



**OECD/RUSSIAN FEDERATION WORKSHOP ON
“BIOSECURITY OF MICROBIAL BIOLOGICAL
RESOURCES – COMPLEMENTING INNOVATION”**

Ministry of Education and Science, Brusov per. 11, Moscow

20 – 21 September 2006

DRAFT PROGRAMME

ABSTRACTS



OECD/RUSSIAN FEDERATION WORKSHOP ON “BIOSECURITY OF MICROBIAL BIOLOGICAL RESOURCES – COMPLEMENTING INNOVATION”

Moscow – Russian Federation – 20-21 September 2006

DRAFT PROGRAMME

Purpose of the Workshop

The Workshop will focus on how to improve research on biosecurity and biosecurity measures in entities handling dangerous biological materials. Specific areas for exploration and discussion are:

- How to integrate biosecurity as a part of quality management in entities handling dangerous biological material?
- How to strengthen the link between the actors involved in preservation of biological material and those involved in R&D especially in the field of infectious diseases?
- What are the drivers for developing internationally agreed rules on biosecurity?
- What challenges do the implementation of biosecurity create for R&D?
- How may R&D and biosecurity measures be mutually balanced?
- What are the new opportunities in collaborative research and technology transfer in the field of biosecurity and infectious diseases?
- What role may the international policy community play in delivering the above items?

The Workshop will be carried out under the auspices of OECD’s Working Party on Biotechnology (WPB).

Workshop Objectives

- i.* Identify opportunities for realising value from pathogenic microbial resources.
- ii.* Discuss the challenge of balancing the needs for controlled access to dangerous biological material and their availability for R&D.
- iii.* Initiate discussions on mutually supportive policies to achieve (*i*) and (*ii*).
- iv.* Identify opportunities for international collaborative research and policy making.

Expected outputs of the workshop

- i.* A Chairman's summary of conclusions will be issued based on materials circulated in advance, discussions at the workshop and rapporteur's report. This report will set-out the issues, opportunities and challenges relating to biosecurity and directions for further work in this area and provide recommendations to the OECD's Working Party on Biotechnology.
- ii.* Recommendations to the OECD Working Party on Biotechnology on Biosecurity on options for further steps towards development of policy recommendations for all entities handling dangerous biological materials.

Outcome:

The Workshop will provide opportunities for participants to identify new partnerships to realise value from pathogenic microbial resources in a safe and secure manner. It will promote improved quality management of such resources as well as international cooperation to assure biosecurity.

Financial Support

Our thanks go to the Russian Ministry of Education and Sciences and the French G8 Global Partnership programme (PMG8) for funding this event.

DAY 1 — WEDNESDAY 20 SEPTEMBER 2006

08:30-09:00 REGISTRATION

09:00-09:30 WELCOME ADDRESS

A.V. KLIMENKO, Deputy Head of the Federal Agency for Science and Innovations of the Russian Federation, Russian Federation

Iain GILLESPIE - OECD

CHAIR OF THE WORKSHOP: **David HARPER**, Director of Health Protection, Department of Health International Health and Scientific Development, United Kingdom

CO-CHAIR OF THE WORKSHOP: **Mikhail P. KIRPICHNIKOV**, Dean of the Faculty of Biology, Moscow State University, Russian Federation

09:30-11:00 KEYNOTE ADDRESSES

09:30-10:00 ACTUAL STATUS OF NATIONAL AND INTERNATIONAL ACTIVITIES IN THE FIELD OF HIGHLY DANGEROUS PATHOGENS AND PERSPECTIVES FOR IMPROVEMENT

G.F. LAZIKOVA, Deputy Chief of the Department of Epidemiological Surveillance, Federal Consumer Rights' Protection and People's Health Agency, Russian Federation

10:00-10:30 FIGHTING NATURALLY OCCURRING OR INTENTIONALLY INDUCED INFECTIOUS DISEASES

Nigel LIGHTFOOT, Director of Emergency Response Division, Health Protection Agency, United Kingdom

10:30-11:00 PATHOGEN SECURITY GUIDELINES AS A PRE-REQUISITE FOR INTERNATIONAL CO-OPERATION

Robert MIKULAK (absent, presented by **Gregory Stewart**), Director, Office of Chemical and Biological Weapons Threat Reduction, Bureau of International Security and Nonproliferation, United States

COFFEE BREAK – 11:00-11:30

**11:30-13:10 SESSION 1: REALISING VALUE FROM PATHOGENIC MICROBIAL
RESOURCES**

Objective of this session: To identify and discuss new opportunities for realising value from pathogenic microbial resources

Chair: Yuri REMNEV, Centre of Modern Medical Technologies (TEMPO), Russian Federation

Discussant: Christine ROHDE, DSMZ Micro-organisms Culture Collection, Germany

Speakers:

11:30-11:50

Application of “Yersinia pestis” for development of diagnostic kits, vaccines and medicines

Andrey ANISIMOV, State Research Centre of Applied Microbiology and Biotechnology, Russian Federation

11:50-12:10

Natural toxins as biological threat: modern approaches to detection and therapy

V.A. NESMEYANOV, Institute of Bioorganic Chemistry, Russian Academy of Science, Russian Federation

12:10-12:30

Genetic databases of bio-threat agents

Florigio LISTA, Health Corps, Army Medical and Veterinary Research Center, Italy

12:30-12:50

Application of GLP in Russian Federation for testing of anti-infectious medical products

Arkadii MURASHEV, Institute of Bioorganic Chemistry, Russian Academy of Science, Russian Federation

12:50-13:10

Evolution of GMP requirements for manufacturing biological products (drugs, vaccines, advanced medicinal products)

Yamina KABRANE, AFSSAPS, Ministry of Health, France

LUNCH – 13:10-14.30

14:30-15:30 ROUNDTABLE DISCUSSION

The Discussant of Session 1 will lead discussions

Questions for discussion:

1. What new biomedical R&D and bio-defence activities make use of pathogenic micro-organisms?
2. Are there barriers impeding R&D that use pathogens and pathogen-derived materials? How may any such barriers be overcome?
3. How may international cooperation reinforce initiatives to capture value from microbial pathogens, *e.g.* standardized diagnostics and maintenance measures?

COFFEE BREAK – 15:30-16:00

16:00-18:30 SESSION 2: ESTABLISHING BIOSECURITY SYSTEMS: RISK ASSESSMENT AND RISK MANAGEMENT OF DANGEROUS BIOLOGICAL MATERIAL

Objectives of this session:

1. Assess existing methodologies for developing biosecurity systems
2. Identify the issues impeding the implementation of biosecurity systems in practice
3. Identify the means by which international initiatives can help further develop harmonised biosecurity systems

Chair: Gregory STEWART, Department of State, Bureau of Internal Security and Nonproliferation, United States

Discussant: Dominique MASSET, AFSSAPS, Ministry of Health, France

Speakers:

16:00-16:20

Laboratory biosecurity risk assessment and management

Reynolds SALERNO, Sandia National Laboratories, United States

16:20-16:40

Feasibility analysis for the implementation of biosecurity measures to the BCCM-IHEM collection of medical fungi

Pierre-Alain FONTEYNE, Scientific Institute of Public health, Mycology Section, Belgium

16:40-17:00

The increasing regulatory framework applying to the exchange and supply of micro-organisms

Barry HOLMES, Head of NCTC, Health Protection Agency Centre for Infections, United Kingdom

17:00-17:20

BioRisk Management

Ottorino COSIVI, Department of Epidemic and Pandemic Alert and Response, World Health Organization

17:20-17:40

Biological Resource Centres (BRCs) and Biosecurity

Louis RECHAUSSAT, INSERM, France

17:40-18:30

ROUNDTABLE DISCUSSION

The Discussant of Session 2 will lead discussions

Questions for discussion:

1. How to assess whether a biological resource is sufficiently dangerous to merit access controls?
2. What types of risk management measures are required to secure pathogenic micro-organisms?
3. What types of facilities possess such material? How many are there? What is needed to increase awareness and improve training of personnel in these facilities?
4. Why is biosecurity risk not the same as biosafety risk? How to ensure that biosecurity measures and biosafety measures are complementary?
5. What impedes the implementation of biosecurity measures?
6. Can an internationally harmonised approach be taken to biosecurity?

COCKTAIL – 18:30-20:00

DAY 2 — THURSDAY, 21 SEPTEMBER 2006 (am only)

09:30-13:00 **SESSION 3: BIOSECURITY REGULATIONS IMPLEMENTATION AND COMPLIANCE: SEEKING BALANCE**

Objectives of this Session:

1. To identify approaches for developing balanced regulations addressing biosecurity issues
2. Identify existing mechanisms which could be used for application of biosecurity regulations and practices
3. Identify the means by which the international policy community can help leverage the above issues

Chair: Maureen ELLIS, Senior Biosafety Advisor, Global Partnership Programme, Canada

Discussant: Terence TAYLOR, President and Director of International Council for the Life Sciences, United States

Speakers:

09:30-09:50 *Biological research, bioterrorism and foreign policy: enhancing international engagement to foster science and security cooperation*

Joseph C. KOWALSKI, Policy Advisor, Office of International Health Affairs, U.S. Department of State, United States

09:50-10:10 *The difficulty in balancing risks and benefits of dual-use research in the implementation of biosecurity*

Kathryn NIXDORFF, Institute of Department of Microbiology and Genetics, TUD, Germany

10:10-10:30 *Needs, development and implementation of biosecurity regulations in France*

Dominique MASSET, AFSSAPS, Ministry of Health, France

10:30-10:50 *A call for action: the St Petersburg workshop addressing biosecurity issues*

Raif G. VASILOV, Vice President, Society for Biotechnology, Russian Federation

COFFEE BREAK – 10:50-11:10

11:10-12:10

ROUNDTABLE DISCUSSION

The Discussant of Session 3 will lead discussions

Questions for discussion:

1. What have States and private actors done to improve the security of dangerous pathogens in laboratories? What challenges have States faced in regulatory compliance, and what impediments have firms faced in co-operation with competitors?
2. How can one best ensure the operational needs of the R&D community that works with highly dangerous pathogens are met while also ensuring against the potential for their abuse?
3. How may mechanisms for quality management be used to ensure application of biosecurity measures?

BREAK – 12:10-12:30

12:10-13:00

CONCLUSIONS

Iain GILLESPIE, OECD

David HARPER, United Kingdom

Mikhail P. KIRPICHNIKOV, Russian Federation

CLOSING REMARKS

Alexandre BARTSEV, OECD

ABSTRACTS

APPLICATION OF *YERSINIA PESTIS* FOR DEVELOPMENT OF DIAGNOSTIC KITS, VACCINES AND MEDICINES

ANDREY P. ANISIMOV

State Research Center for Applied Microbiology, Russian Federation

Plague that has led to the death of millions of people still poses a significant threat to human health and attention has been renewed recently in the possible use of *Yersinia pestis* as a biological weapon by terrorists. Infecting doses of 10 bacteria or less are sufficient to cause lethal infection in naïve rodents and primates. Attempts to treat this deadly disease dates back to the world pandemic eras when such "remedies" as magic means and talismans, mixtures of bird and animal blood, tablets from meat of a rattlesnake or even squeeze from the fresh horse dung were explored. The successful isolation of the plague pathogen by A. Yersin in 1894 led to the beginning of more scientific designs and approaches for the laboratory diagnosis, vaccine prophylaxis, and treatment plague. In the first part of the 20th century this subsequently led to the design of killed and live plague vaccines, specific antibiotic prophylaxis and therapy for *Y. pestis*. Morbidity in humans was reduced down to 2,000 cases reported annually. Mortality rate in vaccinated and/or treated patients also was significantly reduced. The rapid development of the methodology of molecular biology provided the possibility of determining the complete nucleotide sequence of the genome of individual microorganisms; the appearance of PCR technology and biochips, redevelopment of new methods of cell immunology, the wide use of physical methods of studying the structural and functional organization of individual biomolecules, *etc.* have made it possible to begin rational design of diagnostic kits, vaccines and medicines for plague control. The modern approaches of microbial forensics can be used now to identify the source of the microorganisms to assist in resolving biocrimes and/or natural cases of infection.

FEASIBILITY ANALYSIS FOR THE IMPLEMENTATION OF BIOSECURITY MEASURES TO THE BCCM-IHEM COLLECTION OF MEDICAL FUNGI

PIERRE-ALAIN FONTEYNE

Scientific Institute of Public Health, Mycology Section, Belgium.

The BCCM/IHEM Biomedical Fungi and Yeasts Collection (<http://bccm.belspo>) holds over 6,500 strains, mostly filamentous and yeast-like fungi of public health or health related environmental interest. Strains of the public collection are routinely distributed as actively growing cultures on agar slants. Implementation of more stringent biosecurity rules will necessitate important changes in the management of the collection.

Risk analysis

A few fungal spores and metabolites have a bioweaponization potential. *Histoplasma capsulatum* and *Coccidioides immitis* spores could be used with aerosol delivery. Trichothecene mycotoxins could be used to poison food and water sources or released in confined areas. Most authors consider that their use for these purposes would present a number of obstacles with limited impact on public health. Deliberate contamination of large office buildings could however have severe economical costs in absence of an appropriate communication policy. The exhaustive risk analysis of all species in collection represents a huge amount of work that could be shared among multiple BRCs.

Building security

Currently, the access to the stock of biological material was designed according to the biosafety regulations. It is not sufficient. Door locks could be reinforced at a reasonable cost, implementing more restrictive procedures to access the building is possible, but the most difficult task will be the conscientisation of the employees.

Distribution

Packaging and transportation of the material is done according to the international standards and do not require significative improvement. The major difficulty is to appreciate the credibility of clients from abroad. Local regulations inside Europe appear to be extremely variable and information is not sufficient. It is not possible to guarantee that the final user is authorised to handle the pathogen. A practical solution, could be to use a local BRC as an intermediate with the new client.

Networking, sharing information, talking to each other could be the key to a more biosecure world.

THE INCREASING REGULATORY FRAMEWORK APPLYING TO THE EXCHANGE AND SUPPLY OF MICRO-ORGANISMS

BARRY HOLMES

**National Collection of Type Cultures, (NCTC), Health Protection Agency Centre for Infections,
United Kingdom**

The global threat of terrorism has resulted in various legislative changes in many countries. Whilst the author is most familiar with the system in the UK, similar developments are or have taken place within the EU member states and other countries throughout the world.

For dispatching cultures overseas from the UK, export controls on certain micro-organisms have been in place since 1993, regulated by the Department of Trade and Industry (DTI). Registration is required prior to supplying pathogens to countries in either the EU or throughout the rest of the world. For countries outside the EU, an application has to be made for an export licence for each shipment. Apart from the export controls, one also needs an import licence from an increasing number of countries.

For the transfer of cultures within the USA, all facilities holding certain specified pathogens must be registered, cultures can only be supplied to facilities that have also registered and the actual transfer is controlled *via* the Centers for Disease Control and Prevention (CDC), Atlanta. A similar system operates in the UK, controlled by the Specified Animal Pathogens Order (SAPO) 1998 and regulated by the Department for Environment, Food and Rural Affairs (DEFRA). Additionally in the UK, the Anti-Terrorism, Crime and Security Act (ATCSA) 2001 requires that holders of specified pathogens be registered with the Home Office.

If one wishes to import animal pathogens from outside the EU, then an import licence will need to be obtained, as required under the Importation of Animal Pathogens Order (IAPO) 1980. If the pathogen is received from any part of the world, then if it is listed in ATCSA, again one must register with the Home Office.

Finally, current requirements for shipping micro-organisms means a division into Category A or B; the former are prohibited in the mail and require the use of a certain specification of packaging (UN2814; PI 602) and the employment of secure transport mechanisms to ensure they are not misappropriated during transit.

EVOLUTION OF GMP REQUIREMENTS FOR THE MANUFACTURING OF BIOLOGICAL MEDICINAL PRODUCTS

YAMINA KABRANE
AFSSAPS, Ministry of Health, France

Good manufacturing practice is defined as “that part of the Quality Assurance which ensures that products are consistently produced and controlled according to the quality standards appropriate to their use”. In Europe, the principles and guidelines for GMP are stated in two directives for medicinal products to be placed in the market and for investigational medicinal products. General guidelines provide interpretation of these principles and a series of annexes provide more specific requirements for particular category of medicinal products.

Because of the development of new biological products (new vaccines, gene therapy and cell therapy products, products issued from transgenic animals or transgenic plants), specific questions on the GMP requirements for biological medicinal products defined in Annex 2 have been addressed to the EMEA inspectorate services and the GMP guidelines were submitted for modification and reshaping.

Biological medicinal products require very high standards of safety and quality in development, manufacturing, licensing, transport, storage and use. The attainment of this quality objective requires rigorous control of sources materials (cells, tissues, micro-organisms- GMOs,...), specific training of personnel, adapted premises and equipment, adequate documentation/records and adequate quality control. There must be an implemented system of Quality Assurance incorporating GMP and biosafety regulation and where mandatory additional biosecurity measures.

BIOLOGICAL RESEARCH, BIOTERRORISM, AND FOREIGN POLICY: ENHANCING INTERNATIONAL ENGAGEMENT TO FOSTER SCIENCE AND SECURITY COOPERATION

JOSEPH C. KOWALSKI

Bioterrorism, Biodefense, and Health Security, United States Department of State, United States

Recent progress in several scientific fields has led to the development of new tools and knowledge that will serve humanity through advancements in life science research. Unfortunately, in this era of global terrorism and regional instability these incredible advances also raise concerns about security – especially concerns that advances in life science research might be misused by terrorists intent on developing biological weapons. We have reached a moment of both innovation and opportunity, coinciding with an increasing threat from those who wish to harness progress in the life sciences for malevolent purposes. The national security implications of these developments are no longer limited to only a handful of the most developed nations. Instead – and much to the benefit of society – scientists are laboring around the globe to find cures for deadly diseases and to develop new products and processes that benefit the common good. With a pragmatic approach based on solid comprehension of the issues involved, and an understanding of the larger context of science and security, we may be able to foster the forward march of science while protecting the security of the globe’s inhabitants.

FIGHTING NATURALLY OCCURRING OR INTENTIONALLY INDUCED INFECTIOUS DISEASE

NIGEL LIGHTFOOT
Health Protection Agency United Kingdom

Infectious diseases due to the potential biological threat agents continue to occur in small outbreaks around the world. These threat agents include *Bacillus anthracis*, *Clostridium botulinum*, *Yersinia pestis* and *Francisella tularensis* the historic biological warfare agents. In addition recent events point to the potential use of the enteric disease agents, Salmonellae, Shigellae and verocytotoxin producing *Escherichia coli* to maliciously contaminate food and water.

Intelligence assessments indicate current terrorist interest in some these biological agents but perhaps only achievable on a small scale. However we have seen the devastating effects of the anthrax letters in the United States and subsequently we have all gained a lot of experience in responding to hoaxes involving “white powders” The bioterrorism threat is real and we have to balance the needs for public health responses to naturally occurring outbreaks of infectious diseases and the control of these organisms and access to them to prevent malicious use. Controls are necessary and there are some good examples of reasonable approaches that still allow bona fide research workers to continue to develop improved diagnostic tools and therapeutic agents which are essential for public health interventions in naturally occurring disease. These same tools are also necessary to prepare for responses to bioterrorism. The diseases are unusual occurrences but the way forward is for us all to collaborate internationally, to remove duplication of effort, to share high quality biological reference materials and become better prepared to face both challenges in a new secure trusting environment.

GENETIC DATABASES OF BIO-THREAT AGENTS

FLORIGIO LISTA

Health Corps, Army Medical and Veterinary Research Center, Italy

Bio-threat agents are natural occurring pathogenic microorganisms that could be deliberately released to generate terror or more generically damage. Recently, biotechnology advancements made possible virtually all kind of manipulations on harmless bugs to make them very pathogenic. This kind of technology is becoming more and more available even for low level laboratories. On the other hand, natural dispersed agents can cause very serious diseases as the SARS epidemics demonstrated just two years ago. A common need to trace either deliberated or natural agents lead the international community to think about the importance of setting up genetic databases. These databases would be highly valuable to determine the epidemiological characteristics of all sort of infectious disease related events. Furthermore a detailed knowledge of the precise genetic profile of any pathogenic species will enhance the development of new defensive tools against harmful bugs. In order to build a more and more comprehensive database that should be as much representative as possible to describe the whole genetic variations for each specific genera and microorganism, it is recommended to set up a level of collaboration as high as possible. This will improve not only the security of exchanging potential biological agents but will also allow an increase the number of the collected bugs. There is also the need to exchange reproducible methodologies, data and essential materials to make more evident the sharing of real information. Some collaboration are already in place at biodefence as well as civilian level but others are necessary to extend the creation of genetic databases of biological agents as an essential tool for the progress of biosecurity and health worldwide.

NEEDS, DEVELOPMENT AND IMPLEMENTATION OF BIOSECURITY REGULATIONS IN FRANCE

DOMINIQUE MASSET

Toxicological Investigation and Non clinical Evaluation Unit, AFSSAPS, Ministry of Health, France

The rapid expansion of biotechnologies has meant that biological agents are increasingly being used for peaceful purposes. Genetic manipulation of such agents can prove dangerous in some cases. Moreover, laboratories working with these biological agents can be a potential source of supply for terrorist groups and organizations. Recent events have shown that the international dimension of terrorism is closely linked to international trafficking and thus potentially to traffic in biological agents.

Apart from the political and legal consequences that may stem from an act of aggression using biological agents, the release into the environment, whether or not intentionally, of a highly pathogenic biological agent would at first pose a serious public health concern. Legislation on dual-use goods addresses this situation only in part as it does not control exports to certain countries and cannot prevent a dangerous biological agent from being introduced into or used in the French national territory.

It is naturally inconceivable to prohibit biological agents research and development for prophylactic and diagnostic purposes. Biological agents can, however, represent a potential source of local supply for terrorist groups and organizations. The French proposal consists in authorizing and controlling the legal use of micro organisms and toxins with a view to better monitoring and punishing illegal use.

Given that the illicit and/or fraudulent use of agents, pathogenic micro organisms and toxins is likely to be hazardous to public health, it was decided that they should come under legislation on narcotics. This legislation has two advantages:

- It provides for full traceability of the use and flows of these micro organisms and toxins,
- And for the use of a range of criminal rules and regulations to combat use of and illicit traffic in these micro organisms.

By placing special conditions on the use of pathogens as regards activities relating to their production, conversion, applications, import, export, possession, transfer free of charge or against payment, acquisition, and transport. All these operations must be authorized beforehand by the Director General of the French Health Products Safety Agency (AFSSAPS). They can be authorized for the sole purpose of manufacturing human and veterinary health products, conducting research, and teaching. Such authorization can only be given to a natural person.

All acquisition and transfer operations are to be entered in a special register to be shown. The holder of the authorization is required to provide an annual report summarizing for each agent, micro organism, pathogen and toxin the quantities acquired and transferred, and the stockpiles possessed. French Health Products Safety Agency send inspectors to check that legislation is properly implemented.

In order to upgrade these regulations, a law on public health was promulgated on August 9, 2004. It defines a new mission to the French agency with regards to the good application of the dispositions about biological agents.

The application decree to be adopted will reinforce containment measures required, as well as those related to offices and traceability of staff. Measures are taken in harmonisation with the ISO 17025 standard.

PATHOGEN SECURITY GUIDELINES AS A PRE-REQUISITE FOR INTERNATIONAL COOPERATION

ROBERT MIKULAK

United States Department of State, United States

New biological knowledge can help mankind tackle many urgent global problems, including emerging infectious diseases, accumulation of harmful materials in the environment, and economic development.

Modern biological sciences are inherently “dual use” in nature – the same materials and technologies that assist us with advances for peaceful purposes can also be misused for harmful purposes. While the advance of science benefits from sharing of biological materials, willingness to share depends on confidence that dangerous biological materials are being handled in a responsible way. One important step in providing that confidence is the development, promotion, and implementation of international guidelines for ensuring that unauthorized people do not get access to dangerous pathogens in the laboratory, *i.e.*, for pathogen security.

Well-established international guidelines for safe handling of pathogens provide a solid foundation for international pathogen security guidelines. The draft OECD biosecurity guidelines for the proposed Global Biological Resource Centers Network are an important step toward such international guidelines. WHO has also developed guidelines that make an important contribution in this regard.

To ensure that dangerous pathogens are available to the research community, but are handled in a secure manner, we must promote awareness of risks and responsible conduct globally. We must establish international standards for pathogen security practice and promote their adoption, and we must work to ensure that those standards are converted into actual laboratory practice. Collectively, these actions will facilitate the sharing of biological materials in a responsible way and thereby promote the continued scientific progress on which solutions to many global problems depend.

APPLICATION OF GLPS IN RUSSIAN FEDERATION FOR TESTING OF ANTI-INFECTIOUS MEDICAL PRODUCTS

ARKADI N. MURASHEV

Branch of the Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Science, Russian Federation

For testing of anti-infectious medical products there are three main areas of focus for the non-clinical safety package: genetic toxicology battery, rodent and non-rodent toxicology (acute and subchronic) and safety pharmacology (three key organ systems: CNS, cardiovascular and respiratory). These non-clinical studies have to be carried out in compliance with the Good Laboratory Practice (GLP) principles. Principles of GLP apply to all non-clinical health and environmental safety studies required by regulations for the purpose of registering or licensing pharmaceuticals, pesticides, food and feed additives, cosmetic products, veterinary drug products and similar products, and for the regulation of industrial chemicals. GLP is a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.

So far in Russia there are no certified GLP-compliant laboratories. Nevertheless, in the Biological Testing Laboratory (BTL) of the Branch of the Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Science there are the persons, premises and operational units that are necessary for conducting the non-clinical health and environmental safety study. A head of BTL is the person who has the authority and formal responsibility for the organization and functioning of the test facility according to these Principles of GLP. In the BTL there is a Quality Assurance Programme, which is a defined system, including personnel, which is independent of study conduct and is designed to assure test facility management of compliance with these Principles of GLP. Every study in the BTL has a Study Director who has the individual responsible for the overall conduct of it and has a Study Protocol, which is a document which defines the objectives and experimental design for the conduct of it, and includes any amendments. The BTL has a Master Schedule, which is a compilation of information to assist in the assessment of workload and for the tracking of studies at it. In the BTL there are the Standard Operating Procedures which are documented procedures which describe how to perform tests or activities normally not specified in detail in study protocols or test guidelines.

BTL is the first laboratory in Russia, which has AAALAC accreditation (Association for Assessment and Accreditation of Laboratory Animal Care).

NATURAL TOXINS AS BIOLOGICAL THREAT: MODERN APPROACHES TO DETECTION AND THERAPY

VLADIMIR A. NESMEYANOV

Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow

Great variety of living organisms including bacteria, yeasts, plants, animals, etc., produce biological toxins which help them to live or survive in hostile environments. Among these toxins are peptides, proteins, low molecular weight substances. They are highly toxic or even lethal in minute doses. Many of them represent real danger for human beings, for instance, by contaminating food and drinking water. On the other hand toxins are increasingly used as research tools and also in agriculture and medicine.

Nowadays the danger exists that certain biotoxins might be produced and used as biological weapons by terrorists. Therefore sensitive and rapid detection systems and efficient neutralizing tools have to be developed. The modern approach is based on usage of antibodies (monoclonal, recombinant) specific against particular toxin. Different analytical procedures are being developed enabling to detect picogram or nanogram quantities of toxin. Immunoenzyme, immunofluorescent and immunochromatographic procedures are widely used. When biological toxin has to be identified among large number of toxic substances, biochip technology is applied. Biochip might contain several dozens antibodies, immobilized in spots, each specific to particular toxin. If toxin is present, it binds to appropriate antibody, and is detected by special analyzer. Anti-toxin antibodies can be applied also to quickly neutralize biotoxin in human organism. In this case highly desirable to use human antibodies which can be produced, for instance, by phage-display technology, or humanized antibodies, derived on basis of appropriate murine monoclonal antibodies.

Hence, nowadays immunological approaches can provide all necessary tools for biotoxin detection and anti-toxin therapy.

THE DIFFICULTY IN BALANCING RISKS AND BENEFITS OF DUAL-USE RESEARCH IN THE IMPLEMENTATION OF BIOSECURITY

KATHRYN NIXDORFF

Department of Microbiology and Genetics, Darmstadt University of Technology, Germany

Characteristic of the technologies connected with modern forms of research in the life sciences is the explosive rapidity with which new advances occur. In the biomedical sciences these developments are essential for research designed to unravel the mechanisms of disease-causing processes, including the pathogenic mechanisms microorganisms use to cause infectious diseases. However, the same techniques used to improve health and protect against infections can of course be misused to produce new and more effective biological weapons.

Biosecurity measures designed to counteract misuse of biotechnology for biological warfare and bioterrorist purposes will invariably affect biomedical research and must be carefully drafted so as not to impede developments that might be essential for the fight against disease. Because of the pronounced dual-use aspects of biotechnologies, it is not possible to advocate the prohibition of any type of biological research. This will be illustrated by examining an example of dual-use research and applying risk-benefit assessment models. Such models can be very useful as a tool for reflection, leading to heightened awareness of potential risks, and as an aid in steering research in a responsible direction.

However, additional measures that can support risk-benefit analyses are needed as well.

An independent research oversight process would be very useful, depending of course on how it is formulated. Many countries issue licenses or permits to scientists allowing research in the areas of genetic engineering and work with pathogenic microorganisms. The awarding of a license or permit to a principal investigator should be contingent upon receiving instruction about the content of the Biological Weapons Convention and the obligations of the scientist under this treaty, as well as instruction about risk-benefit assessment procedures.

BIOLOGICAL RESOURCE CENTRES (BRCS) AND BIOSECURITY

LOUIS J. RECHAUSSAT
INSERM, France, Chairman of OECD Task Force on BRCs

The initial OECD report on Biological Resource Centres in 2001* already pointed out that “*certain biological agents and toxins (...) can be misused as agents in biological warfare or bioterrorism*” and suggested that “*Governments need to work towards international harmonisation [in order to] discourage inappropriate uses of biological resources*”. The events of September 11, 2001 and the anthrax attacks shortly thereafter prompted the CSTP to invite the Working Party on Biotechnology, and especially its Task Force on BRCs, to investigate biosecurity matters and indicated at its 2nd meeting (March 2002), that the Task Force should incorporate biosecurity measures into its work on standards for BRCs. Several contributions and reports were produced which underlined the particular responsibility of BRCs in storage and distribution of hazardous micro-organisms and toxins. BRCs must be operated such that they reduce the risks of bioterrorism. While biosafety guidelines and standards, based on WHO recommendations, were pretty well adopted everywhere, biosecurity aspects of BRC management needed to be analysed. One of the main issues of these investigations is the fact that each BRC needs a specific risk assessment due to the variety of situations and activities and the evolution of them. Submitted to national regulations, BRCs can play a major role in transfer procedures for a legitimate access by the scientific community.

* "Biological Resource Centres: Underpinning the Future of Life Sciences and Biotechnology", OECD, Paris, 2001 - ISBN: 9264193553"

LABORATORY BIOSECURITY RISK ASSESSMENT AND MANAGEMENT

REYNOLDS M. SALERNO

International Biological Threat Reduction, Sandia National Laboratories, United States

The modern laboratory operating environment should be defined by both biosafety and biosecurity considerations. Risk assessment is a structured process for analyzing the likelihood and consequences of undesired events. This process forms the foundation for a rational approach to both biosafety and biosecurity implementation at the laboratory level. This talk will focus on risk assessment and risk management for bioscience laboratories, specifically covering such issues as why it is important to regularly evaluate risk, how to perform a risk assessment, the shortcomings of the risk assessment process, and the need to ensure that risk management does not unnecessarily disrupt the normal operating activities of the institution.