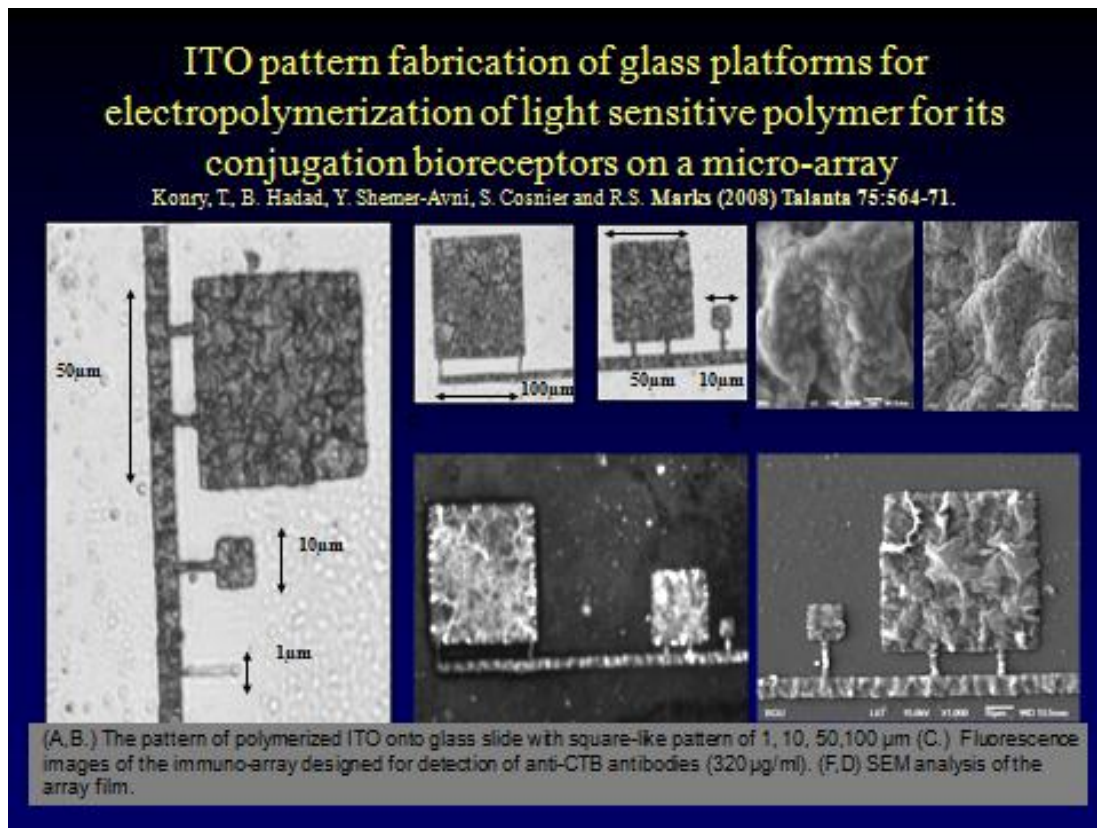
CMOS Lab-on-a-chip Biosensor module



Electrogenerated Indium tin oxide-coated glass surface with photosensitive interfaces: surface analysis

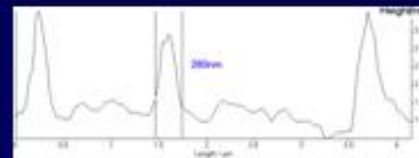
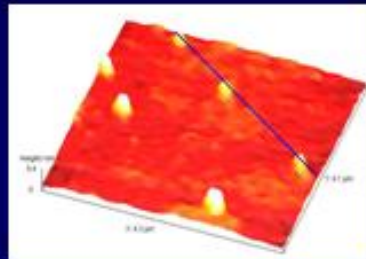
Konry, T.M. Bouhifb, S. Cosnier, M. Whelan, A. Valesia, F. Rossi, R.S. Marks (2007). *Biosensors & Bioelectronics*, 22: 2230-2236





Protein printing with an atomic force sensing nanofountainpen

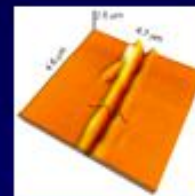
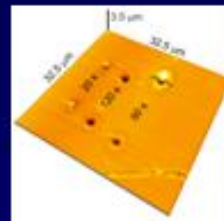
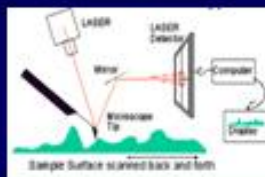
Taha, Hesham, R.S. Marks, L. A. Gheber, I. Rouso, J. Newman, C. Sukenik and A. Lewis (2003). *Applied Physics Letters*. 83 (5) 1041-1043



280 nm in diameter

Nanolithography Using Protease Etching of Protein Surfaces

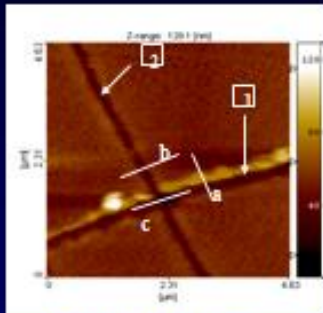
Ionescu, R., R. S. Marks and L. Gheber (2003). *Nano Letters*. 3 (12) 1639-1642



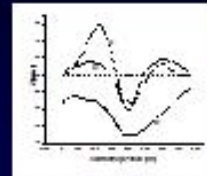
BSA surface;
200 nm pipette (wells)
50 nm pipette (groove)

Manufacturing of nano-channels with controlled dimensions using protease nanolithography

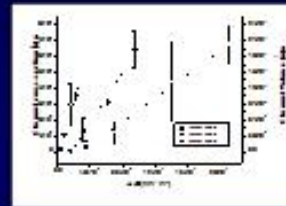
Ionescu, R.E., R.S. Marks and L. Gheber (2005). *Nanoletters*, 5 (5) 821-827



Etching is additive:
the depth of the depression at the intersection of 2 perpendicular channels is the sum of their depths (same pipette; same velocity; '1' made first 60' before '2')



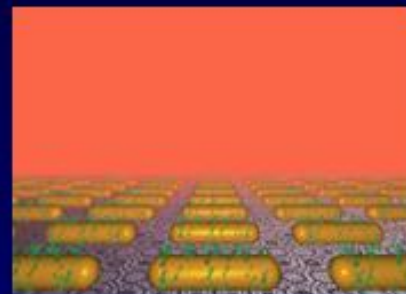
The dotted horizontal line represents the original non-swollen surface. The channel dimensions are similar (a = 17 nm; b = 20 nm; c = 36 nm).



The data splits into three different linear slopes for the three different pipette apertures, where the steepest one belongs to the smallest aperture (100 nm) and the shallowest one belongs to the largest aperture (300 nm).



Nanoantenna: SEIRS & SERS



CCHF



- Fiber optic immunosensor •
- Virus in ticks (immuno & geno) –
- Immunosensor for patients –
- Reverse genetics •
- Drug screening –

NRF CREATE - Singapore

Nanomaterials for Energy & Water
Management

Marks, Magdassi & Ma
Ben Gurion University of the Negev
Hebrew University of Jerusalem
Nanyang Technology University


Solid phase peptide synthesis resin as carrier and adjuvant for oral vaccination

- No cleavage from resin needed
- No purification of peptide needed
- Resin can be given as a bead and/or hydrogel formulation
- Resin belongs to GRAS

Funding



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Pan Stanford ‘High Tech of Biotechnology’

Nanoantenna - Lamy de la Chapelle & Pucci

Fiber optic immunosensors - Marks



Amperometric immunosensors - Cosnier

Protocols in Bioassays & Biosensors - Marks

Luminescent microbial biosensors - Thouand


Advanced techniques in viral detection- Marks,
Lobel & Sall

BGU team

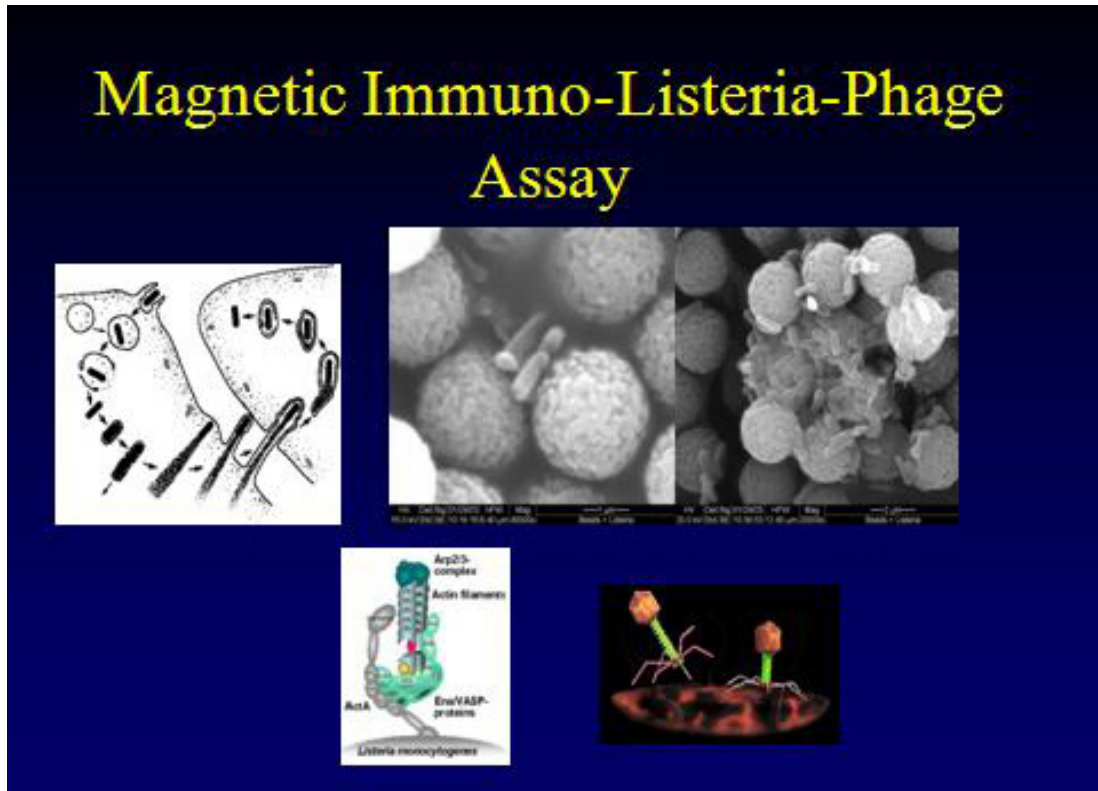
Lindy Kahanovitz
 Hila Rudoy
 Michal Illouz
 Evgeni Eltzov
 Ariel Sobarzo
 Liron Amir
 Avi Ashkenazi

... thank you ...




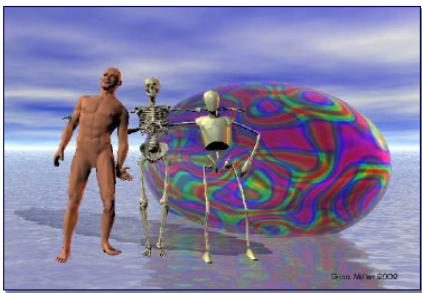

Collaborators




C.2.6 Turkey Nano-Technology Presentation – by Gürer G. Budak

Nanobiotechnology Research in Turkey

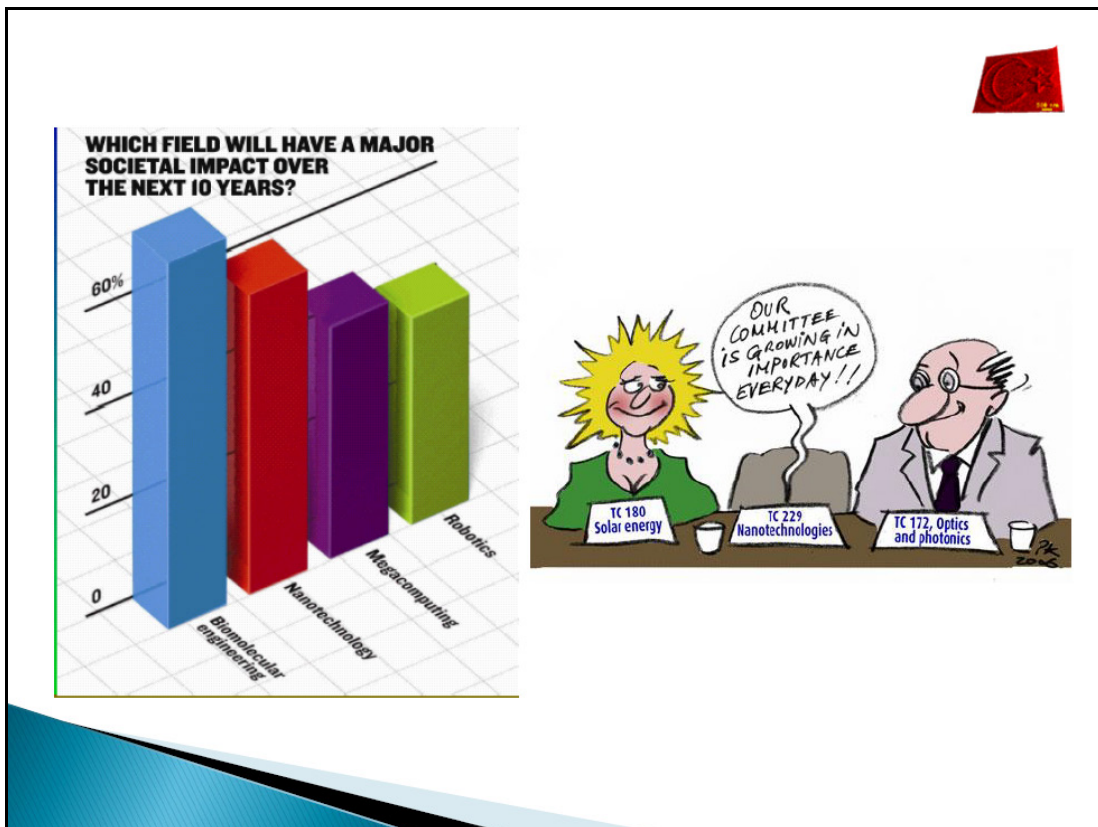
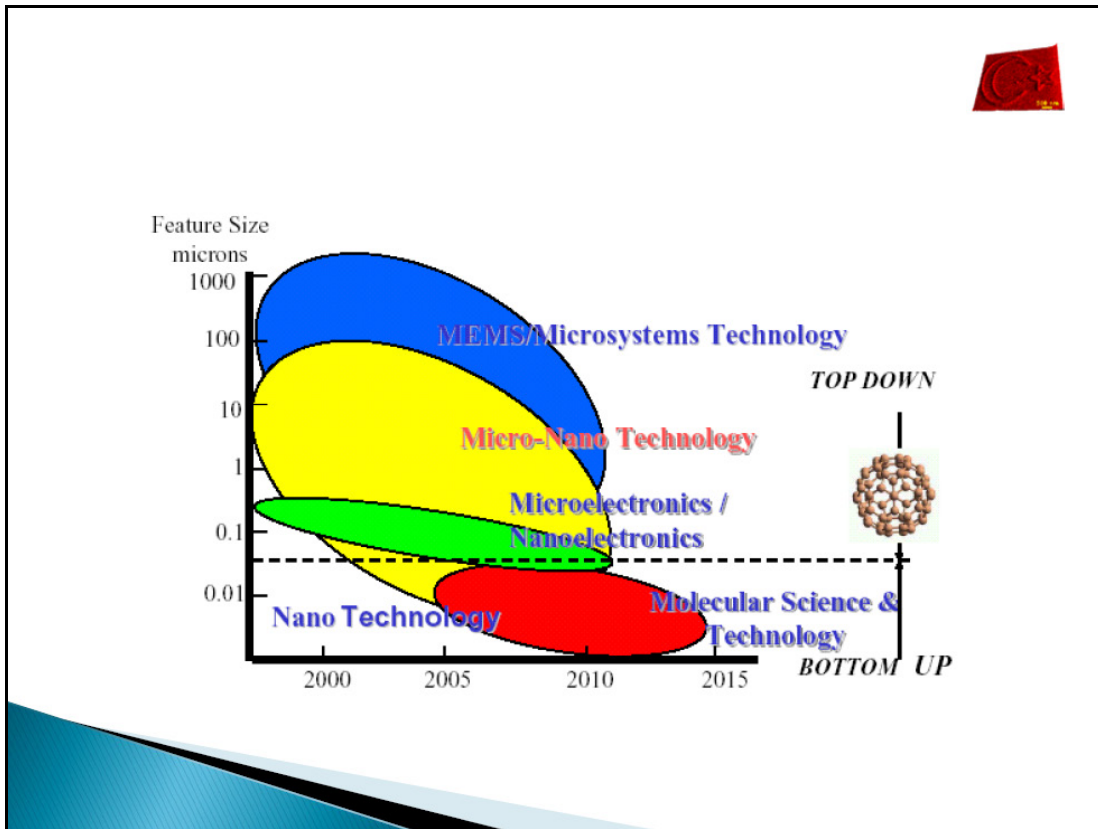





Dr. Gürer G. Budak (MD, PhD, MBA)

- Director, Nanomedicine & Advance Technology Research Center
- Member, European Technology Platform on Nanomedicine
- President, International Academy of Nanomedicine






29 October 2011
NATO HFM 177
Munich-Germany





-AANM
-IANM
-ETP-NM
-CLINAM
-AJNS



**DECISION OF
TURKISH GRAND NATIONAL ASSEMBLY
Decision on the approval of
Ninth Development Plan (2007-2013)
Decision No: 877 Decision Date: 28.06.2006**

16. Developing countries need to base their growth dynamics on productivity increases and on creating new comparative advantages in order to sustain and strengthen their competitiveness in the global arena. To this end, placing an emphasis on innovativeness, increasing scientific and technological capacity, improving human capital, and effective usage of information and communication technologies constitute importance. In the coming period, areas such as biotechnology and nanotechnology will come to the forefront.

482. Towards the future era; nanotechnology, biotechnology, new generation nuclear technologies and hydrogen and fuel battery technologies; research in the sectors to be given priority by the industrial policy; R&D activities that aim to transform local resources into value-added; research in the field of health to increase the quality of life, primarily vaccination and anti-serums; information and communication technologies, and defense and space technologies, will be supported as priority fields.



Governmental Financial Support for Research




State Planning Organization of T.R.



The Scientific and Technological Research Council of Turkey

Nanobiotechnology Research in Turkey



EXCUSE ME, WHERE'S THE NANOTECHNOLOGY DEPARTMENT?

YOU JUST TROD ON IT

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GOPPYARD



- Nanoparticle Fabrication and Characterization Laboratory
- Histo-Pathology Laboratory
- Immunobiology Laboratory
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- ▶ Early Diagnosis and Imaging Systems
- ▶ Targeted Drug Delivery Systems
- ▶ Tissue–Material Science Engineering and Regenerative Medicine



Homepage	Homepage	 <p>Nanotechnology and Nanomedicine Division</p>
About Our Division	<p>NANOTECHNOLOGY AND NANOMEDICINE</p> <p>While the "nanotechnology", which is defined as the scientific and industrial revolution of the 21st century, quickly enters in our life with the products in health, food, agriculture, textile, communication, transporting, defense industry, space and aircraft technologies, also creates new horizons in science and technology with the interdisciplinary research and development activities.</p> <p>Many leading, research and development centers and firms in the world concentrate on the research in nanoscience and nanotechnology in order to increase international competitive capacity. The universities such as Washington, Stanford, Northeastern and institutes like MIT and Stevens found nanotechnology academic programs.</p> <p>Read More</p> <p>The Purposes of Nanotechnology and Nanomedicine (NNT) Interdisciplinary MSc and PhD graduate Program:</p>	
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
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Undersecretariat for Defence Industries Export Portal
International Cooperation Department







MISSION IS:
 To meet the system requirements of Turkish Armed Forces and the government organizations those promote the national defense and security;
 to establish and implement the strategy and procedures
 for the development of defense industry





Undersecretariat for Defence Industries Export Portal
International Cooperation Department



STRATEGIC GOAL 1: TO IMPROVE THE PROCUREMENT ACTIVITIES IN ACCORDANCE WITH THE USER REQUIREMENTS AND INDUSTRIAL GOALS

- 1.1 In order to enhance procurement management capability, project management processes will be improved .
- 1.2 In accordance with achieving the user satisfaction, project cycle times (duration between kick-off and contract awarding) will be shortened.
- 1.3 Quality, test and certification activities will be improved timely and costly.
- 1.4 Decisions given in project management will be consistent with institutional strategies.

STRATEGIC GOAL 2: TO RESTRUCTURE THE DEFENCE INDUSTRY TO BE ABLE TO PROVIDE UNIQUE LOCAL SOLUTIONS AND COMPETE IN THE INTERNATIONAL ARENA

- 2.1 Indigenous share in expenditures for Turkish Armed Forces' defense equipment expenditures shall be enhanced.
- 2.2 Activities that ensure sustainability and improve efficiency in the local defense industry will be actualized.
- 2.3 Integration of SME's and supplier companies to defense industry shall be enhanced.
- 2.4 It shall be ensured that R&D Roadmap and Network of Excellences' operate effectively.

STRATEGIC GOAL 3: TO PARTICIPATE ACTIVELY IN THE MULTINATIONAL DEFENCE AND SECURITY PROJECTS THOSE PROMOTE THE INTERNATIONAL COOPERATION

- 3.1 By fostering the specialization and encouraging the local industry to take place in international supply chain, strategic cooperation efforts will be promoted.
- 3.2 Turkish industry share in NATO defense projects shall be increased.
- 3.3 Export of defense and aeronautics products will be promoted and supported.

STRATEGIC GOAL 4: TO IMPROVE THE ORGANIZATIONAL STRUCTURE

- 4.1 Strategic Human Resources Program will be executed to employ highly qualified staff, to provide necessary training and basis for productive environment and to maintain organizational loyalty.
- 4.2 Knowledge and performance based management approach and strategic management systematic shall be institutionalized.
- 4.3 Governance and security of produced information and sharing of knowledge will be improved in the organization.



 Undersecretariat for Defence Industries Export Portal
International Cooperation Department



Center of Excellence



Autonomous Management



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Center of Excellence



Advanced Materials



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Center of Excellence



Micro & Nanotechnologies





HAZ-MAT ID CWA Detector
sensIR Technologies

Joint Biological Point Detection System (JBPDS) General Dynamic

Joint Service Lightweight Standoff Chemical Agent Detector (JSLSCAD) General Dynamic

M21 Remote Sensing CWA Detector / Alarm (RSCAAL)

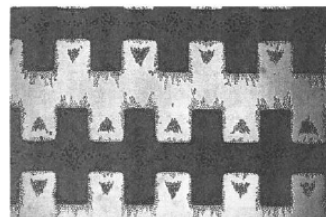
AP2C Remote Sensing CWA Detector / Alarm Proengin Inc.

UV Sentry Toxic Chemical Perimeter Monitor Ocean Optics, Inc.

Nanobiotechnology Research in Turkey

Applications of Biosensors

- Biosensors harness the immensely powerful molecular recognition properties of living systems and engineer these into electronic devices to provide easy-to-use sensing devices.
- Biosensors can be used more generally to measure
 - Disease markers
 - Food safety
 - Environmental quality
 - **To ensure safety and security**

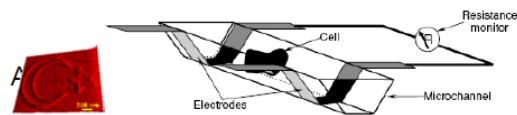
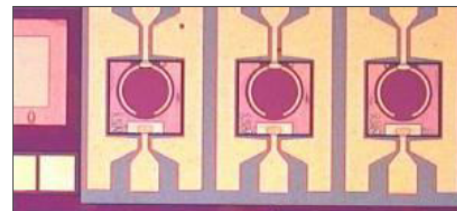
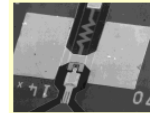


Nanobiotechnology Research in Turkey

Diagnosis and Imaging

□ In Vitro Applications

- chemo-bio nanosensors
- ultra-sensitive biochips
- “lab-on-a-chip” devices
- “cells-on-chips” devices



Biomol Microdevices (2008) 10:321–328
DOI 10.1007/s10544-007-9139-2

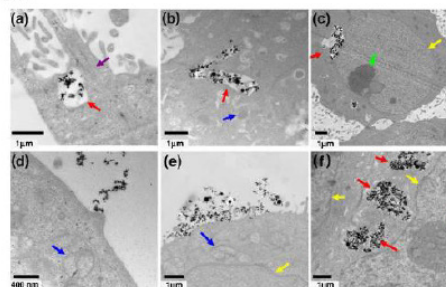


Zeta potential: a surface electrical characteristic to probe the interaction of nanoparticles with normal and cancer human breast epithelial cells

Yu Zhang · Mo Yang · Nathaniel G. Portney ·
Daxiang Cui · Gurer Budak · Ekmel Ozbay ·
Mihrimah Ozkan · Cengiz S. Ozkan

Published online: 29 December 2007
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Fig. 4 Transmission Electron Micrographs of MCF10A cells that were incubated with iron oxide nanoparticles for 30 min (a), 4 h (b) and 24 h (c) at 37°C. Transmission Electron Micrographs of MCF10A cells that were incubated with iron oxide nanoparticles for 30 min (d), 4 h (e) and 24 h (f) at 37°C. All slices were treated with uranyl acetate to stain membranes and lead citrate to stain the nuclear body. Colored arrows represent selected cell organelles: nuclei (yellow), nucleolus (green), mitochondria (blue), and vesicles with iron oxide nanoparticles inside (red), filaments (purple).





ADVANCED MATERIALS

DOI: 10.1002/adma.20702863

Synthesis and Characterization of Iron Oxide Derivatized Mutant Cowpea Mosaic Virus Hybrid Nanoparticles^{90*}

By Alfredo A. Martinez-Morales, Nathaniel G. Portney, Yu Zhang, Giuseppe Desito, Gurer Budak, Ekmel Ozbay, Marianne Manchester, Cengiz S. Ozkan,⁹¹ and Mihrimah Ozkan⁹²

Extensively investigated and mutagenized Cow Pea Mosaic Virus (CPMV) has been demonstrated in a variety of nanossemblies.⁹³⁻⁹⁵ Iron Oxide (IO) has the potential to surpass limits of detection in bioimaging applications. Particularly γ-Fe₂O₃ (magnetite) is considered as one of the most desirable materials for technological and biomedical applications due to its inherent biocompatible nature.^{92,93} Additionally, magnetite nanoparticles could be directed to an organ, tissue, or tumor using an external magnetic field or heated under an alternating magnetic field.⁹⁴ Based on the unique magnetic properties of IO nanoparticles they have been extensively used in biomedical applications, such as magnetic resonance imaging, targeting drug delivery and hyperthermia therapy detoxification and cell separation.⁹⁶⁻¹⁰¹

Combining the two systems can be devised to enhance the local magnetic field strength, by organizing monodisperse IO clusters on a CPMV-T184C mutant viral template. It is known that contrast enhancement is observed by use of superparamagnetic iron oxide nanoparticles (SPIONs) based MRI, by creating large dipolar magnetic field gradients due to their local field inhomogeneity. However, clustering a greater number of IO nanoparticles can further improve contrast beyond free particle SPIONs enhanced MRI, by creating a cumulative dipole effect.¹⁰²

CPMV-T184C is a useful model that has a well characterized structure amenable to surface functionalization.¹⁰³ The smallest repeating structure (asymmetric unit, composed of a "small" (24kD) and "large" (42kD) subunit) displays 5 solvent exposed cysteines used for IO linkage.⁹⁸ By insertion of a cysteine, at residue 184 of the small subunit, anchorage of CPMV to a self assembled monolayer (SAM) on gold substrate pathway can be employed. A previously reported SAM on Au stepwise assembly was used to integrate monodisperse CPMV-IO hybrids for characterization.¹⁰⁰

It is also been shown that aggregation of iron oxide particles can exhibit a greater magnetic dipole, and can be suited for in bio-imaging, provided certain properties are met. Harris et al.¹⁰⁴ demonstrated protease activated aggregation of pegylated iron oxide nanoparticles with enhanced MRI contrast to be most beneficial in improving detection limits of small tumors. Pegylation of CPMV was previously demonstrated to improve circulation times and reduce immunogenicity.⁹² Also, based on enhanced permeability and retention effects (EPR)¹⁰⁵ the longest retention times at tumor sites for nanoparticles occurred for 60-400 nm.¹⁰⁶ Above 300 nm, there is vulnerability to macrophage phagocytosis,¹⁰⁷ and below 10 nm, nanoparticles can leave the systemic circulation via the lymph nodes.¹⁰⁸ Therefore, the IONs-CPMV nanoparticle hybrid system synthesized and MEM characterized in this report could be used for contrast enhanced MRI applications.

In this work the local enhancement of field strength is studied and demonstrated by magnetic force microscopy



⁹¹ Prof. C. S. Ozkan, Y. Zhang
Department of Mechanical Engineering,
University of California Riverside,
92521 Riverside, CA (USA)
E-mail: ozkand@ucr.edu


Prof. M. Ozkan, A. A. Martinez-Morales
Department of Electrical Engineering,
University of California Riverside,
92521 Riverside, CA (USA)
E-mail: mto@ucir.edu

Dr. N. G. Portney
Department of Biomechanical Engineering, University of California Riverside,
92521 Riverside, CA (USA)

Dr. G. Desito, Prof. M. Manchester
Department of Cell Biology, The Scripps Research Institute
92037 La Jolla, CA (USA)

Prof. G. Budak
Faculty of Medicine, Nanomedicine Research Laboratory,
Gazi University
06510 Ankara (Turkey)

Prof. E. Ozbay
Nanotechnology Research Center
Department of Electrical and Electronics Engineering
and Department of Physics
Sakarya University
06800 Ankara (Turkey)





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Size controlled synthesis of sub-100 nm monodisperse poly(methylmethacrylate) nanoparticles using surfactant-free emulsion polymerization

Sevket Tolga Camli¹, Fatih Buyukserin, Oguz Balci, Gurer Guven Budak

Nanomedicine and Advanced Technologies Research Center, Gazi University, 06830 Ankara, Turkey

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Surfactant-free emulsion polymerization
Monodisperse
Dynamic light scattering

ABSTRACT

Surfactant-free emulsion polymerization (SFEP) is a well-known technique for the production of polymeric nanoparticles that does not require post-synthetic cleaning steps. Obtaining hydrophobic particles at sub-100 nm scale, however, is quite challenging with this polymerization method. Here, we demonstrate a single step synthetic approach that yields poly(methylmethacrylate) (PMMA) nanoparticles with controlled sub-100 nm size and relatively high resultant solid content. Dynamic light scattering (DLS) was used for the particle characterization. Spherical and uniformly sized nanoparticles were confirmed by atomic force microscopy (AFM) and scanning electron microscopy (SEM). Acetone was used as a cosolvent in order to obtain monodisperse sub-100 nm diameter particles. Stable PMMA nanoparticle dispersions were obtained for all formulations where the persulfate initiator causes the negative charges on the particle surface. The effects of acetone, monomer and initiator concentration were studied to optimize average particle hydrodynamic diameter and polydispersity index of the final particles. Non-crosslinked monodisperse PMMA nanoparticles (polydispersity index less than 0.05) with diameters from 32 nm to 72 nm were synthesized by using this method.

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Colloids and Surfaces A: Physicochem. Eng. Aspects 366 (2010) 141–146

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Colloids and Surfaces A: Physicochemical and Engineering Aspects

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Fine-tuning of functional poly(methylmethacrylate) nanoparticle size at the sub-100 nm scale using surfactant-free emulsion polymerization

Sevket Tolga Camli*, Fatih Buyukserin, Mustafa Selman Yavuz, Gürer Güven Budak

Nanomedicine and Advanced Technologies Research Center, Gazi University, 06830 Ankara, Turkey

ARTICLE INFO

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 Surfactant-free emulsion polymerization
 Monodisperse
 Dynamic light scattering

ABSTRACT

Functional poly(methylmethacrylate) (PMMA) nanoparticles are of great use in various research areas from photonic band gap materials to biomolecule delivery vehicles. Herein, we introduce a conventional surfactant-free emulsion polymerization (SFEP) method that enables the production of functional sub-100 nm PMMA nanoparticles without the need of microwave irradiation. Cross-linked PMMA latex having monodisperse size distribution can be prepared. Particle characterization studies were carried out using dynamic light scattering (DLS). Spherical and uniformly sized nanoparticles were observed by scanning electron microscopy (SEM). Stable cationic PMMA nanoparticle dispersions were obtained for all formulations where the particle charge stems from the amidine initiator. The presence of the amidine moieties was confirmed by using an isothiocyanate containing fluorophore. An important appealing feature of this method is the ability to fine-tune the resultant particle size at the sub-100 nm scale by simply varying the monomer concentration.

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RESEARCH ARTICLE

Antibody-functionalized nano test tubes target breast cancer cells

Alihan R. Akbulut¹, Ceylan P. Akbulut², Mehmet P. Akbulut³, Aydin Akbulut⁴, Mustafa Selman Yavuz⁵, Mustafa Selman Yavuz⁶, Mustafa Selman Yavuz⁷, Mustafa Selman Yavuz⁸, Mustafa Selman Yavuz⁹, Mustafa Selman Yavuz¹⁰


*1*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *2*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *3*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *4*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *5*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *6*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *7*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *8*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *9*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey; *10*Department of Chemistry, Faculty of Sciences, Gazi University, Ankara, Turkey


AIM: To develop nano test tubes that will deliver a biomedical payload to a specific cell type. **METHODS:** The template-synthesis method was used to prepare silica nano test tubes. An antibody that is specific for breast cancer cells was attached to the outer tube surface. A fluorescent dye was attached to the inner surface of the nano test tubes. The tubes were incubated with the breast cancer cells and the extent of attachment to the cell surface was investigated by fluorescence microscopy. **RESULTS:** Tubes modified on their outer surface with the target antibody showed enhanced attachment to breast cancer cells, relative to tubes modified on their outer surfaces with a spacer and spacer-mustard control antibody. **CONCLUSIONS:** This work is a first step toward demonstrating that nano test tubes can be used as cell-specific delivery vehicles.

Nanoparticles, such as nano spheres, tubes and wires, have been proposed for use in various biomedical applications (1), including imaging (2-4), drug/gene/protein (5) and biomolecule delivery (6-8). In particular, the use of nanoparticles in biomolecule delivery offers a number of advantages, such as increased efficacy (9), protection of the drug (10) or genetic material (11), payload and reduced drug toxicity (10). Spherical nanoparticles are often chosen, used because this shape is most amenable to spherical particles can be synthesized from a diverse range of materials, such as lipids (12), polymers (13), dendrimers (14) and various inorganic compounds (15,16).

Nanotubes are an alternative to spherical nanoparticles; however, to date, there have only been a few reports of their use in biomedical contexts, mostly through carbon (17,18), silica (19,20) and polymer based nanotubes (21). We have pioneered a methodology called template synthesis, for preparing nanotubular structures of nearly any size and composed of nearly any material (22-24). These template-synthesized nanotubes have a number of attributes that make them potential candidates for biomolecule delivery applications. First, for any aspect ratio above unity, a nanotube will have a larger inner volume than a spherical nanoparticle of the same diameter. This should enable nanotubes to carry a correspondingly larger payload. In addition, the template method enables differential chemical functionalization of the inner versus the outer surfaces of the nanotubes (25). Multifunctional delivery vehicles could be obtained by this differential modification strategy. Such delivery tools have attracted great interest in biomedical applications; for example,

Figure 3. Transmission electron microscopy image of silica nano test tubes.





nature materials

LETTERS

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Gold nanocages covered by smart polymers for controlled release with near-infrared light

Mustafa S. Yavuz*, Yiyun Cheng*, Jingyi Chen*, Claire M. Cobley, Qiang Zhang, Matthew Rycenga, Jingwei Xie, Chulhong Kim, Kwang H. Song, Andrea G. Schwartz, Lihong V. Wang and Younan Xia[†]

Photosensitive caged compounds have enhanced our ability to address the complexity of biological systems by generating effectors with remarkable spatial/temporal resolutions^{1–3}. The caging effect is typically removed by photolysis with ultraviolet light to liberate the bioactive species. Although this technique has been successfully applied to many biological problems, it suffers from a number of intrinsic drawbacks. For example, it requires dedicated efforts to design and synthesize a precursor compound for each effector. The ultraviolet light may cause damage to biological samples and is suitable only for *in vitro* studies because of its quick attenuation in tissue⁴. Here we address these issues by developing a platform based on the photothermal effect of gold nanocages. Gold nanocages represent a class of nanostructures with hollow interiors and porous walls⁵. They can have strong absorption (for the photothermal effect) in the near-infrared while maintaining a compact size. When the surface of a gold nanocage is covered with a smart polymer, the pre-loaded effector can be released in a controllable fashion using a near-infrared laser. This system works well with various effectors without involving sophisticated syntheses, and is well suited for *in vivo* studies owing to the high transparency of soft tissue in the near-infrared region⁶.

Figure 1a shows a schematic of the controlled-release system. solution drops to 90% of the original value⁸. By incorporating acrylamide (AAm) into the polymer chain, we obtained pNIPAAm-co-pAAm copolymers with LCSTs being tuned to anywhere in the range of 32–50°C (Supplementary Fig. S1 and Table S1; ref. 8). For *in vivo* applications, the LCST should be tuned to a value above the body temperature (37°C) but below the hyperthermia temperature (42°C). Here, we have focused on two types of polymer: pNIPAAm and a pNIPAAm-co-pAAm copolymer with an LCST at 32 and 39°C, respectively. Both were prepared using atom-transfer radical polymerization^{11,12}.

We covalently anchored the smart polymer to the surface of Au nanocages by means of gold-thiolate linkage. One way to achieve this is to include a disulfide bond in the middle of the polymer chain by using a disulfide initiator¹³ (Fig. 1b). As thiolate has a stronger binding towards the Au surface than the C=O group of poly(vinyl pyrrolidone) (PVP), we could replace the PVP on nanocages with the smart polymer. After the displacement, the absorption peak of the nanocages redshifted by ~13 nm, which could be offset during the nanocage synthesis. As shown in Fig. 1c by transmission electron microscope (TEM) imaging, the pNIPAAm-co-pAAm coating had a relatively uniform thickness of ~9 nm in the dry state. This result is in reasonable agreement with the value (~5 nm) estimated from the thermogravimetric analysis and gel permeation chromatography data shown in Supplementary Fig. S2 and S3.





EU FRAMEWORK PROGRAMME 7
PEOPLE SPECIFIC PROGRAMME
MARIE CURIE ACTIONS
Marie Curie International Reintegration Grants
FP7-PEOPLE-IRG-2009

Project Title : MULTIFUNCTIONAL COMPOSITE SILICA NANOTUBES FOR TARGETED DELIVERY, “MuCoSiNT”

Primary Investigator : Dr. Fatih Büyükserin (PhD)

Project Coordinator : Prof. Dr. Gürer G. Budak (MD, PhD, MBA)

Institution : Nanomedicine & Advanced Technologies Research Center, Gazi University, Ankara, Turkey

Budget : 75.000 Euro

Period : 36 months (2009-2012)

Source : European Union



**EU FRAMEWORK PROGRAMME 7
PEOPLE SPECIFIC PROGRAMME
MARIE CURIE ACTIONS
Marie Curie International Reintegration Grants
FP7-PEOPLE-IRG-2009**

Project Title : SELF-ASSEMBLED THERMO-NANOPROBES ON HOLLOW GOLD NANOPARTICLES FOR THERAGNOSTIC APPLICATIONS, "TNP-HGNs"

Primary Investigator : Dr. Mustafa Selman Yavuz (PhD)

Project Coordinator : Prof. Dr. Gürer G. Budak (MD, PhD, MBA)

Institution : Nanomedicine & Advanced Technologies Research Center, Gazi University, Ankara, Turkey

Budget : 75.000 Euro

Period : 36 months (2010-2013)

Source : European Union



Thank You !

Dr. Gürer G. Budak (MD, PhD, MBA)

- Director, NanoMedicine & Advance Technology Research Center
- Member, European Technology Platform on Nanomedicine
- President, International Academy of Nanomedicine

C.2.7 BioMedAC Presentation – by François Thibault



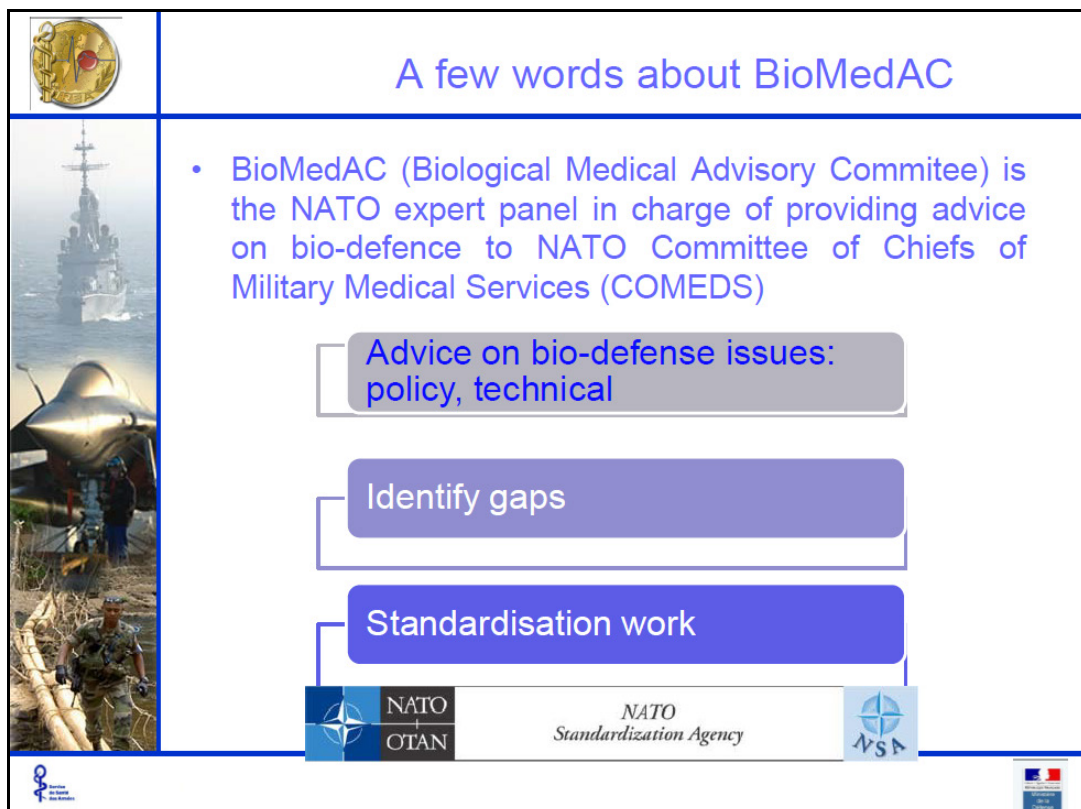
2011 • Munich • Germany
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 Medical
 Conference

25 - 28 October 2011
 Bundeswehr Medical Academy, Munich

Rapidly Deployable Outbreak Investigation Team (RDOIT):
The NATO toolbox for suspect outbreak investigations

Pharm. Col. François THIBAUT
 IRBA/CRSSA, La Tronche, FRANCE

Presentation given on the behalf
 of the NATO BioMedAC Expert Panel



A few words about BioMedAC

- BioMedAC (Biological Medical Advisory Committee) is the NATO expert panel in charge of providing advice on bio-defence to NATO Committee of Chiefs of Military Medical Services (COMEDS)

Advice on bio-defense issues:
 policy, technical





Identify gaps





Standardisation work

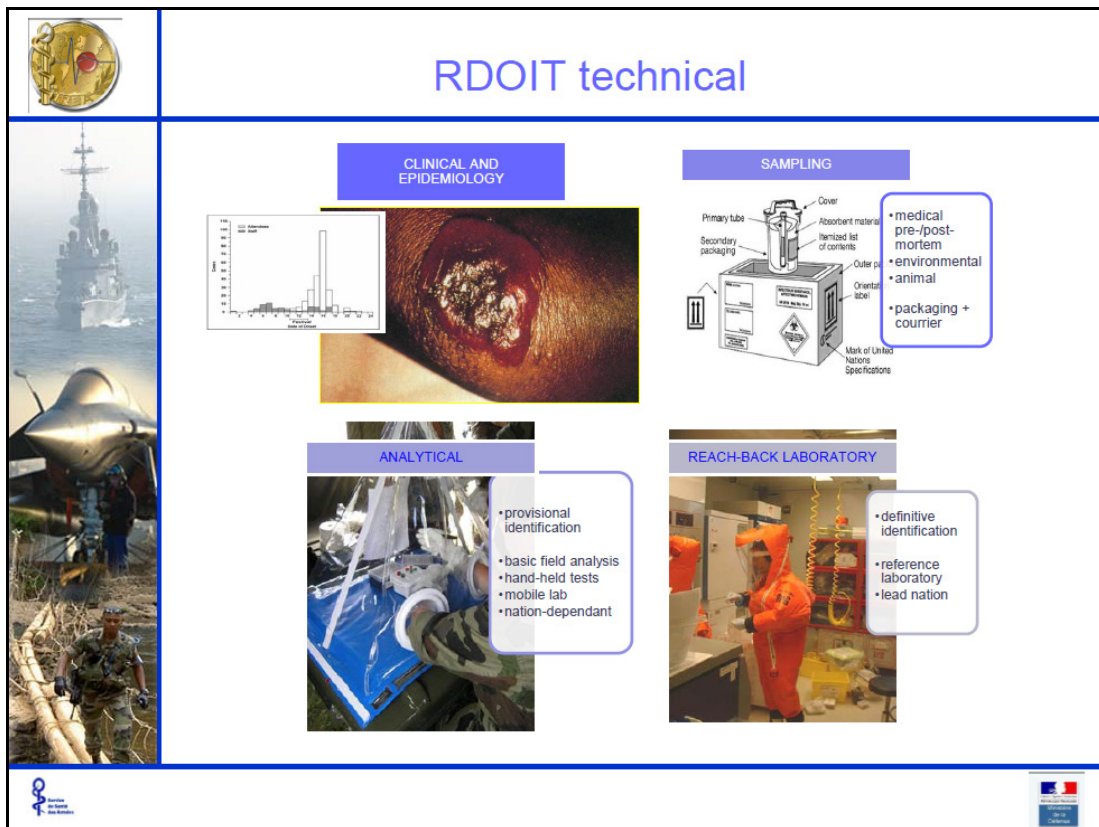
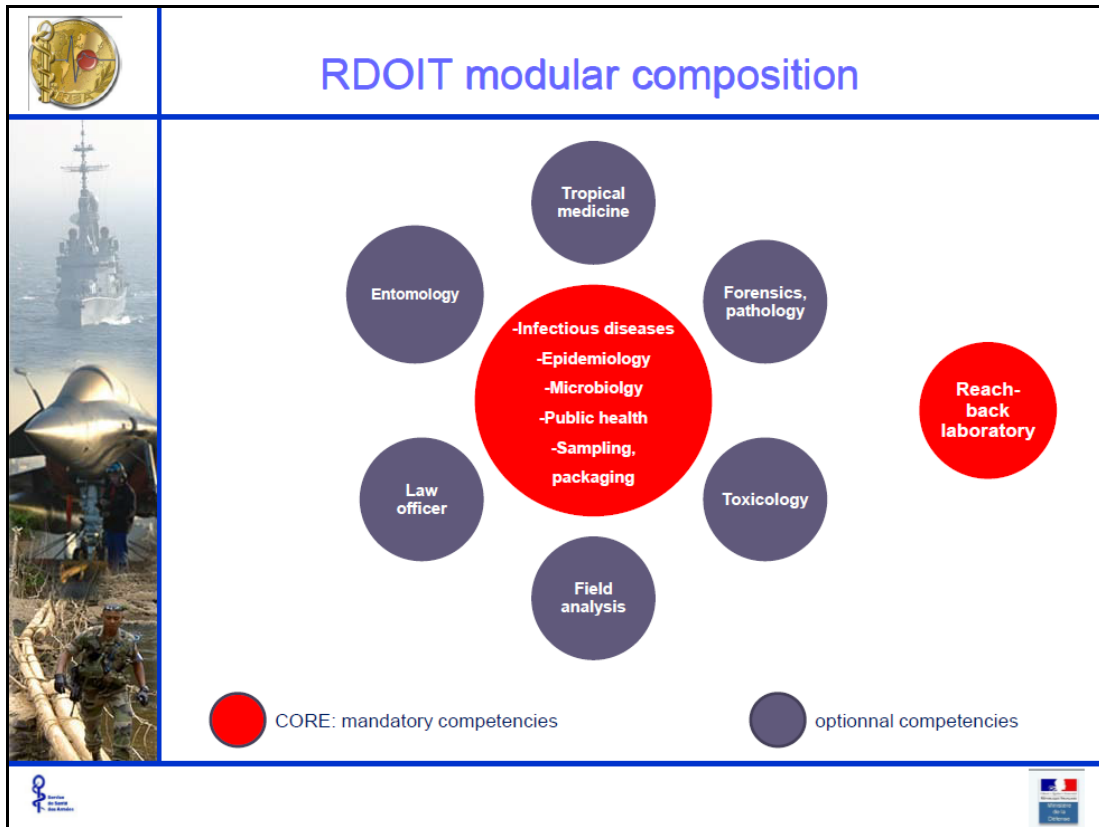
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 VSA


	<h2 style="text-align: center;">Some BioMedAC EP deliverables</h2>
	<ul style="list-style-type: none"> • Expert advice <ul style="list-style-type: none"> • biological threat “dirty dozen” • decontamination “how clean is clean” • smallpox vaccine, deployable laboratory,... • Standardisation documents <ul style="list-style-type: none"> • NATO handbook on the medical aspects of NBC defensive operations (AMedP-6) • Concept of operations of medical support in CBRN environments (AMedP-7) • Planning guide for the estimation of CBRN casualties (AMedP-8) • Rapidly deployable outbreak investigation team (RDOIT) for suspected use of biological warfare agents (STANAG 2529) • ...

	<h2 style="text-align: center;">Impact of biological threat on NATO operations</h2>
	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>High morbidity/mortality rates</p> <ul style="list-style-type: none"> • Highly pathogenic agents <p>Dramatic clinical course</p> <ul style="list-style-type: none"> • Aerosol route (unusual clinical presentation) <p>Risk of epidemic spread</p> <ul style="list-style-type: none"> • Contagious diseases (smallpox, plague) </div> <div style="text-align: center;"> <p>Delayed diagnosis</p> <ul style="list-style-type: none"> • Uncommon forms of uncommon diseases <p>Delayed agent identification</p> <ul style="list-style-type: none"> • Specialised diagnostic tools needed • Limited field capabilities </div> </div> <div style="display: flex; justify-content: space-around; margin-top: 20px;"> <div style="background-color: #444; color: white; padding: 5px; width: 40%;">Overwhelmed medical resources</div> <div style="background-color: #444; color: white; padding: 5px; width: 40%;">Limited field expertise</div> </div> <div style="background-color: #444; color: white; padding: 5px; text-align: center; margin-top: 10px;"> Unnecessary casualties Mission failure </div> <div style="background-color: red; color: white; padding: 10px; text-align: center; margin-top: 10px; font-weight: bold; font-size: 1.2em;"> CAPABILITY GAP </div>


	<h2>Rapidly deployable outbreak investigation team (RDOIT)</h2>
	<ul style="list-style-type: none"> • To send highly (and adequately) specialised staff to the theater... • ...to compensate lack of expertise on the field • ...to investigate outbreak(s) or incident(s) where intentional use of biological agents (biowarfare, bioterrorism or biocrime) cannot be excluded • ...to support operational decision-making <ul style="list-style-type: none"> • advise on prevention and control measures • assist commander and medical authorities
	


	<h2>RDOIT characteristics</h2>
	<div style="display: flex; justify-content: space-around;"> <div data-bbox="494 1288 750 1825" style="background-color: #1a3d7a; color: white; padding: 10px;"> <p>Technical</p> <ul style="list-style-type: none"> • Autonomous team • Tailored to the mission <ul style="list-style-type: none"> • modularity • Small footprint • Mobility • Reach-back laboratory </div> <div data-bbox="766 1288 1021 1825" style="background-color: #4a69bd; color: white; padding: 10px;"> <p>Staff</p> <ul style="list-style-type: none"> • High-level of expertise • Core + optional competencies • Operationally trained </div> <div data-bbox="1037 1288 1292 1825" style="background-color: #6a8bd9; color: white; padding: 10px;"> <p>Operational</p> <ul style="list-style-type: none"> • Multinational composition <ul style="list-style-type: none"> • lead nation • 48h notice-to-move • Op control: Theatre Commander </div> </div>
	








RDOIT triggering mechanism






- Triggering events can be very diverse
- Data from the medical treatment facilities
 - Identification among military or civilians of case(s) of an infectious disease:
 - not known to be endemic in the region of deployment
 - when incidence is much higher than usually encountered
 - spreading with such a high casualty rate that treatment facilities are likely to be overwhelmed
 - All cases of infectious diseases known or considered likely to be suitable for use as a BW agent, which should be regarded as suspicious.
- Data from the disease surveillance system
- Preserve RDOIT efficiency
 - Limited resource, no continuous deployment











RDOIT in a multinational environment



International	<ul style="list-style-type: none"> • Civilian organisations/agencies • Health reporting regulations
Host nation	<ul style="list-style-type: none"> • Public health authorities • Hospitals/clinical labs.
Theater	<ul style="list-style-type: none"> • Field Commander • Medical treatment facilities • CBRN assets






Where we are

- RDOIT concept has been transcribed into a Standardisation Agreement (STANAG 2529)
 - ratified by 18 nations
 - promulgated in 2009
- RDOIT in use or in development in several countries
- The way ahead:
 - planning guidance document

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NATO STANDARDIZATION AGENCY
AGENCE OTAN DE NORMALISATION



MILITARY COMMITTEE MEDICAL STANDARDIZATION BOARD (MCMedSB)

29 October 2009 NSA(MED)1179(2009)CBRNMED/2529

MCMedSB

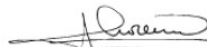
STANAG 2529 CBRN/MED (EDITION 1) – RAPIDLY DEPLOYABLE OUTBREAK INVESTIGATION TEAM (RDOIT) FOR SUSPECTED USE OF BIOLOGICAL WARFARE AGENTS

Reference: NSA(MED)G208(2009)CBRNMED/2529 dated 18 February 2009 (Edition 1) (Ratification Draft 1)

1. The enclosed NATO Standardization Agreement, which has been ratified by nations as reflected in the NATO Standardization Document Database (NSDD), is promulgated herewith.
2. The reference listed above is to be destroyed in accordance with local document destruction procedures.

ACTION BY NATIONAL STAFFS

3. National staffs are requested to examine their ratification status of the STANAG and, if they have not already done so, advise the MCMedSB, NSA, through their national delegation as appropriate of their intention regarding its ratification and implementation.






Juan A. MORENO
Vice Admiral, ESP(N)
Director, NATO Standardization Agency

Enclosure:
STANAG 2529 (Edition 1)

NATO Standardization Agency – Agence OTAN de normalisation
B-1110 Brussels, Belgium Internet site: <http://nssa.nato.int>
E-mail: joint@nssa.nato.int – Tel 32.2.707.5573 – Fax 32.2.707.5718


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









RDOIT in FRANCE : EMIBE

- "mobile element for biological and epidemiological investigation "
 - based on mobile lab for parasitology investigation
 - technical :
 - self-contained (transport boxes)
 - serology
 - real-time PCR
 - pathogen identification and culture
 - pre-development phase
 - DGA contract



	<h2>CONCLUSION</h2>
	<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="background-color: #4a7ebb; color: white; padding: 10px; width: 30%;"> <h3>RDOIT concept</h3> <ul style="list-style-type: none"> • modularity • small footprint • autonomy • reach-back laboratory </div> <div style="background-color: #4a7ebb; color: white; padding: 10px; width: 30%;"> <h3>Challenges</h3> <ul style="list-style-type: none"> • developments needed • national specificities • multinational training </div> <div style="background-color: #4a7ebb; color: white; padding: 10px; width: 30%;"> <h3>Liaisons</h3> <ul style="list-style-type: none"> • field laboratory • hand held tests • disease surveillance system • applications of Nano and Bio-Technology </div> </div>
	

	
	<p>Thank you for your attention</p> <div style="display: flex; justify-content: center; align-items: center; gap: 20px;">    </div>
	<p style="display: flex; justify-content: space-between;"> Medical Biodefense Conference 2011 RDOIT  </p>



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Agent	Chemical										
Analytic	Deployable laboratory										
Biological	Radiological										
CBRN	Warfare										
14. Abstract	<p>The NATO STO Human Factors and Medicine panel chartered a Research Technical Group (HFM-177 RTG) to study "Deployable Laboratory Applications of Nano- and Bio-Technology", which focused on deployable NATO CBRN laboratory advance technologies. Over 20 expert representatives from the Czech Republic, France, the Republic of Georgia, Germany, Israel, Turkey, United Kingdom and United States participated. Each country discussed their CBRN deployable laboratory capabilities and challenges. The RTG recognized different approaches taken by each country in the development of their deployable laboratory for their country's mission. The review resulted in findings of potential novel options to customize the level of response required for NATO missions. A RTG sub-group developed a survey that aided documentation of state-of-the-art technical advances employed in current laboratories that may allow NATO to apply a customized response team depending upon the threat scenario. Many countries' found enhancement approaches from others' lessons-learned that were applicable to their deployment laboratory activities. The HFM-177 RTG meetings were great successes that allowed knowledge gathering resulting in a technical report addressing current capabilities and future directions. The RTG recommends that these findings be forwarded to the NATO Army Armaments Group, Joint Capability Group on CBRN Defence, and the Sampling and Identification of Biological, Chemical and Radiological Agents sub-group for their consideration of asset applications and for determining country agreement development for capability application in a NATO bio-response.</p>										





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Streitkräfteamt / Abteilung III
Fachinformationszentrum der Bundeswehr (FIZBw)
Gorch-Fock-Straße 7
D-53229 Bonn

GRECE (Point of Contact)

Defence Industry & Research General
Directorate, Research Directorate
Fakinos Base Camp, S.T.G. 1020
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