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RESEARCH AND TECHNOLOGY ORGANISATION

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RTO TECHNICAL REPORT **TR-HFM-057**

Biotechnologies for Assessment of Toxic Hazards in Operational Environments

(Utilisation des biotechnologies pour l'évaluation des risques toxiques en environnement opérationnel)

Final Report of HFM-057/RTG-009.

Published June 2008

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The Research and Technology Organisation (RTO) of NATO

RTO is the single focus in NATO for Defence Research and Technology activities. Its mission is to conduct and promote co-operative research and information exchange. The objective is to support the development and effective use of national defence research and technology and to meet the military needs of the Alliance, to maintain a technological lead, and to provide advice to NATO and national decision makers. The RTO performs its mission with the support of an extensive network of national experts. It also ensures effective co-ordination with other NATO bodies involved in R&T activities.

RTO reports both to the Military Committee of NATO and to the Conference of National Armament Directors. It comprises a Research and Technology Board (RTB) as the highest level of national representation and the Research and Technology Agency (RTA), a dedicated staff with its headquarters in Neuilly, near Paris, France. In order to facilitate contacts with the military users and other NATO activities, a small part of the RTA staff is located in NATO Headquarters in Brussels. The Brussels staff also co-ordinates RTO's co-operation with nations in Middle and Eastern Europe, to which RTO attaches particular importance especially as working together in the field of research is one of the more promising areas of co-operation.

The total spectrum of R&T activities is covered by the following 7 bodies:

- 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 bodies are made up of national representatives as well as generally recognised 'world class' scientists. They also provide a communication link to military users and other NATO bodies. RTO's scientific and technological work is carried out by Technical Teams, created for specific activities and with a specific duration. Such Technical Teams can organise workshops, symposia, field trials, lecture series and training courses. An important function of these Technical Teams is to ensure the continuity of the expert networks.

RTO builds upon earlier co-operation in defence research and technology as set-up under the Advisory Group for Aerospace Research and Development (AGARD) and the Defence Research Group (DRG). AGARD and the DRG share common roots in that they were both established at the initiative of Dr Theodore von Kármán, a leading aerospace scientist, who early on recognised the importance of scientific support for the Allied Armed Forces. RTO is capitalising on these common roots in order to provide the Alliance and the NATO nations with a strong scientific and technological basis that will guarantee a solid base for the future.

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Explanation of Acronyms, Abbreviations and Nomenclature

ACGIH	American Society for Governmental Industrial Hygienists (USA)
ADI	Acceptable Daily Intake
AFPMB	Armed Forces Pest Management Board
ANAM	Automated Neuropsychological Assessment Metric, an experimental computerized system for cognitive function testing developed by the US Army Medical Research and Materiel Command
Apoptosis	Early changes in pathways leading to programmed cell death; used as a marker of accelerated cell death associated with toxic chemical exposures
ATSDR	Agency for Toxic Substances and Disease Registry (USA)
BAT	Biologischer Arbeitsstofftoleranzwert (Biological Tolerance Value for Occupational Exposures)
BDU	Battle Dress Uniform
Br_2CA	cis- 3 -(2,2-dibromovinyl)- 2,2-dimethylcyclopropanol- carboxylic acid (pyrethroid metabolite)
BW	Body Weight
Cl_2CA	see DCCA
C/T	Ratio of Exposure Concentration to TLV
CAS-Nr.	Chemical Abstracts Service Number
CEPA	Canadian Environmental Protection Act (CAN)
CFR	Code of Federal Regulations (USA)
CHPPM	Center for Health Promotion and Preventive Medicine (USA)
CONUS	Continental USA
CPR	Controlled Products Regulations (CAN)
CULTEX	A system for in vivo testing of the effects of toxic gases on lung cells
CW	Chemical Weapons
DCCA	3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (cis or trans) another common abbreviation = Cl_2CA (Pyrethroid metabolite)
DEET	Diethyl toluamide
DFG	Deutsche Forschungsgemeinschaft (German Research Foundation)
DNA	Desoxyribo-Nucleic Acid
DoD	Department of Defense (USA)
EKA	Expositionsequivalente für krebserzeugende Stoffe (Exposure Equivalents for Carcinogenic Substances)
EPI	Exposure/Potency Index
F-PBA	4-fluoro-3-phenoxybenzoic acid (pyrethroid metabolite)
GC-MS	Gas chromatography Mass Spectrometry
GHS	Globally Harmonised Systems

HI	Hazard Index
HPLC	High Performance Liquid Chromatography
HSDB	Hazardous Substances Databank (USA)
ICP-MS	Inductively Coupled Plasma – Mass Spectrometry
IDAA	Individual Dynamic Absorption Application (US Army)
IPCS	International Programme of Chemical Safety
IRIS	Integrated Risk Information Service (USA)
ISS	Integral Search System
JP8	A jet fuel, kerosene-based. It is a replacement for the JP-4 fuel. The U.S. Navy uses a similar formula to JP-8, called JP-5. It was first introduced at NATO bases in 1978. Its NATO code is F-34. It is specified by MIL-DTL-83133 and British Defence Standard 91-87. Commercial aviation uses a similar mixture under the name Jet-A. JP-8 in addition contains icing inhibitor, corrosion inhibitors, lubricants, and antistatic agents.
LC/MSMS	Liquid Chromatography Tandem Mass Spectrometer
LOAEL	Lowest Observed Adverse Effect Level
MIP	Molecular Imprinting
MRL	Minimal Risk Levels
MSDS	Material Safety Data Sheet
NIEHS	National Institute of Environmental Health Sciences (USA)
NIOSH	National Institutes for Occupational Safety and Health (USA)
NOAEL	Non Observed Adverse Effect Level
NOHSC	National Occupational Health and Safety Commission (AUSTRALIA)
NSAID	Non-Steroidal Anti-Inflammatory Drug
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational Exposure Limits
OSHA	Occupational Safety and Health Administration (USA)
PAH	Phenylalanine hydroxylase
PBPK	Physiologically-Based Pharmacokinetic Modelling
PBPK/PD	Physiologically-Based Pharmacokinetic Modelling/Pharmacodynamic
PCR	Polymerase Chain Reaction
PEI	Polyethyleneimine
PEL	Permissible Exposure Limit
Pyrethroids	Broad-spectrum insecticides-- chemicals used to kill a variety of insects. Permethrin is referred to as a synthetic pyrethroid insecticide because, while manmade, it resembles naturally-occuring chemicals with insecticidal properties, called pyrethrins. Pyrethrins are found especially in chrysanthemums.
RAM	Restrictive Access Material
RfD	Reference dose (US EPA)
SCOEL	Scientific Committee on Occupational Exposure Limits (EU)
STEL	Short Term Excursion Limits

TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
TDI	Tolerable Daily Intake
TLV	Threshold Limit Value
TTD	Target-organ Toxicity Dose
TWA	Time-weighted Averages
UNECE	United Nations Economic Commission for Europe (UN)
USEPA	Environmental Protection Agency (USA)
WHMIS	Workplace Hazardous Materials Information System
WHO	World Health Organisation
WOE	Weight of Evidence Modification

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- Paris, France
- Fort Detrick, Frederick, Maryland, USA
- Schloss Orienstein, Dietz, Germany
- TNO Prins Maurits, Rijswijk, Netherlands
- Toronto, Canada
- NBC-skydd, FOI, Umea, Sweden
- Leopold's Kazerne, Gent, Belgium
- Natick, Massachusetts, USA

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Biological indicators	Health monitoring	Physical interactions
Biomarkers	Health risk communication	Sensitivity
Biomarkers of exposure	Inhalation hazards	Susceptibility
Biotechnology	JP8 and other petroleum products	Threat evaluation
Dermal exposure hazards	Models	Toxicology
Dosage	Neuropsychological measures	Vulnerability
Exposure	Neurotoxicological	

14. Abstract

Protection against toxicological threats that impair health and performance of military members requires identification of risks and methods to assess exposure. This group focused on markers of exposure for assessment of neurotoxicological threats from non-threat agents. Two model systems were examined in detail, permethrin and JP8. These represent relevant chemical mixtures that are inhalation and dermal exposure hazards with neurotoxicological potential. The group reviewed and reported research on approaches to assessing health and performance risks from these two models, ranging from neurobehavioral testing to special in vitro exposure test systems and cellular biomarkers. Interactions with physical factors (e.g., heat, dust, work/exercise), psychological stress, and other chemical exposures were evaluated. Research gaps in health risk communication strategies to mitigate risk and achieve optimal compliance with protective measures were also discussed. Two international Environmental and Industrial Health Hazard (EIHH) workshops paralleled the efforts of this panel and expanded contributions to this work. Further work in these areas is being conducted with agreements to continue sharing of information on approaches to assess neurotoxicological risks. Recommendations were made for further development of efficient processes for early predeployment consideration of potential threats, assessment and monitoring of neurochemical hazards, and lifecycle health monitoring of exposed individuals.

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