# Nanotechnology – Toxicological Issues and Environmental Safety

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# Nanotechnology – Toxicological Issues and Environmental Safety

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## PREFACE

The North Atlantic Treaty Organization (NATO), through the NATO "Security Through Science Program," sponsored an Advanced Research Workshop (ARW) entitled "Nanotechnology – Toxicological Issues and Environmental Security" that was held August 12–17, 2006 in Varna, Bulgaria.

The purpose of the workshop was to bring to focus and discuss the toxicological, ecological, and environmental safety issues surrounding the development, manufacture and use of nanomaterials. This represented the first international workshop organized specifically to share concerns and discussions on these issues between scientists from NATO and Partner countries. Scientists, representing the fields of toxicology, risk assessment, molecular biology physics, nanotechnology, ecology, epidemiology, medicine, public health, scientific ethics, and environmental protection from Belgium, Bulgaria, Czech Republic, Hungary, Moldova, Republic of Macedonia, Romania, Russian Federation, and the United States participated. Their main goal was to exchange experience in nanotoxicology and risk assessment, identify the most important gaps in knowledge, and draw directions for future research and collaborations in the field of nanotechnology regarding safe application and development.

The ARW was opened with two introductory lectures that summarized the global directions and issues in nanotechnologies, as well as the status and perspectives of nanotechnologies in the Partner countries. This was followed by sessions on nanomaterials/nanoparticles – toxicological issues; risk assessment, and control measures; public participation and educational/ethical issues and lastly; institutional mechanisms and status reports from various countries. There were two spirited round table discussions. The first dealt with toxicological issues of nanomaterials and nanoparticles and the second with risk assessment and control measures. Some of the questions addressed in the discussions included the following: How do we determine/select which nanomaterials should be tested for toxicity (prevalence, potential use, properties)? What are the minimum physiochemical properties that should be established before animals or *in vitro* tests are undertaken? What types of equipments are required for this characterization (and their availability)? Are there any opportunities to employ *in vitro* screening approach or computational toxicology? How important and how feasible is it to do toxicokinetics/distribution studies? What are the main sources and routes of human exposure (occupational, environmental)? What exposure metrics are most predictive of biological effect (e.g., mass, number, surface area)? Are the current environmental fate and transport models applicable to nanomaterials? What methodologies should be used for detection and characterization of occupational and environmental exposures? Are the

current personal - protection equipment, including respirators, adequate for all nanomaterials? What are the major gaps in knowledge needed for risk assessment of nanomaterials? Do we have adequate guidelines for working safely with nanomaterials? Do we have enough information to initiate monitoring of health effects of nanomaterials in workers? What institutional mechanisms and approaches for risk management should be developed – international and/or specific dependent on the country infrastructure and economy? These intensive and provocative discussions held during the workshop are summarized in the section entitled "Conclusions and Recommendations." A shared hope of the workshop was that it will serve as a stepping-stone for future collaborations between countries in fostering the safe use of nanotechnology.

The ARW was funded by a NATO award provided by the Assistant Secretary General for Public Diplomacy upon consideration by the Advisory Panel on Chemistry/Biology/Physics and the Program Director Dr. F. Pedrazzini. The co-directors of the workshop were P. Simeonova (United States) and N. Opopol (Moldova). Other members of the organizing committee were F. Kaloyanova (Bulgaria) and D. Solodoukhina (Russian Federation). We appreciate the financial support and the organization which made the workshop possible.

We should like to express our particular thanks to A. Maynard and E. Kuempel (United States) for their help in organizing the discussion round tables and preparing the Conclusions and Recommendations of the workshop.

Finally we gratefully acknowledge the help of Springer and the publishing editor Annelies Kersbergen with this book.

Coeditors:
P.P. Simeonova
N. Opopol
M.I. Luster

## CONCLUSIONS AND RECOMMENDATIONS

### NATO Advanced Research Workshop (ARW) "Nanotechnology – Toxicological Issues and Environmental Security," August 12–17, 2006, Varna, Bulgaria

Nanotechnology is one of the fastest growing technological fields of the 21st century. However, the success of the emerging nanotechnology applications will depend on dynamic development of nanomaterial toxicology, risk and exposure assessment. The objectives of the NATO ARW were to provide an exchange of experience in nanotoxicology and risk assessment between scientists from NATO and Partner countries, to identify the most important gaps in knowledge, and to identify directions for future research which will ensure safe application and development of nanotechnology.

The NATO ARW concluded that many NATO and Partner countries are involved in development of nanotechnologies. These emerging technologies, although only in the research stage in some countries, will impact numerous industries, including daily consumer products, health care, energy, and transportation. Little is known about the potential adverse health and ecological effects of exposure to engineered nanomaterials, the main components of many nanotechnologies. Concerns are coming from the initial toxicological studies as well as the research and epidemiological reports on ultrafine particle toxicity. The most attractive properties of nanomaterials for medical and technological applications, including their small size, large surface area, and high reactivity, may also lead to new and unusual toxicity. Both country-specific and global issues were identified at the workshop and detailed recommendations were made related to nanomaterial characterization, toxicity tests, exposure and risk assessment, development of protective and prevention stratagies, risk communications and managements in nanotechnologies. Concerns about nanomaterials' potential toxicity and impact on human health and the environment must be addressed while the field is still developing and exposure is limited. Corresponding political measures will provide equality of nanotechnology opportunities and sustainable development of NATO and Partner countries.

### General Recommendations

1. *Potential risk:* Evaluation of potential risk must be an integral part of nanotechnology development in all countries.
2. *Product development:* Nanotechnology product development cycles should incorporate an evaluation of potential risk and risk reduction from the earliest stages.

3. *Strategic research:* Organizations investing in nanotechnology research should invest in strategic research to evaluate potential health and environmental impact, and to develop effective risk management and risk-reduction strategies. Governments need to fund basic and general research, while enabling industry to support relevant product and material-specific research. Mechanisms are needed to ensure the transparent release of information relevant to understanding and managing potential risk.
4. *Information exchange:* Countries investing in nanotechnology should partner to share information and resources when researching potential risk and developing risk-management policies. Information sharing is particularly encouraged between developed and developing economies. Regional networks should be initiated to share information, coordinate research, and establish research infrastructures.
5. *International harmonization:* International agreement is needed on strategic risk research needs and aims. International organizations, such as NATO should take a lead in ensuring a global response to potential nanotechnology risk management through international partnering, coordination, and information sharing.
6. *Multidisciplinary research:* Collaboration between diverse scientific disciplines should be encouraged and supported in order to develop effective risk assessment and management methods for nanotechnologies.
7. *Risk communication:* There must be dialogue (between government, industry, academics, nongovernmental organizations and the public) on the benefits and risks of nanotechnology based on relevant and high-quality science. Nanotechnology risk-research programs and publications should be subject to high standards of scientific peer review to ensure a high quality of published studies.
8. *Continuing education and training:* International issue-specific workshops should be held to support coordinated nanotechnology risk research and policy. Education and training, including participation of NATO and non-NATO country experts, is needed to ensure the safe handling and use of nanomaterials.

## Recommendations for Research Needs

### Characterization of nanomaterials

- Methods and tools should be developed to identify and characterize engineered nanomaterials in biological matrices (e.g., exploring the use of interactions between nanostructures and electromagnetic radiation could lead to new methodologies).
- Nano-specific tools for characterizing the physical and chemical properties of nanomaterials in risk research should be developed, through

collaborations and partnerships with researchers characterizing nanomaterial functionality and applicability. Centers of excellence should be developed that provide access to analytical tools.

- Research to define and characterize biologically active surface area of engineered nanomaterials should be a high priority.
- Novel methods of evaluating potential impact *in situ* should be developed, including the use of biomonitoring and the development of instruments that combine measurements of exposure with an analysis of potential hazard (such as reactive oxygen species, ROS, production). These should complement more conventional exposure-evaluation methods.
- Terminology and nomenclature standards should be developed for nano technologies and nanomaterials that are specific to addressing potential impact.

**Exposure**

- Universal personal aerosols samplers should be developed that measure particle mass, number, and surface-area concentration simultaneously.
- International guidance should be developed on the effective exposure control of engineered nanomaterials.

**Hazard/Toxicity**

- Well-characterized stable benchmark and reference materials should be developed and used for toxicology studies. The applicability of these materials should be assessed regularly against the properties and characteristics of newly developed nanomaterials.
- Rapid cellular assays should be agreed upon and used for screening and preliminary hazard ranking of engineered nanomaterials.
- Nanomaterials must be appropriately characterized in toxicity tests. International guidelines on minimum physical and chemical characterization requirements and toxicity screening tests for engineered nanomaterials should be developed, agreed upon, and applied (e.g., as criteria for peer-reviewed publication).
- Priorities for toxicity testing should include materials that are close to commercial use, or are already being used in substantial quantities.
- The relevance of all significant exposure routes should be investigated, including the main routes of oral, inhalation and dermal exposure.
- While *in vivo* tests will remain essential, alternatives should be developed that minimize reliance on animal testing for new engineered nanomaterials.

- Information should be developed on potentially confounding influences in toxicity studies on engineered nanomaterials (e.g., the role of photoactivity and differential adsorption of proteins).

**Risk Assessment**

- Research into assessing and managing the potential impacts of nanotechnologies in the workplace is a high priority, including measuring worker exposure, controlling nanomaterials release, and safe disposal of nanomaterials.
- Life-cycle analysis methodologies should be developed for evaluating the potential impact of engineered nanomaterials and products on human health and the environment, from production to disposal.
- The kinetics and dynamics of nanomaterials in the body and the environment should be studied (including material disposition, dispersion, transformation and accumulation).
- Data are needed on human exposure, biomonitoring, and health outcomes that might be related to exposure.

**Recommendations for Risk Communication and Management**

**Risk Communication**

- Education and training is needed for researchers, manufacturers, and users of nanomaterials regarding the safe development and use of nanomaterials.
- Open access to nanotechnology risk-relevant information within industries is needed, including toxicity data, exposure data, and best available working practices. Centralized web-based portals should be established, providing access to global resources for assessing and managing the potential risks of nanotechnologies. These should include international databases on nanomaterial risk, including published data, research, products and risk assessment and management methods.
- Clear and transparent communication with consumers is needed on the potential benefits and risks of products developed using or containing nanomaterials.
- Products that contain nanomaterials should clearly state on the ingredients list which components are present as nanomaterials.

**Risk Management**

- Existing regulations should be evaluated for their applicability to engineered nanomaterials, and where necessary new regulations should be developed.

- Chemical regulations should be extended and enforced so that MSDS for engineered nanomaterials contain accurate and relevant information on potential risks of engineered nanomaterials, and acknowledge where information is not currently available.
- International guidance should be developed and shared on the best available practices for working with engineered nanomaterials. Guidance should be categorized by process and use.
- Criteria should be developed for when and how medical screening is conducted when exposure to engineered nanomaterials potentially occurs.

The recommendations reflect the perspectives of meeting participants, and provide a valuable resource for developing further international collaborations and actions to ensure the potential risks of emerging nanotechnologies are assessed and managed appropriately.

**Note:** These are the individual views of the participants, and do not necessarily reflect the views of the countries and organizations represented at the meeting.