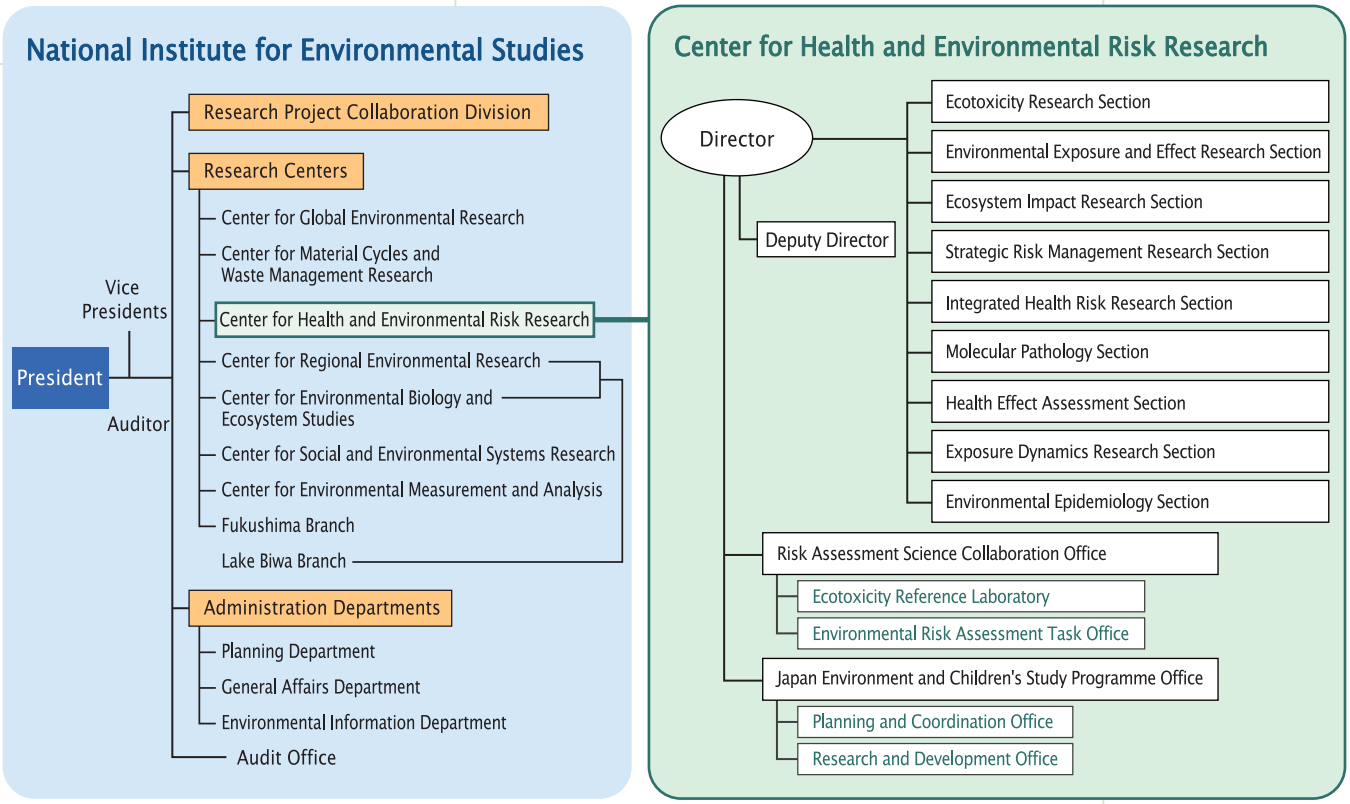
Research Center: Overview

Overview

The Center for Health and Environmental Risk Research conducts research to help realize a safe and secure society. The center integrates activities in the environmental risk research field and environmental health research field and the activities of the Health and Environmental Safety Research Program and of two projects administered by the Risk Assessment Science Collaboration Office (RASCO) and Japan Environment and Children's Study (JECS). In the environmental risk research field, the center is developing advanced ecotoxicity testing and assessment methodologies and environmental analyses of the effects of exposure to environmental chemicals, and is conducting chemical fate and exposure studies to provide data for the management of the risks posed by environmental chemicals. In the environmental health research field, the center is developing methods to determine the health impacts of exposure to environmental chemicals, the potential impacts of environmental chemicals on future generations, and the mechanisms of toxicity of environmental chemicals. The center is also conducting experimental and epidemiological studies to elucidate factors hazardous to the environment. RASCO is conducting official risk assessments under the *Chemical Substance Control Law* and other governmental frameworks, and disseminating the center's databases and research outcomes. The JECS Programme Office provides core management services for the 15 regional centres involved in the JECS.

Organization

The Center for Health and Environmental Risk Research is one of eight research centers in the National Institute for Environmental Studies. The center includes nine research sections—Ecotoxicity Research, Environmental Exposure and Effect Research, Ecosystem Impact Research, Strategic Risk Management Research, Integrated Health Risk Research, Molecular Pathology, Health Effect Assessment, Exposure Dynamics Research, and Environmental Epidemiology—that collaborate on basic research and task-oriented research programs. In addition, the center has two offices, RASCO and the JECS Programme Office, that oversee outreach research projects. We believe that the effective integration of our activities covering basic research, issue-oriented research, and the two outreach research projects is the defining characteristic of our center.



Research Program: Overview

Health and Environmental Safety Research Program

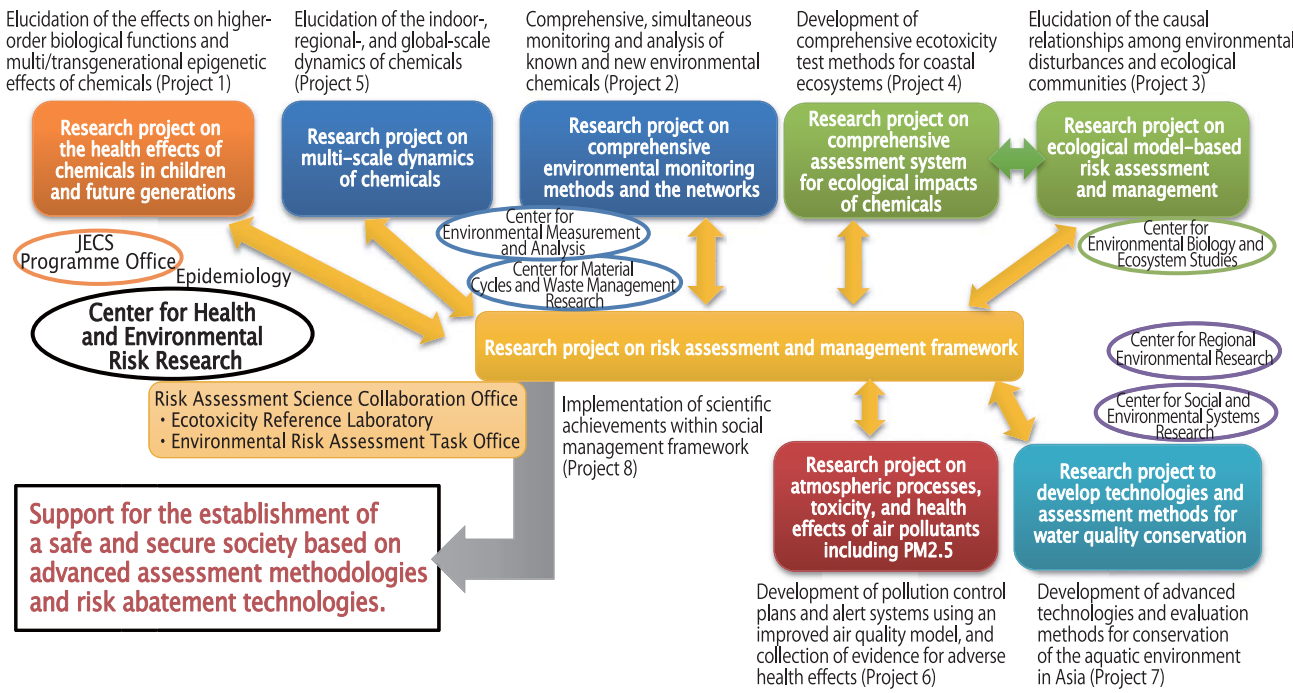
Systematic development of risk sciences to achieve the goal of safe and secure society

To ensure the establishment of safe and secure society, we must address current environmental concerns regarding chemical contamination and ensure that major environmental pollution events, such as the outbreak of Minamata disease in Japan, do not happen again. This is the basis of establishment of all other sustainable goals of low-carbon society, sound recycle-oriented society or society in harmony with nature. The aim of this research program is to provide scientific support through development of new findings on hazard, analytical technologies, fate processes and models, and abatement technologies, and also advanced risk assessment methodologies and management framework for environmental chemicals. To achieve this aim, the program is using a multi-faceted, systematic approach to find out new insight of health and environmental hazards, develop methods for assessing health and environmental risks, and abatement technologies to the risks, posed by environmental chemicals. The program is examining the effects of chemicals on higher-order biological functions and multi/transgenerational impacts, developing new systems for assessing the ecological impacts of chemical bioaccumulation and advanced high-throughput chemical analyses to obtain a more comprehensive understanding of the dynamics of environmental chemicals. In addition, the project is examining the atmospheric processes and the adverse health effects associated with exposure to PM2.5 and other air pollutants, and developing advanced methods for the conservation of regional aquatic environments.

The program comprises the following eight research projects:

- Project 1 is assessing the health effects of chemicals in children and future generations, and is examining the effects of chemicals on the development of immune and metabolic diseases, developmental neurotoxicity, and multi/transgenerational epigenetic inheritance.
- Project 2 is developing comprehensive environmental monitoring methods and networks, and is developing multicomponent simultaneous analysis and non-targeted analysis methodologies for the detection of biological effects and elucidating the potential chemical contaminants.
- Project 3 is developing ecological risk assessment and management based on ecological models, and is developing models to elucidate the causal relationships between environmental disturbances and ecological communities to predict environmental disturbances within ecosystems.
- Project 4 is developing a system for the comprehensive assessment of the ecological impacts of environmental chemicals, and is developing advanced methodologies for determining the ecotoxicity of environmental chemicals, assessing the integrity of coastal ecosystems, and determining the effects of mixtures of chemicals on the environment.
- Project 5 is examining the dynamics of chemicals on several spatio-temporal scales by developing analytical techniques and global-scale models for investigating the movement of toxic heavy metals through the environment, by examining the emission and behavior of chemicals on the regional scale, and by examining the dynamics of chemicals on the indoor scale.
- Project 6 is examining the atmospheric processes, toxicity and health effects of air pollutants including PM2.5 to propose pollution control plans, to collect evidence of adverse health effects and to construct alert systems.
- Project 7 is developing improvement technologies and assessment methods of water quality for the conservation of aquatic environments.
- Project 8 is developing an advanced risk assessment and management framework, and is developing a novel framework for assessing and managing the risks posed by environmental chemicals through interdisciplinary discussions on strategies and social actions.

By combining the research outcomes of these eight projects, the program aims to establish advanced systems for the detection and assessment of the health and environmental risks posed by known and new environmental chemicals for which there is currently no established approach, as well as to develop comprehensive and rapid monitoring and prediction systems and management technologies for environmental chemicals.



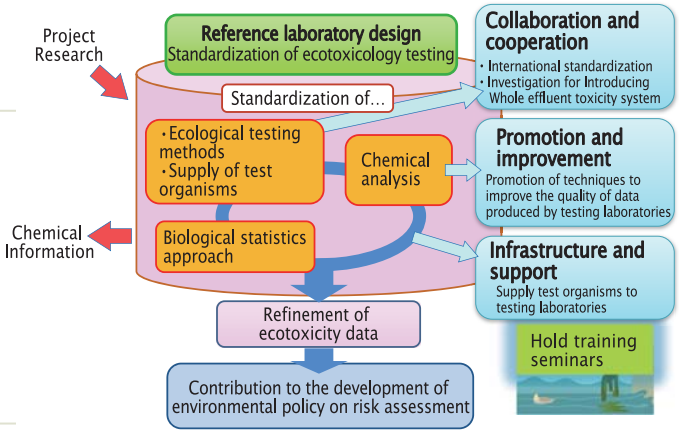
Outreach Research Projects

Risk Assessment Science Collaboration Office

The Risk Assessment Science Collaboration Office provides domestic leadership for the promotion of regulatory science with the aim of achieving a safe and secure society. The office conducts ecological toxicity research, promotes international collaboration for the development of advanced testing methods, supports the standardization of test implementation, promotes infrastructure development, and conducts other efforts to support regulatory policies and measures. The office also assesses environmental risks scientifically under the collaboration with other organizations, constructing databases, and disseminating knowledge and technical methodologies. The office focuses on implementing research projects to provide the latest research outcomes that can be used as the basis for new regulatory policy measures.

Ecotoxicity Reference Laboratory

The Ecotoxicity Reference Laboratory contributes to the realization of a safe society by proactively promoting regulatory science as a leading "reference laboratory for ecotoxicological research". To this end, the laboratory conducts ecotoxicological research to contribute administrative chemical management system such as the *Chemical Substances Control Law* or *Agricultural Chemicals Regulation Law*, develops new ecotoxicity test methods through collaboration with the Organisation for Economic Co-operation and Development (OECD) and the US Environmental Protection Agency, participates as the Japanese representative in international ring tests, supports the International Organization for Standardization (ISO) and OECD for the standardization of test methods, supplies stable test organisms for ecotoxicity testing, and conducts education seminars on ecotoxicity test techniques. In collaboration with domestic universities and local environmental laboratories, the laboratory also promotes ecotoxicity testing and performs scientific risk assessment. The laboratory provides the latest research results to domestic and international institutions, and conducts fundamental research for the development of more effective administrative measures to regulate environmental risk of chemicals.



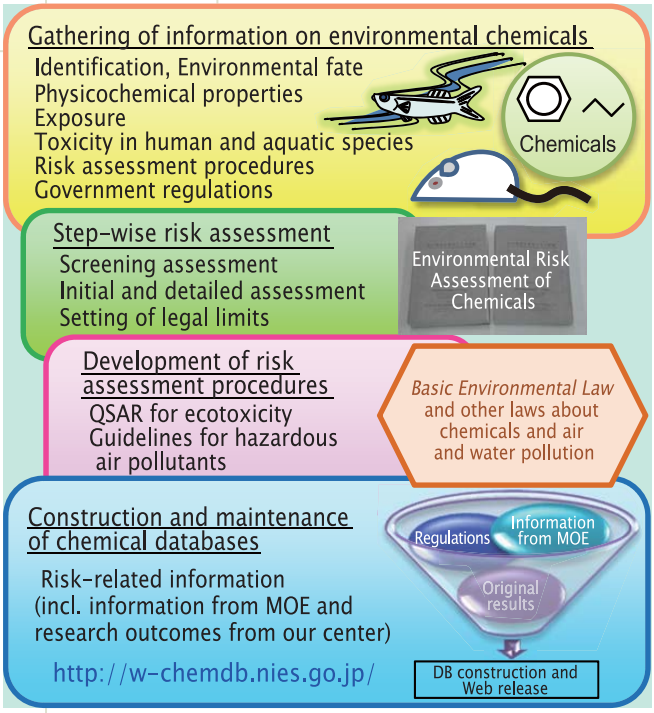
The Ecotoxicity Reference Laboratory functions as a core organization for the standardization of ecotoxicity testing both domestically and internationally

Test organisms to be supplied

Environmental Risk Assessment Task Office

The Environmental Risk Assessment Task Office promotes research to support the assessment and management of the risks posed by environmental chemical substances, provides risk-related information to the government and public, and conducts scientific risk assessments with the knowledge and experience it accumulates. The office also collects a variety of information on environmental chemicals (e.g., physico-chemical properties, toxicity) and assesses their risks through methodologies that range from simple screening to detailed assessment to support the risk assessment conducted under the laws enacted by the Ministry of the Environment.

Under the *Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc.* (*Chemical Substances Control Law*), which mandates the pre-production evaluation of new chemical substances, three ministries—Ministry of Economy, Trade and Industry; Ministry of Health, Labour and Welfare; and Ministry of the Environment—conduct risk assessments of chemical substances for their continuous management after going to market. The office supports this with step-wise risk assessments, that is, screening assessment followed by detailed assessment for Priority Assessment Chemical Substances. The office also studies the prediction of ecological toxicity by using quantitative structure-activity relationship models and organizes the annual Chemical Substances Control Law seminar as a platform to disseminate information to help manufacturers understand the laws concerning the production and distribution of chemical substances. In



QSAR: Quantitative structure-activity relationship; MOE: Ministry of the Environment

addition, the office performs initial risk assessments for chemical substances in the environment and publishes the assessment results of health and ecological risks associated with these substances as an evaluation document titled *Environmental Risk Assessment of Chemicals*.

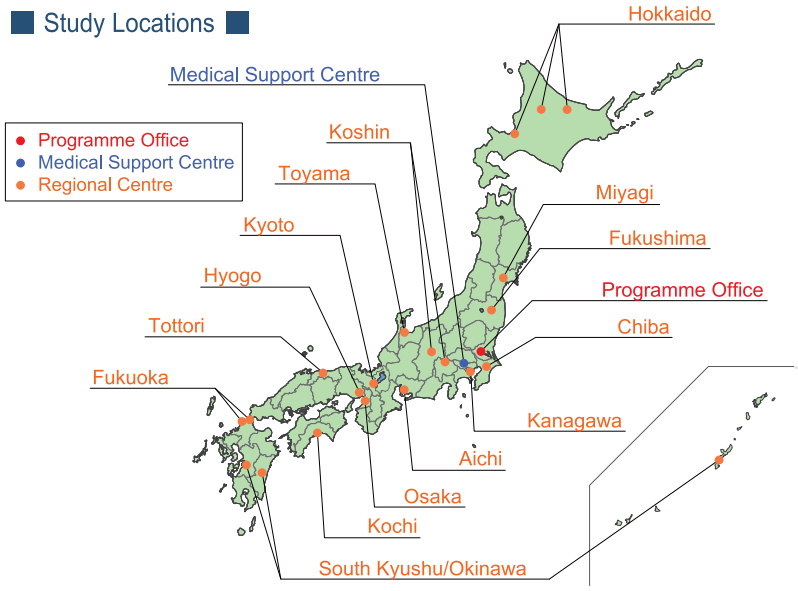
To ensure water quality and protect aquatic life, the office supports the setting of environmental quality standards for water pollution and the registration of withholding standards for agricultural chemicals based on the *Basic Environment Law* and *Agricultural Chemicals Regulation Law*, respectively; and to ensure air quality, it oversees the revision of domestic guidelines stipulating the guideline values for hazardous air pollutants. Through these activities, the office contributes to the management of the risks posed by environmental chemicals.

The office also administers several web-based databases such as the chemical database WebKis-Plus and the environmental measurement methods database EnvMethod. These databases are updated annually with risk-related information regarding the latest laws and regulations including environmental standards, the volumes of the manufacturing or import of chemical substances and the shipment of agricultural chemicals, information obtained from environmental monitoring, risk assessment results and risk analysis procedures, and research outcomes from the Center of Health and Environmental Risk Research.

Japan Environment and Children's Study Programme Office

The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that is being conducted by the National Institute for Environmental Studies (NIES) to identify environmental factors that affect the health and development of children. JECS is conducted in collaboration with the National Centre for Child Health and Development, which serves as the Medical Support Centre and contributes medical expertise to the study, as well as with 15 Regional Centres based at universities and research institutes throughout Japan. The Programme Office provides core administrative and technical support for the Regional Centres, which recruit participants and collect study data from their geographical area.

Recruitment of pregnant women to the study began in 2011, and by the end of 2014 more than 100,000 mother-child pairs had been recruited. The Regional Centres are responsible for collecting data starting from conception and will follow the children until they are 13 years of age. In the main study, biannual questionnaires are used to collect information on the participants, such as their health and development, and the environmental factors to which they are exposed. A sub-cohort study will involve 5,000 children randomly selected from the main cohort, and more in-depth measurement methods such as home visits, ambient air measurements, psycho-developmental tests, and pediatrician examinations will be used to more thoroughly investigate the correlations between environmental factors and outcome variables.



To ensure that the correct data is collected and analyses are conducted in accordance with the study protocols, the Programme Office is responsible for developing standard operation procedures, centralizing the data collected by the Regional Centres, administering the data management system, maintaining the repository of biological and environmental samples, and performing exposure measurements. The Programme Office is also responsible for risk management and participant retention. In addition, the Programme Office takes a leadership role in facilitating collaboration among the domestic and international research groups involved in the environmental birth-cohort study and provides a platform for the efficient exchange of information among the various research groups involved.

Storage of biospecimens collected as part of JECS.

Environmental Research Fields Relevant to the Center

Environmental Risk Research Field

Using science to reduce environmental risks and to achieve a safe society

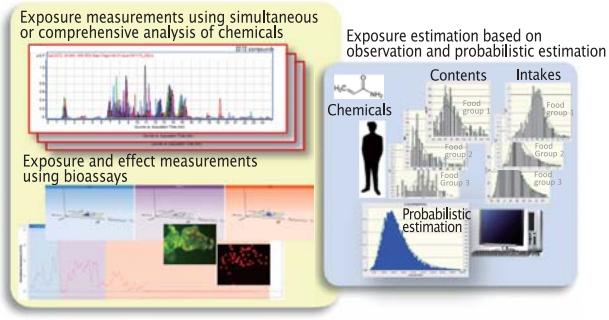
In the field of environmental risk, our research includes the development of advanced ecotoxicity testing methods, assessment systems to elucidate the ecological impacts of chemicals, methods to determine environmental exposure and the impact of environmental chemicals, and measures to clarify exposure and impacts of chemicals on inshore ecosystems through field surveys and laboratory experiments. We are also conducting studies of the environmental fate and assessing the exposure of ecosystems to chemicals, and conducting systematic management of the risks associated with environmental chemicals. This research is conducted collaboratively with the center's projects in the field of environmental health related to the impact of environmental chemicals on human health. The findings from this research are being applied in the real world as risk assessment science.

The Ecotoxicity Research Section is developing ecotoxicity test methods and models to assess the ecological impact of chemicals from molecular to organism level such as quantitative structure activity relationship (QSAR), *in vivo* testing, and statistical analysis.

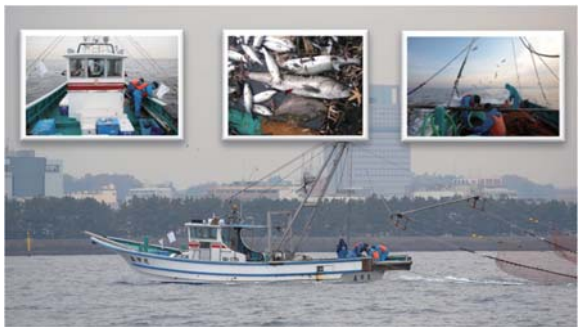
The Environmental Exposure and Effects Research Section is developing methods to determine exposure to environmental chemicals and the impacts of environmental chemicals on human health and the environment. This section focuses on developing advanced analytical methods to detect chemical substances with ligand-receptor binding activities, high molecular-weight biological substances, and mutagenic or carcinogenic substances in the environment. The section is also conducting research to elucidate the relationships between exposure to environmental chemicals and their effects on health.

The Ecosystem Impact Research Section is using field studies, laboratory experiments, and ecosystem model analyses to develop countermeasures for the recovery of biotas and environmental remediation based on historical data and assessment of the present state of coastal ecosystems exposed to various anthropogenic stressors arising from human activities.

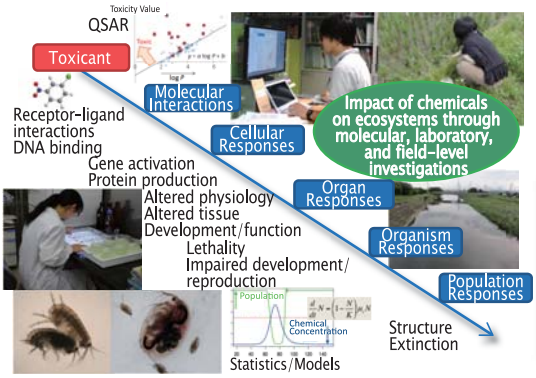
The Strategic Risk Management Research Section is studying aspects important for modeling the environmental fate and emissions of chemicals, assessing the exposure and risks of environmental chemicals, assessing the ecological impacts of environmental disturbances, and systematically managing the risks to health and the environment posed by environmental chemicals while taking into consideration the many risk factors.



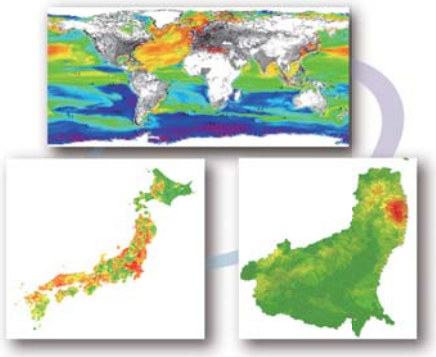
Development of advanced analytical approaches for detecting and assessing exposure to chemical substances and chemical effects



Field surveys of the environment and biota in Tokyo Bay, Japan



Molecular-to-organism level modeling to investigate the ecotoxicity of chemicals



Prediction of multimedia fate of chemicals in the environment

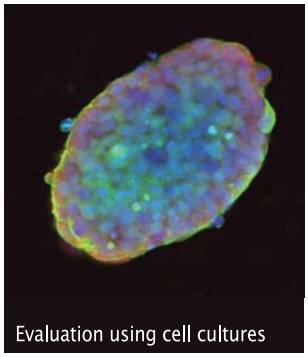
Research Facility

Environmental Risk Research Laboratory: This research laboratory is the core of the center's environmental risk research. The laboratory conducts research on the ecological impacts of environmental chemicals and assesses the health effects of exposure to environmental chemicals. The first floor is dedicated to research on the ecological impact of environmental chemicals in aquatic organisms. The second floor houses various instruments for chemical analyses (e.g., gas chromatography- tandem mass spectrometry and liquid chromatography-tandem mass spectrometry) and a confocal laser microscope. *In vitro* bioassays to assess environmental quality are also conducted on the second floor. The fourth floor is divided into two areas: one for gathering, analyzing, and assessing information regarding the risks associated with chemical substances; and one for conducting animal testing to clarify the health risks associated with exposure to environmental chemicals.

Environmental Risk Research Laboratory

Environmental Health Research Field

Preventing adverse health effects associated with environmental factors and reducing these risks for future generations


Evaluation using cell cultures

Whole-body inhalation chambers for nanoparticle experiments

Our research in the field of environmental health aims to experimentally investigate and assess the health impacts of environmental factors and the underlying modes of action, develop simple and fast systems to assess exposure and impact, and conduct epidemiological surveys and studies to identify the impacts of environmental chemicals on health. Specifically, we are working to assess the health impacts of environmental chemicals, metals, atmospheric pollutants, and nanomaterials; and to establish, improve, and verify methods of assessing these impacts. We are also using genomics and epigenetics studies to clarify the mechanisms of action underlying the effects of environmental chemicals. In addition, we are working to integrate, systematize, improve, and refine the epidemiological assessment of these health impacts.

The Molecular Pathology Section is evaluating the effects of environmental substances, including environmental chemicals, on the pathology of diseases such as immune and metabolic diseases. This research also focuses on the molecular mechanisms underlying changes in biological crosstalk and epigenetic changes.

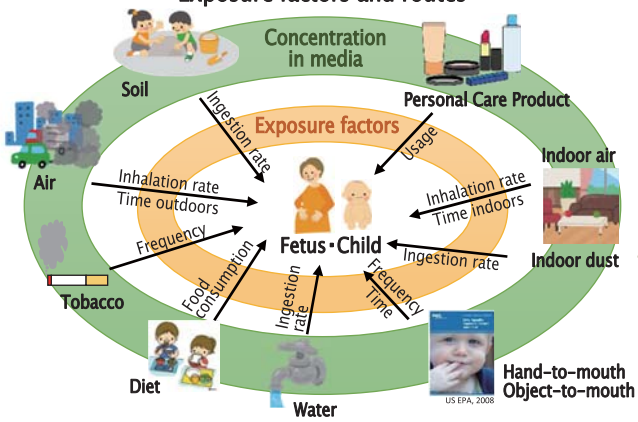
The Health Effect Assessment Section is developing methodologies to evaluate the neuropathological and social behavioral effects of environmental factors, and contributes to the identification of health-threatening chemicals, reduction of the adverse effects of environmental chemicals, and development of precautionary approaches.

The Integrated Health Risk Research Section is developing biomarkers of neurotoxicity, immunotoxicity, reproductive and developmental toxicity, genotoxicity, and inhalational toxicity based on the physico-chemical characteristics of harmful environmental substances such as fibrous nanomaterials.

The Exposure Dynamics Research Section is focusing on measuring and estimating lifetime exposures to environmental stressors that may cause adverse health effects. These environmental stressors include chemical substances, the physical environment, and diet, as well as the socio-economic and community environment. Human biomonitoring and exposure modeling are key tools in this research.

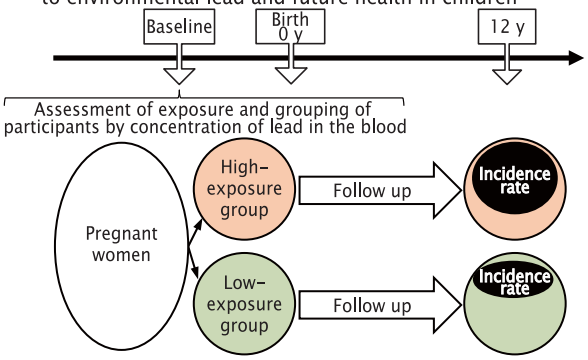
The Environmental Epidemiology Section is involved in developing epidemiological methods and applications for estimating and assessing the health impacts of exposure to harmful environmental chemicals.

Exposure factors and routes



Schema of a cohort study

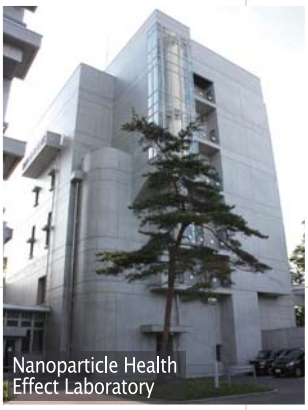
Examining the association between prenatal exposure to environmental lead and future health in children



Research facilities

Animal Laboratory: This laboratory conducts experiments using laboratory animals and tissue and cell cultures to investigate the effects of various environmental chemicals on human health and determine whether environmental pollutants have adverse effects on human health.

Nanoparticle Health Effect Laboratory: The urban atmosphere remains polluted with particulate substances emitted from automobiles. Therefore, this laboratory investigates the effects of ultrafine particles contained in diesel exhaust and environmental nanoparticles on human health. The Nanoparticle Health Effect Laboratory is connected with the Animal Laboratory building and is equipped with advanced inhalational exposure chambers.


Nanoparticle Health Effect Laboratory

Animal Laboratory

Databases and websites managed by the Center for Health and Environmental Risk Research

Grid-Catchment Integrated Environmental Modeling System (G-CIEMS)

http://www.nies.go.jp/rcer_expoass/gciems/gciems.html (Japanese only)

G-CIEMS is a spatially resolved and geo-referenced, dynamic, multimedia environmental fate model. This model predicts the concentrations of chemicals in the atmosphere, surface water, surface-water sediments, and surface soil based on environmental emissions and physico-chemical properties of a target substance and on geographical and meteorological information.

KAshinhou Tool for Ecotoxicity (KATE)

http://kate.nies.go.jp/ (Japanese only)

KATE is a web-based software service that can be used to predict ecotoxicity values such as fish acute toxicity (median lethal concentration [LC_{50}]) and daphnia immobilization (median effect concentration [EC_{50}]) by using original quantitative structure-activity relationship models that assess the quantitative relationship between the physico-chemical characteristics of a chemical and its biological activities.

Chemical Substance Database (WebKis-Plus)

http://w-chemdb.nies.go.jp/ (Japanese only)

WebKis-Plus database contains information on physicochemical properties, regulations (related mainly to environmental pollution), environmental concentrations from surveys conducted by the Ministry of the Environment, volumes of chemical substances manufactured or imported, volumes of agricultural chemicals shipped to each Japanese prefecture, Pollutant Release and Transfer Register (PRTR) emissions and transportation amounts, the results of risk assessments performed by several external organizations, and other relevant information related to chemical substances.

Environmental Analytical Method Database (EnvMethod)

http://www.nies.go.jp/emdb/ (Japanese only)

EnvMethod is a database containing information on environmental measurement methods that is searchable by chemical name, relevant regulation, reference, analytical method, and/or environmental medium. This database is linked to WebKis-Plus database.

Simulation Models and Tools for Exposure Assessment

http://www.nies.go.jp/rcer_expoass/index.html (Japanese only)

This suite of tools contains G-CIEMS, an integrated tool for assessing environmental risk, the Multimedia Simplebox-systems Environmental Model (MuSEM), a tool for visualizing geographic information system data containing simulation results from G-CIEMS, and other tools for assessing exposure to environmental chemicals.

Health Effects Alert System (HEALS)

http://project.nies.go.jp/heals/

HEALS (Health Effects Alert System) includes four subsystems—ChemToxGen, ChemArrayDB, pCEC, and MulCEH— that can be used to evaluate the effects of environmental chemicals by using a variety of databases and algorithms. This system classifies chemicals that act on cells and tissues from the viewpoint of gene expression signatures, cellular functions, and organ toxicities. Furthermore, a high-performance Bayesian network system, RX-TAOGEN in MulCEH can be used to predict the underlying mechanisms of chemical toxicity by examining gene expression and cellular phenotypes.

The fourth five-year plan (2016-2020)
Center for Health and Environmental Risk Research 2017.03

National Institute for Environmental Studies
Center for Health and Environmental Risk Research

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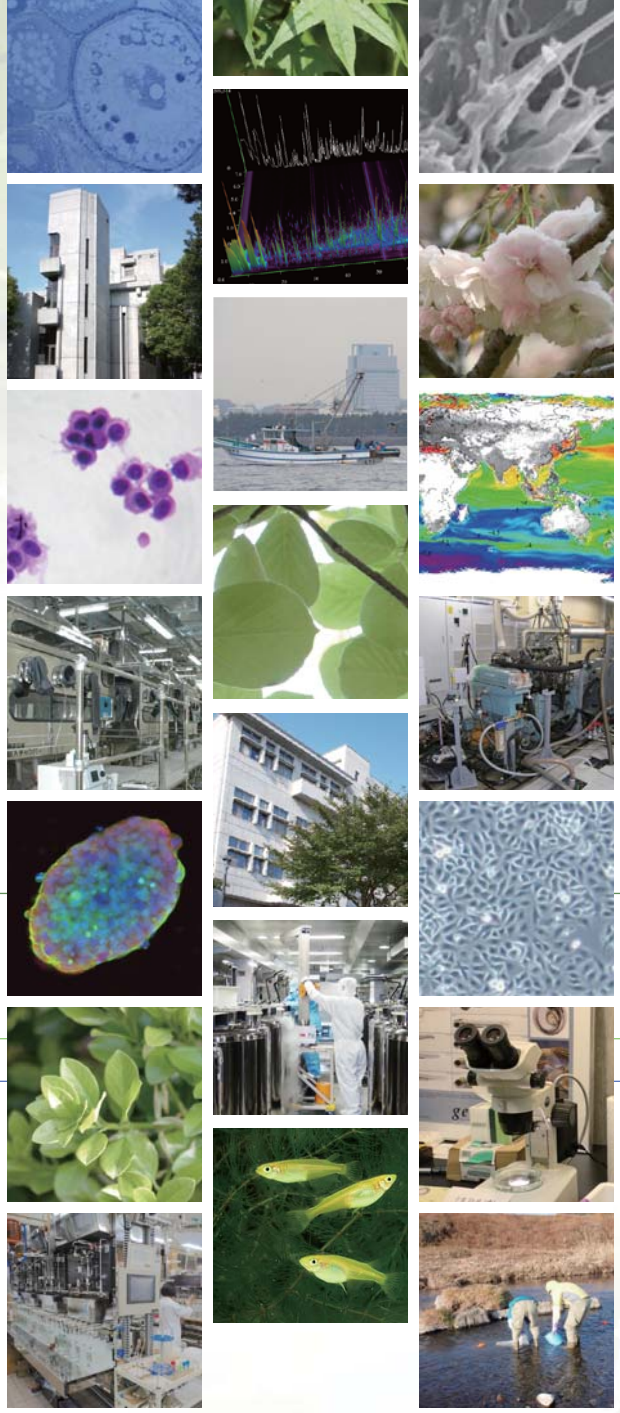

National Institute for Environmental Studies

Center for Health and Environmental Risk Research