TA Note 01

Recent Trends in the Assessment and Management of Risks of Multi-walled Carbon Nanotubes

Responding to a Precautionary Measure from the Ministry of Health, Labour and Welfare

These notes present suggestions and organize information regarding recent trends in the assessment and management of risks of multi-walled carbon nanotubes. They were compiled in the hope of serving as a reference for the Council for Science and Technology Policy (CSTP) during the establishment of the 4th Science and Technology Basic Plan and other activities. In particular, due to the apparently large societal impacts of two academic papers released in 2008 related to the toxicity of multi-walled carbon nanotubes, as well as the Ministry of Health, Labour and Welfare's "notification on present precautionary measures for the prevention of exposure at workplaces manufacturing and handling nanomaterials," the goal was to promptly organize a report focusing on this problem. Accordingly, the specific characteristics, risks, and benefits of a variety of nanomaterials, as well as the wide range of their societal impacts including trends overseas, are not dealt with in this investigation.

This investigative research, commissioned by the Research Institute of Science and Technology for Society (RISTEX) within the Japan Science and Technology Agency (JST), is being conducted as one part of the "Innovation and Institutionalization of Technology Assessment in Japan" project, which is planned to run from 2007 to 2011. Technology assessment refers to systems or activities that support problem identification and decision making with regard to technology and society. This is accomplished by anticipating various future societal impacts during the early stages of development of emerging technologies which challenge existing systems of research, development, and innovation or present problems in terms of compliance with legal systems. As practiced in Europe and the United States, a wide variety of related parties and citizens are involved, differences in each group's point of view regarding benefits, safety, and risks are acknowledged, and this dialogue guides the developmental direction of science and technology. These kinds of activities are being carried out in a fragmentary nature in Japan, but in terms of obtaining a comprehensive view of problems and giving thought to both uncertainties and diverse values, they are insufficient to respond to the needs of policymakers or acquire the trust of society. Institutionalizing the assessment of emerging technology's societal impacts will make a long-term, strategic contribution to the introduction and promulgation of such technology in society, as well as supplement existing policymaking systems.

Searching for ways in which technology assessment can be institutionalized and established in Japan in the future, this project also offers practical examples of nanotechnology in fields like medicine, food, and energy, while actually carrying out the process of technology assessment itself.

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Summary

1. Knowledge about the Toxicity and Risks of Multi-walled Carbon Nanotubes

In the most recent research considering the toxicity of multi-walled carbon nanotubes, one type of nanomaterial, the occurrence of mesothelioma similar to that resulting from exposure to asbestos was observed following direct intraperitoneal dosage of the material in mice. In order to estimate the risks that multi-walled carbon nanotubes pose to the human body and the environment, it is necessary to make an assessment in relation to toxicity and exposure. However, there are apparent differences in perspective as to what the principal objective of such an assessment should be. Additionally, opinions differ among researchers about whether this material's structural similarities with asbestos determine its hazard, as well as about whether or not there is a threshold dosage amount which displays toxicity. Detailed results of exposure assessments are not currently available, but because the volume of multi-walled carbon nanotubes in use is small and the chances for direct exposure to large quantities are limited, this material does not seem to pose a level of immediate risk which would justify categorization as "another asbestos."

2. Precautions

Following the public release of multi-walled carbon nanotubes' toxicity on mice, at an early stage of events on the global scale, a notification requesting that organizations in Japan using this material take precautionary measures with regard to nanomaterials as a whole was issued by the Ministry of Health, Labour and Welfare (MHLW). Although its content was vague and it did not provide a clear basis for taking such measures, the notification—reported on by the media—had a significant social impact, and some businesses experienced stagnation in the nanotechnology sector due to reaction from banks and downstream companies.

3. Cooperation among Related Agencies

The MHLW; The Ministry of Economy, Trade and Industry (METI); and the Ministry of the Environment are each independently investigating the impacts of nanotechnology on the environment, health, and safety. In contrast, the Cabinet Office is aiming for cooperation between these ministries' nanotechnology research efforts. However, the Cabinet Office has yet to compare and assess in a unified manner the most up-to-date scientific knowledge regarding the environmental, health, and safety impacts of nanomaterials and articulate a strategic policy regarding measures to be taken, and in this respect, their efforts toward collaboration are not functioning effectively.

Responsive Steps for the Future

1. Deepening the Discussion about Risk Assessment and Risk Management for Multi-walled Carbon Nanotubes

There are a variety of viewpoints on the assessment of multi-walled carbon nanotubes, for example about whether more importance should be placed on assessing toxicity or exposure. Because of this it is necessary for the Cabinet Office to gain a systematic understanding of the current fundamental thinking of researchers, both in Japan and abroad, regarding toxicity and risk assessment for nanomaterials. Based on this understanding, it is imperative to deepen the discussion about multi-walled carbon nanotubes. We must consider the level of safety that should be incorporated in precautionary measures, and also costs such as the actual burdens on industry and opportunity loss, viewing these in comparison with the benefits that Japan stands to gain by competing internationally in research and development, innovation, and industrial expansion.

2. Precautionary Measures Related to Multi-walled Carbon Nanotubes

Making clear what kinds of information and systems we currently lack is essential in order to take effective precautionary measures. In deciding on such measures for the future, we must supplement these insufficiencies and utilize a process which will create decision-making results acceptable to society as a whole. Specifically, a forum is needed that will allow for ongoing examination and reformulation of responses and regular discussion of risks, based on the sharing of up-to-date information by related parties. It is desirable to enact specific, workable precautionary measures that are based on both this kind of discussion and an accurate understanding of the current situation. Based on the results of this kind of dialogue, there is also a responsibility to provide reliable information to society as a whole.

3. Nanomaterials Management Systems and Cooperation between Related Parties

The Cabinet Office should further develop inter-agency cooperation and make management systems more substantive through the creation of a science-based network. Deepening organizational cooperation—including industry, academia, public research institutions, NGOs, and consumer organizations—is another desirable objective. For example, the establishment of a database compiling information about nanomaterials risks through university-industry-government collaboration, and risk communication which allows citizens to access that information, could be expected. Further, we should increase the opportunities for this kind of diverse knowledge to be brought together with human resources, and through the Nanotechnology Business Creation Initiative (NBCI), promote public interest in the societal impacts of nanomaterials and support combined, voluntary efforts by related businesses.

Introduction

On February 7, 2008, the MHLW issued a notification to related business associations and other parties requesting that they take precautionary measures to prevent exposure at workplaces where nanomaterials are handled. Following this, as considerations regarding the handling of nanomaterials continued at concerned ministries, the media reported that multi-walled carbon nanotubes, a type of nanomaterial, may affect the human body in the same way as asbestos, based on results obtained in the most recent domestic and international risk-related research. As a result, certain groups are expressing concerns over safety. How well do we understand the risks of carbon nanotubes, and how far has research into these risks progressed? What is the current state of risk management and communication? These notes compile information on recent trends viewed in light of these questions.

What Are Nanomaterials?

Generally, the term "nanotechnology" refers to technology involving objects and phenomena on the scale of nanometers (nm), or billionths of one meter. As described in the 2nd Science and Technology Basic Plan, this ability to handle and manipulate such revolutionary phenomena and functions, unable to be viewed on a conventional scale, is important. The United Kingdom has defined the field of nanoscience, which seeks to further understand these phenomena and functions, and nanoscience activities in the United States include research aimed at understanding the characteristics of the nanoscale.[1]

The term "nanomaterials" generally applies to synthetic materials measuring between approximately 1 and 100 nm in one dimension, even with minimal basic structure.[2] Within this category, a "nanoparticle" is defined as a spherical object with a diameter between 1 and 100 nm, however this term is often used interchangeably with "nanomaterial." Nanomaterials have different physical characteristics than conventional materials, and are expected to bring large benefits to society in a variety of fields as a next-generation fundamental industrial technology with the ability to break conventional technological barriers. On the other hand, the extremely small nature of these materials makes them both biologically invasive and highly bioreactive, leading some to point out the potential for negative impacts on humans and the environment as well as the presence of ethical problems.[3]

Following the indication of issues related to nanotechnology and the environment, health, and safety by the United States' National Nanotechnology Initiative (NNI) in 2000, guidelines for risk assessment and management have been issued in the United States, the UK, Germany, and other western countries.[4] In 2004, the UK's Royal Society and Royal Academy of Engineering released a report stating that nanotechnology could bring great benefits, but that it will require responsible development. Regarding the impacts of nanotechnology on health and the environment, in particular the report depicted inhalation during the nanomaterial manufacturing process and environmental pollution as problems, and stated the need for consideration of safety throughout the life cycle of products incorporating nanomaterials, from production to disposal.[5] In the midst of these developments, the Organisation for Economic Co-operation and Development (OECD) established a Working Party on Manufactured Nanomaterials in 2006, and is moving forward with international partnership efforts including nanomaterials hazard data collection and the consideration of assessment methods.[6]

In Japan as well, efforts to understand the societal impacts of nanotechnology have intensified since fiscal year 2004,[7] and continuing discussion centered around the Cabinet Office has been held by related government agencies, universities, public bodies, and industry groups.[8] Combined with these activities and based on the support of related ministries, research on the assessment of nanotechnology's impacts on the environment, health, and safety continues.[9]

"Nanomaterial risk assessment" refers to "risk (danger level)," expressed as a combination of "hazard," indicating how hazardous the target material is, and "exposure," indicating the frequency, range, and amount that the material comes in contact with a human body or the environment, and assesses this risk scientifically and quantitatively. Accordingly if exposure is managed properly, it is possible to minimize risks even with a highly hazardous material.

Multi-walled Carbon Nanotubes: Background Information

1. What Are Carbon Nanotubes?

A “carbon nanotube” (CNT) is a type of nanomaterial; more specifically, a one-atom thick carbon sheet rolled into a tube. Compared with a quantity of iron weighing the same amount, this material is several hundred times stronger, and is thin and light. Consumer products using carbon nanotubes already exist and include sports supplies like tennis racquets, bicycle handlebars, and baseball bats. Applications include semiconductors, because carbon nanotubes become semiconductors based on differences in three-dimensional structure, television displays, due to high electrical conductivity and the ability to emit electrons at low voltages, and heat sinks, owing to excellent thermal conductivity. Because they bond well with hydrogen, it is also expected that they will be used as hydrogen storage material for fuel cells.[10] Further, carbon nanotubes have gained attention as a material which could be used to realize a space elevator, extending from the earth into geostationary orbit.[11]

Japan has been a leading research and development region since the theoretical discovery of carbon nanotubes in 1991, and as of the 2006 fiscal year is still at the forefront of production technology and the fields of highly functional materials, energy, and the environment. Also, the research and development of electronics-related applications is seen as occupying an important position in Japan.[12] The scale of the global market in this area was an estimated 20 billion yen as of 2004, and according to some forecasts it could be at 100 billion yen by 2010 if steady growth continues.[13]

A multi-walled carbon nanotube (MWCNT) is a layered tube created by concentrically nesting multiple individual carbon nanotubes of differing diameters and lengths, as shown in Figure 1. While the diameter of a single-wall carbon nanotube is on the order of a single nanometer, that of a multi-walled carbon nanotube is in the tens of nanometers (Figure 2). Market prices vary based on type, purity, and other factors, but it is estimated that single-wall nanotubes sell for between 10,000 and 100,000 yen per gram, with multi-walled carbon nanotubes selling for between hundreds of yen and 20,000 yen per gram.[14] During 2006 approximately one hundred kilograms of single-wall carbon nanotubes were estimated to have been used in Japan, compared with an estimate of approximately sixty tons for multi-walled carbon nanotubes. Almost all of these multi-walled carbon nanotubes were mixed with plastic for use in semiconductor trays. Use in conductive paste, power storage devices, and fuel cells, as well as medical applications, are expected in the future.[15]

Figure 1: A multi-walled carbon nanotube[16] (diameter 10-100 nm)

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Figure 2. Usage amounts and particle sizes of primary nanomaterials[17]

Omitted

2. Social Trends Related to the Safety of Multi-walled Carbon Nanotubes

Looking beyond the many expectations surrounding carbon nanotubes, there are also considerable concerns regarding their safety. The facts that carbon nanotubes may behave similarly to asbestos inside the human body, and that appropriate research is required, were being pointed out in as early as 1998.[18] Research results claiming that the nanocarbon material fullerene (C_{60}) was present in the brains of fish raised in a tank into which it had been dispersed were released and sensationalized by the media in 2004.[19] These developments have led to more active recent research on the safety of nanomaterials. From 2003, a sudden increase in the number of scientific papers on the risks of carbon nanotubes has taken place, with 46 items in 2006 compared to only one in 2000.[20] The United States' National Institute for Occupational Safety and Health (NIOSH) has been advancing assessment research on single- and multi-walled carbon nanotubes since the early 2000s.[21] In Japan as well, since 2005 METI and the MHLW have been supporting the same kinds of research.

In 2008, two independent reports from Japan's National Institute of Health Sciences (NIHS) and the University of Edinburgh garnered broad attention by reporting that in their experiments, intraperitoneal administration of multi-walled carbon nanotubes in mice caused mesothelioma similar to that resulting from exposure to asbestos. The NIHS group administered multi-walled carbon nanotubes to the abdominal cavities of mice which had been made deficient in genes which act to suppress cancer. In February 2008, having claimed the occurrence of mesothelioma in this experiment, this group published a paper in a Japanese academic journal indicating that multi-walled carbon nanotubes might cause the same kind of mesothelioma that asbestos does,[22] with the Mainichi Daily News running the headline "Cancer-inducing?"[23] The Tokyo Metropolitan Institute of Public Health, which had cooperated with the research,[24] carried out an experiment in which multi-walled carbon nanotubes were administered to the abdominal cavities of normal rats without genetic alteration. The occurrence of mesothelioma was observed, and the results were announced on the Tokyo Metropolitan Government's homepage on February 22.[25] The mesothelia are membranous structures which surround various body cavities. These include the pleura, which encloses the thoracic cavity, and the peritoneum, surrounding the abdominal cavity (Figure 3).

Following these events, the University of Edinburgh research group in the UK conducted experiments using normal, healthy mice in which a variety of multi-walled carbon nanotubes and asbestos were used, in order to assess the impact that differences in characteristics such as fiber length and diameter would have. These results, claiming an increase in foreign-body giant cells and in the size of affected areas in the case of multi-walled carbon nanotubes and asbestos having longer fibers, were announced in an online academic journal on May 20, 2008[26]. On the same day as the announcement of the University of Edinburgh research findings, major foreign media concurrently reported that carbon nanotubes produce a response similar to that of asbestos in experiments with mice.[27] Two days later media outlets in Japan as well, such as Nihon Keizai Shimbun and NHK News, reported on the risk that carbon nanotubes could cause mesothelioma.[28] Certain NGOs, viewing the results of this research in a grave manner, have recommended the establishment of guidelines, standards, and laws relating to nanotechnology safety measurement, the participation of citizens in the decision-making process, and a moratorium on the manufacturing and import of nanotechnology products until safety has been confirmed.[29]

In response to these developments, on February 7, 2008 the MHLW sent the "notification on present preventive measures for the prevention of exposure at workplaces manufacturing and handling nanomaterials"[30] (hereafter referred to as "Notification") to related business associations, industrial-safety organizations, and the directors of prefectural labour bureaus. On February 22, the Tokyo Metropolitan Government mentioned the research of NIHS and the Tokyo Metropolitan Institute of Public Health in announcing a "Request for proposals on safety measures related to carbon nanotubes and other materials."[31] This document requests that the MHLW further promote health-risk assessment research, enact measures to prevent workplace exposure and dispersion into the environment, and distribute information based on an accurate understanding of carbon nanotubes. A similar request was submitted by a member of the Diet in June.[32]

In its Notification, the MHLW indicated that investigative commissions of experts in the field would be established, and in March the first of these meetings was held jointly with the Labour Standards Bureau and the Pharmaceutical and Medical Safety Bureau. As a step towards improving the efficacy of countermeasures for nanomaterials in the workplace, the Labour Standards Bureau's "Study Group on Preventive Measures for Exposure of Personnel to Chemical Substances with Unknown Human Toxicity (Nanomaterials)" indicated a detailed management method, giving consideration to the realities of workplaces and considering the facts and issues related to exposure prevention countermeasures, summarizing these findings in a report released in November.[33] The Pharmaceutical and Medical Safety Bureau's "Study Group on Safety Measures for Nanomaterials" is planning to release its findings by the end of fiscal year 2008. This report will be based on an understanding of the state of nanomaterials development, current scientific knowledge, and related regulations, and will indicate specific responses for the future and current barriers to the implementation of safety measures.

Figure 3. Position of the mesothelia[36]

Omitted

Table 1. Principal events related to carbon nanotube risk assessment and risk management[38]

1998 Research paper indicating that carbon nanotubes may behave similarly to asbestos in the human body is announced
2001 United States: NNI decides to conduct research on the impacts of nanomaterials on health, safety, and the environment (renewed in 2004)
2004 United Kingdom: The Royal Society and Royal Academy of Engineering release the report “Nanoscience and nanotechnologies: opportunities and uncertainties” (July) MHLW: Research related to nanomaterials safety measures begins
2005 Ministry of Education, Culture, Sports, Science and Technology (MEXT): Research project on facilitation of public acceptance of nanotechnology Woodrow Wilson International Center for Scholars initiates a project on nanotechnology (April) **♦ High expectations for expanding nanomaterial applications, especially for carbon nanomaterials**
2006 MHLW: Study of the current state of nanomaterials in workplaces (April) MEXT: Multi-disciplinary expert panel on societal implications of nanotechnology National Institute of Advanced Industrial Science and Technology (AIST): Initiates research and development related to nanoparticle characteristic assessment methods National Institute for Environmental Studies (NIES): Initiates research on the biotransformation of nanoparticles, etc., in the environment and health effect assessment OECD: Establishes the Working Party on Manufactured Nanomaterials under the Chemicals Committee (September) The Consumers Union of Japan sends an open letter with questions regarding the safety of nanotechnology to the MHLW, METI, and the Japan Cosmetic Industry Association (September 15) **♦ Careful examination of the synthesis method for carbon nanotubes** **♦ Little progress visible on the road to product development**
2007 CSTP: Establishes “Developing Nanotechnologies and Engaging the Public” coordination program MHLW: Initiates investigation on nanomaterials safety measures National Institute of Occupational Safety and Health, Japan (JNIOSH): Begins study on actual exposure conditions, research into measurement devices, etc. METI: Announces management method guidelines for nanotechnology research and production sites (March) **♦ Prospects for a carbon nanotube mass-production method** **♦ Many manufacturers promote achievements**
2008 MHLW: Notification on precautionary measures for exposure prevention (February 7) Tokyo Metropolitan Institute of Public Health: Releases experiment results on homepage (February 22) NIHS: Publishes research paper in academic journal (February 26) MHLW: Establishes investigative commission related to nanomaterials safety measures (March 3) University of Edinburgh: Publishes research paper in academic journal (May 20) Member Masamichi Kondo submits a memorandum on questions regarding carbon nanotube safety and preventive measures to the House of Councillors (June 3) Ministry of the Environment: Establishes investigative commission related to the environmental impacts of nanomaterials (June 16) MHLW: Releases investigative committee report related to preventive measures (November 26) METI: Establishes research group on nanomaterials safety measures (November 27) **♦ Business attitudes cool down**

In June, the Ministry of the Environment launched an “expert committee on the environmental impact of manufactured nanomaterials," indicating the basic view that even at an inconclusive stage of hazard assessment, from a precautionary perspective, it is beneficial to create systems of manufacture and usage that focus on exposure prevention. The “guidelines for preventing the environmental impact of manufactured nanomaterials” were released in March 2009. They compiled information on the status of usage in Japan, toxicity, environmental management technology, and other topics.[34]

The METI Manufacturing Industries Bureau’s “Research Group on the State of Safety Measures among Nanomaterial Manufacturers" began considering voluntary safety measures being taken by nanomaterial manufacturers in November 2008, and released a report in March 2009 detailing areas targeted for consideration—the definition and range of nanomaterials, safety efforts in Japan and abroad, basic trends in responses, and detailed responses.[35]

Figure 4. Magnified photographs of carbon nanotubes (above) and asbestos (below)[37]
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Recent Toxicity and Risk Assessment Research on Multi-walled Carbon Nanotubes[39]

This section examines the implications of representative recent research on the assessment of toxicity and risk.

1. Research by NIHS and the University of Edinburgh Group

Based on the fact that carbon nanotubes are fibrous, in the intraperitoneal application experiment mentioned above, NIHS was testing the Stanton-Pott hypothesis[40]. This hypothesis originated in the 1980s, when Stanton and Pott proposed a general rule that fibrous matter which is durable, thin, and long has carcinogenic properties in biological systems regardless of chemical composition or crystalline structure, especially fibers less than 0.25 µm in width and greater than 8.0 µm in length, which are most likely to cause mesothelioma. Phagocytes (cells that engulf and destroy foreign matter) present in biological systems are unable to ingest long, thin multi-walled carbon nanotubes, and it is thought that their resultant accumulation can cause cancer (Figure 5).

However, metal elution (purity), surface modification, specific surface area, size effect, and aggregating effect are also all possible causes of toxicity. Knowledge in this area is still insufficient.[42] Additionally, the Stanton-Pott hypothesis itself, which states that toxicity is based on fiber length, is not a established theory, and there is not currently a sufficient basis to argue that it should receive more emphasis than other possible factors.

Further, the NIHS research group has taken the stance that, since even minimal exposure to asbestos or carbon nanotubes can have irreversible impacts on the human body over a long period of time, there is no lower limit or threshold dosage for displaying toxicity. In contrast, some hold the view that a threshold dose does exist for carcinogenic materials like asbestos.[43] One argument states that detailed investigation of the relationship between the material dosage amount and biological response (dose-response relationship) is needed,[44] with some research on this dose-response relationship for carbon nanotubes being conducted.[45]

In actuality, opinions regarding this research are varied. Aside from the dose-response relationship, a number of experts have pointed out that some experimental methods are based on intraperitoneal dosage, which is unlikely to occur in the real world, and the fact that it is necessary to investigate the probability that nanotubes inhaled in actual manufacturing processes would arrive at the pleura or abdominal cavity.[46] On the other hand, in experiments with fibrous substances such as asbestos using mice, because inhalation toxicity is not indicated as clearly in the case of humans, some have expressed the opinion that intraperitoneal dosage is useful to a certain extent in confirming the hazard of such materials.[47]

2. NEDO Project (Research by AIST and the University of Occupational and Environmental Health et al., Japan)

Beginning in fiscal year 2006, AIST and the University of Occupational and Environmental Health, Japan (UOEH) have been advancing research and development aimed at establishing a method for evaluating the risks of manufactured nanoparticles, including multi-walled carbon nanotubes, through the “Research and Development of Nanoparticle Characterization Methods” project of the New Energy and Industrial Technology Development Organization (NEDO).[48]

In contrast to the research efforts of NIHS and the University of Edinburgh, the NEDO project is furthering hazard evaluation for carbon nanotubes using tests similar to those for other nanomaterials.[51] For the three materials which have generated the most interest (fullerene, single-wall carbon nanotubes, and multi-walled carbon nanotubes), more realistic inhalation exposure tests, tracheal injection experiments consistent with these, and test tube experiments are all being performed, including hazard evaluation. At the same time, simple test-tube experiments with approximately 50 types of materials are being performed in an effort to determine hazard based on relative relationships to specified nanomaterials.

Exposure assessment is conducted by comprehensively analyzing the following three things: 1) emission scenarios (through what activities and in what quantities are materials emitted?); 2) the material’s behavior and changes in the environment; and 3) exposure scenarios (in what situations does exposure take place and what are the levels of exposure?). Because of this, in addition to measurements at workplaces using nanomaterials, they are also conducting emission simulation tests in which nanomaterials are agitated and dispersed and particles are measured. Additionally, they are attempting to analyze the life cycle of products using nanomaterials through literature review and investigative hearings.

Interim evaluations of the NEDO project have offered praise for its more realistic inhalation exposure tests and efforts to establish a structure for hazard evaluation. However, the evaluators also comment that the thinking behind connecting exposure under actual usage conditions with hazard evaluation testing needs to be made more organized and clear. Also, because current risk assessment tends to be unilinear, it is expected that considering estimation with a broader range, sensitivity analysis, and exposure and risk analysis corresponding to the stages of development will restructure risk evaluation and management frameworks.[52]

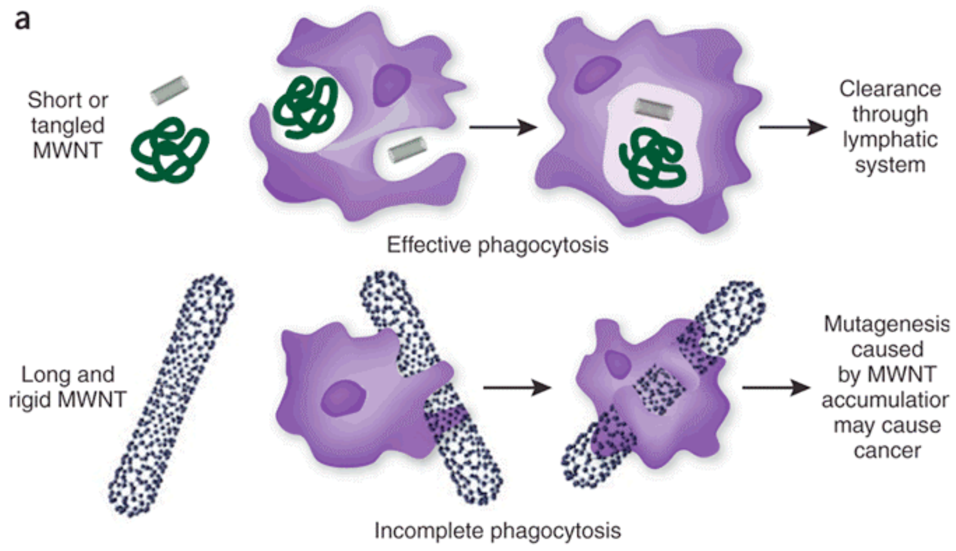

Figure 5. Relation between the long, thin nature of multi-walled carbon nanotubes and their hazard in organisms[41]

3. Other Research in Japan

JNIOSH is carrying out "Research on Risk Assessment for Nanoparticles, Material for Advanced Industry,"[53] which began during fiscal year 2007 and is scheduled to last for three years. This project aims to assist in health administration for workers in nanotechnology industries by acquiring basic data necessary for regulating nanoparticles, including carbon nanotubes, and establishing a hazard assessment method for nanoparticles. Research related to measurement methods for particulate concentration in the air, exposure assessment methods, and ecological assessment methods had been planned, but the establishment of hazard assessment methods, not exposure assessment, is the research theme. In external ex-ante evaluation of this research, a number of evaluation committee members pointed out the importance of examining information in order to perform exposure assessment in realistic workplaces, and of setting experimental conditions.[54]

NIES has initiated research on the chronic effects of intraperitoneal administration of carbon nanotubes, and in the course of observation for 18 months following administration, it was confirmed that the groups of mice which had been administered 2 µg and 10 µg of multi-walled carbon nanotubes had lower survival rates.[55] Aside from this, a group at Tohoku University is conducting research on hazard in relation to the length and surface of carbon nanotubes.[56]

Table 2. Primary recent research on the toxicity and risks of carbon nanotubes

	Primary objectives	Characteristics	Primary points raised by external parties
NIHS	Confirm hazard based on the Stanton-Pott hypothesis	Identification of mesothelioma following intraperitoneal administration in genetically deficient mice	Unrealistic bodily entry pathway and administration dosage[40,46,49]
Tokyo Metropolitan Institute of Public Health		Identification of mesothelioma following intraperitoneal administration in normal rats	
The University of Edinburgh	Confirm hazard based on the Stanton-Pott hypothesis	Identification of mesothelioma following intraperitoneal administration in normal mice	Unrealistic bodily entry pathway[49]
NEDO Project	Establish risk assessment method	Usage in test of samples characterized from sample-preparation technology development; inclusion of exposure assessment and societal considerations in project	Unclear link between exposure during actual use and hazard assessment; unilinear risk assessment[51]
JNIOSH	Research risk evaluation for use in occupational risk management	Understanding of actual usage situations for exposure study; hazard assessment	Need for examination of information necessary to assess exposure in real-life workplaces[50,54]
NIES	Research chronic effects of carbon nanotubes	Confirmation of decreased survival rate following intrathoracic administration in normal mice	Lack of investigation as to whether manifestation of health impacts resulted from physical stimuli or were chemical reactions[55]

4. Are Multi-walled Carbon Nanotubes Another Asbestos?

Risk, as mentioned above, is expressed as a product of hazard and exposure. Accordingly, when comparing the risks of multi-walled carbon nanotubes to those of asbestos, we must consider not only hazard but exposure as well. While the yearly production volume of multi-walled carbon nanotubes is approximately 60 tons, that of asbestos is around 300,000 tons, with a cumulative 10 million tons having been used up to the present.[57] Additionally, multi-walled carbon nanotubes are not used as a building material in large quantities or in a way which releases them directly into the environment, as with asbestos. For these reasons, it is plausible to say that multi-walled carbon nanotubes do not immediately create a level of risk which would justify equating them with asbestos. However, carbon nanotubes are one nanomaterial upon which global expectations have been placed, and in reflecting on the way in which research and development has been pursued, the need for substantial risk assessment and risk management efforts cannot be ignored.

5. Conclusions

NIHS and the University of Edinburgh research group have focused on the similarity of carbon nanotubes and asbestos as fibrous materials, and are assessing the hazard of multi-walled carbon nanotubes based on the Stanton-Pott hypothesis, which states that the thinness and length of materials are related to hazard. However, whether or not the thin, long nature of the material is the controlling factor, whether or not there is a threshold dose, and whether or not nanotubes will actually reach the abdominal cavity have all yet to be confirmed. On the other hand, the NEDO project has established a hazard assessment testing method for carbon nanotubes that uses tracheal inhalation, a natural entry path, and is aiming for risk assessment combined with exposure assessment. As with the establishment of an inhalation exposure testing method, it is thought that there are still many issues in creating appropriate exposure scenarios, based on actual environmental data, which can be used for exposure assessment. Furthermore, regarding all of this research, hazard has been displayed in experiments with animals, but there is still much room for debate as to how to postulate from this the level of risk for humans.

Trends in Risk Management and Communication Associated with Nanomaterials

1. Risk Management in Government and Industry

"Risk management" refers to acquiring an understanding of risk occurrence, indicating what kind of response will be taken with regard to risks that occur, and actually responding to such risks. The first two aspects are represented by METI's guidelines and the MHLW's Notification. Examples of the latter component are environmental, health, and safety efforts being carried out at factories and research organization workplaces, and crisis management by business administrators.

In 2007 METI contracted with a private research firm to investigate the status of research organizations and manufacturers conducting research or manufacturing activities related to nanotechnology, at the same time investigating management case examples abroad and releasing voluntary management guidelines.[58] These indicated basic guidelines in areas including nanomaterials manufacturing and processing, operations management, cleaning and waste material management, and protective equipment. While providing these guidelines to member companies of nanotechnology-related organizations, METI has also been urging voluntary efforts based on their content.[59] Measures which should be taken by companies producing nanomaterials, such as multi-walled carbon nanotubes, concerning matters such as production equipment and processes, work management, and protective equipment are also indicated in the Notification released by the MHLW in February 2008. Because of the need to indicate more specific management methods that take workplace realities into account and to further consider the current situation and challenges regarding exposure-prevention measures, the investigative committee that was subsequently launched continued its deliberations, and in November compiled a report indicating such specific management methods.

Carbon nanotube research and development has progressed smoothly in the United States since 2000, but has seemed sluggish in Japan since 2002. The reason given for this is that because projects in Japan receiving public funding mixed basic and objective-oriented research, despite success in synthesizing high-quality carbon nanotubes, there was no commercialization concept. On the other hand, although preliminary products using the "nano" image circulated in the marketplace as a result of the nanotech boom created by the media, because the most important research and development did not bring technological achievements, the boom peaked in 2002.[60] For example, at "nanotech," a representative Japanese international exhibition related to nanotechnology and nanomaterials, despite the fact that the number of exhibitors and guests has increased steadily over the years, the number of exhibitors announcing displays related to carbon nanotube materials remains stagnant.[61] Even in this situation, electronics-related Japanese firms are steadily acquiring patents, moving forward with research and development, and displaying successes through commercialization.[62]

However, according to companies, the Notification released in 2008 by the MHLW had a greater impact on business than on workplace activities. The actual responses of companies to the Notification have been described as falling into two broad categories. First, companies that had been carrying out production up until that time were using a minimal amount of equipment to counteract conventional dust pollution while handling nanomaterials. These situations were conceived of as best-practice procedures, resulting in little if any action in response to the Notification. Second, companies that were just beginning nanomaterials-related manufacturing adopted a wait-and-see stance.[63] After receiving the Notification, some nanomaterials-related companies provided product users with cautionary notifications[64] or articulated environmental safety management systems.[65] However some suspect that viewed from the standpoint of business, the possibilities of wasted investment and diminished company images resulting from future regulations, risks to business management,[66] and current risk information have all put businesses in a negative position.[67]

In actuality, some venture companies handling nanomaterials such as carbon nanotubes stopped receiving financing from banks following turmoil regarding safety. Aside from businesses where research and development were frozen, some carbon nanotube producers were notified of a discontinuation by downstream companies, and some decided to voluntarily wait for movement in end markets.[68]

2. Precautionary Approach

Reflecting on problems caused by asbestos in the past, the government has expressed the conclusion that even though related ministries and agencies responded in accordance with scientific knowledge at the time, awareness of a "precautionary approach" and coordination between related ministries and agencies may not have been sufficient.[69] A "precautionary approach" refers to the attitude that "if there is a chance of serious harm, even if not completely scientifically verified, countermeasures must not be delayed." This is viewed as different from "prevention"—enacting preventive regulations in order to avoid harm from risks for which the causal relationships have been scientifically proven[70]—but confusion is frequently apparent among government and experts.[71]

One view holds that the MHLW's response to nanomaterials took into account conclusions drawn from past experience, applying a precautionary approach,[72] and that it was allegedly the fastest response among regulatory authorities of any nation.[73] This is seen as being based on the research accomplishments of NIHS,[74] but no official explanation has been given. The facts that the Notification was not limited to carbon nanotubes but rather targeted all nanomaterials, and that its measures are uniform, not based on the individual characteristics of nanomaterials, are reasons why it is difficult to ascertain its basis. Also, while concerns regarding occupational safety and health impacts in the production industry have been studied,[75] the government has not yet carried out an investigation of the realities of industry concerns such as those mentioned above, regarding research and development, innovation, and business promotion in light of the MHLW's precautionary measures. In other words, because balanced consideration of both the risks and benefits has not taken place, with an unchecked cool-down lasting for years in the market for carbon nanotubes, opportunities for the expansion of nanotechnology-related business are being lost.

On the other hand, substantive debate by deliberative councils up until this point has been extremely scarce with regard to defining safety. One opinion is that the lack of understanding with regard to safety is due to the fact that a testing method has not yet been established.[76] However, without a clear definition of "safety" itself, the basis for risk management is lacking.

3. Communication between Related Government Agencies and Organizations

A number of deliberative councils are debating the state of cooperation between related government agencies and organizations with regard to nanomaterials safety efforts.[77] As understood by committee members participating in the METI and CSTP project teams, this kind of cooperation is being achieved,[78] and was further promoted by the establishment of the Coordination Program of Science and Technology Projects.[79] Through this Coordination Program, the CSTP sets "nationally and socially important themes that should be promoted through the cooperation of related government agencies," eliminates unnecessary and redundant related policies, and strengthens and actively promotes cooperation.

JNIOSH provides an example of cooperation between research organizations. They are exchanging information with industry organizations and domestic and international research bodies, and also studying nanomaterials-related occupational health jointly with AIST while avoiding research overlap.[80] However, even though the research projects of NIHS and AIST are in the same coordination program, differences in risk assessment policies between the two have not been clearly identified. Also, because the MHLW's Notification was released by the Labour Standards Bureau, the research organization that will have responsibility from this point on is JNIOSH, but the question of how to carry on with NIHS's risk assessment structure and research achievements presents a challenge. This kind of strategic diversification and decentralization in public research organizations' attitudes and efforts related to the evaluation and management of toxicity and risks was not an intended outcome.

Unbalance can also be observed among experts involved with communication. Regarding progressing with research related to nanotechnology risks, there are extremely few experts in the field of risk assessment, so much so that some have pointed out the fact that Japanese research in toxicology and occupational health engineering lags behind that of the USA and some European countries.[81] Also, some members of the CSTP's project teams in the fields of nanotechnology and materials are of the opinion that a range of experts necessary to handle safety problems is lacking.[82]

4. Communication with the General Consumer and Society

From the point of view of the general consumer and society, the benefits of nanotechnology are expected rather than real. The usefulness of this technology has yet to be publicly acknowledged, making it susceptible to damage from harmful rumors.[83] Also, regarding coverage in the mass media, there are problems with the accuracy of information, and some have made the criticism that dangers tend to be sensationalized.[84]

Let's look at efforts in other countries for perspective on what constitutes appropriate communication.[85] One example in the United States is an international organization which includes businesses, universities, government, and NGOs, called the International Council on Nanotechnology (ICON) and based at Rice University. This organization's activities include holding forums and events related to the health and environmental risks of nanotechnology, building knowledge databases with items such as peer-reviewed research papers, providing high-level technological information useful in decision making, and building a basis for communication so that a variety of stakeholders can easily understand complex data.[86] Also in the United States, the Woodrow Wilson International Center for Scholars, a nonpartisan think tank, began a project on nanotechnology in 2005. As one part of this project, they are advancing the creation of a database of global public research projects related to the health and environmental impacts of nanotechnology.[87] Through these activities cooperation between public and private research is accelerated further, with the promotion of international research cooperation as a primary objective. Also, the Royal Commission on Environmental Pollution is an organization in which experts from the business, academic, and public sectors participate on an individual basis. Although they receive financial contributions from the UK's Department for Environment, Food and Rural Affairs, they carry out independent activities and have numerous connections not only with government agencies and parliament, but also with research organizations, the business community, environmental organizations, and other parties. The Royal Commission issued a press release regarding nanomaterials in November 2008.[88]

In Japan, although only a single-year project, the MHLW is creating a database through a far-ranging literature review.[89] The Council for Science and Technology Policy's Coordination Program of Science and Technology Projects is also advancing research aimed at the development and operation of a database targeting nanomaterials measurement methods, physical information, etc.[90] However, in all of these instances emphasis tends toward hardware-oriented database building, with very little clear awareness of which segments of the population should be offered useful services. Also, due to the impermanent nature of these systems, uncertainties about accumulating information and knowledge in the future remain. In the private sector, the NBCI was established by volunteers from the business community in 2003 to conduct and promote business matching. This organization is currently engaging in exchange of the most up-to-date technology information; the sharing of information between entrepreneurs, researchers, and investors; human exchange between researchers and technicians; research and development strategy recommendations to government; venture business support; standardization; outreach and education. However, cooperation with a wide variety of related organizations such as universities, public research organizations, and NGOs is still developing. Activities such as promulgating nano-related safety information as a representative the nanotech industry and promoting the existence of the NBCI itself are also being considered, but have not yet been realized due to insufficient human resources and other factors. It is also thought that because nanotechnology is related to a variety of fields, and businesses in diverse areas are affiliated with NBCI, the group was not able to provide unified opinions or recommendations with regard to government policymaking.[91] Looking at NGOs, one can observe that they are striving to achieve scholarly nanomaterials risk assessment and management;[92] introducing information from around the world related to nanotech-associated risks, the establishment of nanotech safety standards, and regulatory trends;[93] and conducting investigatory research on the safety of nanotech cosmetics and the opinions of researchers associated with nanotechnology.[94] Currently, however, they have little power of influence, and do not seem to have the kind of stable operations systems which would be capable of playing a central role in communication.

Conclusions

1. Knowledge about the Toxicity and Risks of Multi-walled Carbon Nanotubes

In the most recent research considering the toxicity of multi-walled carbon nanotubes, one type of nanomaterial, the occurrence of mesothelioma similar to that resulting from exposure to asbestos was observed following direct intraperitoneal dosage of the material in mice. In order to estimate the risks that multi-walled carbon nanotubes pose to the human body and the environment, it is necessary to make an assessment in relation to toxicity and exposure. However, there are apparent differences in perspective as to what the principal objective of such an assessment should be. Additionally, opinions differ among researchers about whether this material's structural similarities with asbestos determine its hazard, as well as about whether or not there is a threshold dosage amount which displays toxicity. Detailed results of exposure assessments are not currently available, but because the volume of multi-walled carbon nanotubes in use is small and the chances for direct exposure to large quantities are limited, this material does not seem to pose a level of immediate risk which would justify categorization as "another asbestos."

2. Precautions

In Japan, following the public release of multi-layer carbon nanotubes' harmful effects on mice, at an early stage of events on the global scale, a notification requesting that organizations using such materials take precautionary measures with regard to nanomaterials as a whole was issued by the MHLW, but its content was vague and it did not provide a clear basis for taking such measures. Despite this the notification—reported on by the media—had a significant social impact, and some businesses experienced stagnation in the nanotechnology sector due to reaction from banks and downstream companies.

3. Cooperation among Related Agencies

The MHLW; METI; and the Ministry of the Environment are each independently investigating the impacts of nanotechnology on the environment, health, and safety. In contrast, the Cabinet Office is aiming for cooperation between these ministries' nanotechnology research efforts. However, the Cabinet Office has yet to compare and assess in a unified manner the most up-to-date scientific knowledge regarding the environmental, health, and safety impacts of nanomaterials and articulate a strategic policy regarding measures to be taken, and in this respect, their efforts toward collaboration are not functioning effectively.

Responsive Steps for the Future

1. Deepening the Discussion about Risk Assessment and Risk Management for Multi-walled Carbon Nanotubes

There are a variety of viewpoints on the assessment of multi-walled carbon nanotubes, for example about whether more importance should be placed on assessing hazard or exposure. Because of this it is necessary for the Cabinet Office to gain a systematic understanding of the current fundamental thinking of researchers, both in Japan and abroad, regarding toxicity and risk assessment for nanomaterials. Based on this understanding, it is imperative to deepen the discussion about multi-walled carbon nanotubes. We must consider the level of safety that should be incorporated in preventive measures, and also costs such as the actual burdens on industry and opportunity loss, viewing these in comparison with the benefits that Japan stands to gain by competing internationally in research and development, innovation, and industrial expansion.

2. Precautionary Measures Related to Multi-walled Carbon Nanotubes

Making clear what kinds of information and systems we currently lack is essential in order to take effective precautionary measures. In deciding on such measures for the future, we must supplement these insufficiencies and utilize a process which will create decision-making results acceptable to society as a whole. Specifically, a forum is needed that will allow for ongoing examination and reformulation of responses and regular discussion of risks, based on the sharing of up-to-date information by related parties. It is desirable to enact specific, workable precautionary measures that are based on both this kind of discussion and an accurate understanding of the current situation. Based on the results of this kind of dialogue, there is also a responsibility to provide reliable information to society as a whole.

3. Nanomaterials Management Systems and Cooperation between Related Parties

The Cabinet Office should further develop inter-agency cooperation and make management systems more substantive through the creation of a science-based network. Deepening organizational cooperation—including industry, academia, public research institutions, NGOs, and consumer organizations—is another desirable objective. For example, the establishment of a database compiling information about nanomaterials risks through industry-academic-government collaboration, and risk communication which allows citizens to access that information, could be expected. Further, we should increase the opportunities for this kind of diverse knowledge to be brought together with human resources, and through NBCI, promote public interest in the societal impacts of nanomaterials and support combined, voluntary efforts by related businesses.

Additional Statement

In creating these notes, interviews with Ms. Yukako Itakura, Mr. Takeshi Yasuma, and two other individuals related to these contents were carried out. Additionally, the rough draft of these notes was reviewed by each of the individuals above, as well as by Mr. Masashi Gamo, Mr. Jun Kanno, Ms. Ayumi Kojima, and Mr. Seishiro Hirano. We would like to express our gratitude to all of these individuals. Comments received from a number of I2TA project members, including Gaku Ichihara, Akifumi Ueda, Tomoko Tsuchiya, and Shintaro Munakata also served as reference. The I2TA project group is solely responsible for these notes.

References

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