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INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

CRI's ICEIT has been designated as a
"UNEP Centre of Excellence for Environmental and Industrial Toxicology".

# Framework for Risk Assessment of PFAS

Per- and polyfluoroalkyl substances (PFAS) are a class of synthetic organic substances with perfluoroalkyl moieties that are highly resistant to environmental and metabolic degradation. Most PFAS are either non-degradable or transform into other stable PFAS metabolites. Under EU chemicals regulation, they are classified as very persistent substances.

Among all PFAS, perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) have been the most widely studied, due to their toxic effects on living beings and their common use in consumer and industrial applications. It has been scientifically accepted that the diversity of these substances, in terms of properties, behavior, hazards, and risks, is a significant criterion for risk classification.

A number of epidemiological, animal, and *in vitro* studies have found links between PFAS and health effects, including developmental toxicity, carcinogenicity, weight gain, hormonal imbalance, and immunity-related effects.

Human health effects for some PFAS exposures have also been reported from animal models. However, a longer half-life, no metabolism, and high resorption of these chemicals make extrapolation from animal models to humans complicated.

Establishing health effects guidelines requires a careful review of the strength of evidence, consistency of evidence across studies, species concordance, strength of effect associations in epidemiological studies, and selection of effects for determining which potential impacts are either severe, or of great concern.

The present study has reviewed and summarized the influence of PFAS exposure on health, pointing the quality of evidence, and applied translational techniques to integrate evidence for PFAS policy making.

This review emphasizes some of the shortcomings in existing research and introduces an improved framework for assessing risk.

This is the first review which collected highly referred articles on PFAS used for policymaking by several regulatory agencies and evaluated them based on the review guidelines developed by the US National Toxicology Program's Office of Health Assessment and Translation (OHAT).

Several limitations were observed, including co-exposure to multiple chemicals and limited measurement of primary and secondary outcomes related to specific toxicity. However, data from all these studies provided a moderate to strong level of confidence for links between PFAS exposure and different adverse outcomes.

Advances in computational toxicology and availability of experimental data is beginning to shift the focus of research on PFAS towards translation of risk from exposure scenarios to health risk assessment using *in silico* tools.

Translational toxicology involves the integration of pharmacokinetics, pharmaco-dynamics, systems biology, and adverse outcome pathways (AOPs) in order to understand the interactions among chemicals and living beings at different levels of biological organization.

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## *Framework for Risk Assessment of PFAS*

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*In silico* tools such as physiologically based pharmacokinetic (PBPK) models, are currently being utilized to estimate daily exposure based on serum levels found in the population, together with additional evidence from epidemiology and animal studies.

Inter-species dose extrapolation was performed to compare with humans, the relevance of dosing scenarios used in animals.

With some recent evidence of selected PFAS involvement in immune hazards to humans, future human studies must characterize wider immune outcomes including (but not limited to) immune effects from early exposure during pregnancy and the possible role of PFAS's in initiating allergic and auto-immune processes. More longitudinal epidemiology studies are required with additional susceptible human endpoints.

Significant toxicokinetic differences have been observed in various animal and human studies. In rodents, half-life varies from a few hours to several weeks, being in general much shorter than that in humans. The half-life of PFAS has been a major controversial issue, with varying PFAS half-lives in humans differing by years.

Although PBPK models for some PFAS are well developed for health risk assessment, they still need to be further developed, optimized, and validated for other PFAS. Experimental evidence is needed to understand and quantify the association between PFAS and blood lipids (cholesterol levels) and the role of enterohepatic recirculation and glomerular reabsorption, including organic anion transporters.

In the case of mixture toxicity, "an additive reference dose (RfD) approach" compared to a "relative potency factor (RPF) approach", should be considered. However, for most PFAS, RPF values are still lacking for susceptible hazard endpoints.

The development of new approaches to determining PFAS toxicity must consider tissue-specific modes of action. New approaches should rely on molecular interactions involving enzymes, storage, transport proteins, and ability to alter cell membrane fluidity within a particular organ/system.

Overall, a framework for translation of risk was proposed based on the conclusions of this review with the goal of improving policymaking. The current review can improve the methodological protocols for PFAS experimental studies and encourage the utilization of *in silico* models for translating risk.

A greater emphasis on developing workable and effective risk assessment methods for human health, including adverse outcome pathways to support regulatory processes and development of relevant policy-related strategies are clearly necessary.

***Source:*** Environmental Research, Vol. 208, Article 112722, May 2022.

# Immunomodulatory Effects of Pesticides on Macrophage Functions

Increased pesticide use raises environmental and public health concerns. Emerging evidence suggests that exposure to environmental contaminants plays a role in the development of cancers and neurological, skin, and metabolic diseases, which are related to immune system dysregulation, and potentially to macrophage dysfunction.

Macrophages are a group of heterogeneous cells that are partly derived from blood monocytes. In addition to their role in triggering inflammation, macrophages play a key role in resolving inflammation, contribute to repairing and remodeling tissue, and participate in restoring tissue homeostasis.

The present study evaluated *in vitro* immunomodulatory effects of two insecticides: chlorpyrifos and thiacloprid, and four fungicides: thiophanate, boscalid, dithianon, and captan which have in common their wide use in apple arboriculture in France.

The researchers used human monocyte-derived macrophages (hMDMs) from several screened donors, in contrast to most studies that have used murine or human macrophage cell lines. The hMDMs were cultured for 4 or 24 hours with or without pesticides (0.01, 0.1, 1, and 10 μmol/L).

The findings demonstrate that among the tested pesticides, only boscalid between 0.01 and 10 μmol/L had no effect on human monocyte-derived macrophages effector functions.

Thiacloprid promoted the ability of macrophages to produce reactive oxygen species (ROS) in response to zymosan and induced the production of IL-10 in response to lipopolysaccharide.

Chlorpyrifos and thiophanate increased the production of ROS at low doses (0.01-0.1 μmol/L) while at high doses, chlorpyrifos, captan and dithianon have shown immunosuppressive effects through the reduction of ROS and pro-inflammatory cytokines such as IL-1β and TNF-α production.

The researchers established that dithianon (0.01-1 μmol/L) and captan (0.1, 1 μmol/L) induced mRNA expression of *NQO1 (NADPH dehydrogenase quinone 1)* and *HMOX1 (Heme oxygenase 1)* antioxidant enzymes. Dithianon also induced the mRNA expression of catalase, superoxide dismutase-2 at 10 μmol/L.

In conclusion, these results show that exposure to chlorpyrifos, dithianon, and captan induce immunomodulatory effects that may influence the disease fighting properties of monocytes/macrophages while pesticides such as thiacloprid, thiophanate and boscalid have little influence.

The information obtained from this study could be used to guide policy and regulations relating to the doses of these pesticides to minimize occupational health risks.

***Source:*** Food and Chemical Toxicology, Vol. 163, Article 112992, May 2022.

# Toxic Effects of Glyphosate on the Nervous System

Glyphosate is the most widely used herbicide in the world and can persist in the environment for days or months. Glyphosate-based herbicides (GBH) represent approximately 60% of the global market for non-selective herbicides. Its intensive and large-scale use can constitute a major environmental and health problem.

The mechanism of action of glyphosate is associated with its ability to block the shikimic acid pathway, which is involved in the synthesis of aromatic amino acids in plants, fungi, and some micro-organisms. The absence of the shikimate pathway in animals has led to the conclusion that GBH does not pose a health risk to animals and humans.

Many investigations on glyphosate toxicity in animals have suggested the low toxicity of this compound, the adverse effects of which have only been observed after exposure to relatively high doses. These data led to the classification of glyphosate in the least toxic category (category IV, practically non-toxic and non-irritating) by the United States Environmental Protection Agency (EPA).

Although the concentrations of glyphosate residues that persist over time are relatively low, it is possible that due to extensive use on a large scale, they may accumulate and become a risk to animal and human health, as they are chronically exposed to residues in the water and food they consume.

Based on research on the chronic side effects of glyphosate, the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) reclassified glyphosate as probably carcinogenic to humans in 2015.

Numerous commercial formulations of glyphosate contain several adjuvants, which improve the penetration of the active ingredient into the target plants and increase their efficacy. It has been postulated that the activity of GBH is not exclusively due to the active ingredient but could be due to the intrinsic toxicity of the adjuvants or the possible synergy between glyphosate and the other ingredients of the formulation.

In fact, polyethoxylated tallow amine, the predominant surfactant in several commercial formulations, has been found to increase glyphosate-induced toxicity by facilitating its penetration through plasma membranes. Therefore, it is important for research to evaluate the toxicity of both commercial formulations and pure glyphosate.

The present systematic review investigates the current state of our knowledge related to the effects of glyphosate and mechanisms of action of glyphosate and its commercial formulations on the nervous system of various animal species and humans. The main objective of this review is to understand the risks arising from increasing exposure to glyphosate residues in the environment and in food.

The information provided indicates that exposure to glyphosate; its main metabolite, AMPA (amino-methylphosphonic acid); or its commercial formulations induces several neurotoxic effects in all the species studied.

The main modes of action include changes in the development of the nervous system and in the neurotransmission systems, oxidative stress, neuroinflammation, processes that lead to neuronal death, and the appearance of behavioral changes. Changes in the structure and function of neurons lead to the development of neuropathology, encephalopathology, and sensory and motor dysfunctions.

Exposure to glyphosate during the early stages of life can severely affect normal cell development by deregulating some of the signaling pathways involved in this process, leading to alterations in differentiation, neuronal growth, migration, and myelination.

Nevertheless, it appears that in adult humans, glyphosate does not produce toxic effects immediately after exposure but takes one or two days to do so. It is possible that this delay is due, at least in part, to the fact that the pesticide takes time to alter the integrity of the blood-brain-barrier (BBB), cross it, and subsequently distribute itself in the central nervous system.

Glyphosate also seems to exert a significant toxic effect on neurotransmission, with the glutamatergic system being one of the most affected systems. Glyphosate was found to increase glutamate release and decreased its reuptake, in addition to activating N-methyl-D-aspartate receptor (NMDAR) and L-type voltage-dependent calcium channel (L-VDCC), thus increasing the influx of $Ca^{2+}$ into neurons.

The results analyzed herein reflect the capacity of glyphosate to induce oxidative stress, neuroinflammation, and mitochondrial dysfunction, processes that lead to neuronal death by autophagia, necrosis, or apoptosis, as well as the appearance of behavioral and motor disorders.

The doses of glyphosate that produce these neurotoxic effects vary widely but are lower than the limits set by regulatory agencies.

Although there are important discrepancies between the analyzed findings, it is unequivocal that exposure to glyphosate produces important alterations in the structure and function of the nervous system of humans, rodents, fish, and invertebrates.

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***Source:*** International Journal of Molecular Sciences, Vol. 23, No. 9, Article 4605, April 2022.

# Air Pollution as A Risk Factor for Cognitive Impairment No Dementia

Cognitive impairment no dementia (CIND) describes individuals whose cognitive functioning falls below normal but does not meet dementia criteria. Importantly, CIND potentially identifies a subgroup at higher risk of developing dementia.

Although a certain degree of decline in cognitive functions can be considered a normal consequence of aging, the identification of modifiable risk factors for mild cognitive changes should be urgently prioritized, as these may be essential for the prevention or postponement of dementia development.

Exposure to air pollution can cause substantial adverse health effects at all stages of life, and especially in the more vulnerable people such as the children and elderly.

The effect of air pollution on cognitive functioning and dementia incidence in older adults have been studied with mixed or sometimes contradictory findings. The inconsistent results may be due to differences in assessment of cognitive performance, types of air pollutants, and length of the exposure period.

The present study aimed to investigate the longitudinal association of long-term residential exposure to particulate matters ($PM_{2.5}$ and $PM_{10}$) and nitrogen oxides (NOx) and cognitive impairment and its further progression to dementia in older adults residing in an urban area in Sweden.

CIND was assessed by a comprehensive neuropsychological battery (scoring ≥1.5 standard deviations below age-specific means in ≥1 cognitive domain).

In the present study, researchers included a long follow-up period of up to 12 years and air pollution exposure over 10 years. The strongest effects of long-term exposure to $PM_{2.5}$ on cognition showed that 1-$\mu g/m^3$ increase in 5-year average $PM_{2.5}$ exposure was associated with about an over 3-fold increased risk of mild cognitive impairment and a 2-fold increased risk of incident dementia among 1572 US old population. Weaker associations were found for $PM_{10}$ and NOx.

Several biological mechanisms underlying the relationship between air pollution and cognition have been proposed, including neuroinflammation, oxidative stress, and vascular damage. Air pollutants might pass the blood-brain barrier and enter the central nervous system via the olfactory bulb. Exposure to air pollution may also stimulate the inflammatory response and increase cytokine release to the circulation.

Among those with CIND at baseline (n = 607), 118 participants developed dementia during follow-up. The results also show that exposure to air pollution was a risk factor for the conversion from CIND to dementia.

Thereby, these results might shed light on future studies to better understand the role of air pollution on the relationship between cognitive impairment and developing dementia.

This is the first longitudinal study that has not only investigated the impact of air pollution on CIND but also its progression to dementia, considering various air pollutants. Moreover, researchers were able to assess long periods of air pollution exposure from the detailed spatiotemporal model also considering the moving status during follow-ups.

Future studies are warranted to investigate the mechanism underlying the risk of air pollution for cognitive impairment.

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***Source:*** Environment International, Vol. 160, Article 107067, February 2022.

# Children Health Impacts from Indoor Exposure to $PM_{2.5}$ and Metals

Among compounds that influence indoor air quality (IAQ), the World Health Organization (WHO) emphasizes risks associated with exposure to particles arising from the combined effects of chemical composition and particle size.

Fine particulate matter ($PM_{2.5}$) in the particle fraction is most strongly associated with negative human health effects, since it penetrates deeply into the lungs and causes a variety of negative health outcomes. For non-organic compounds, metals comprise 1-2% of atmospheric $PM_{2.5}$ but cause different health effects.

As indoor exposure often dominates overall human exposure to $PM_{2.5}$ and children spend most of their time indoors, it is important to evaluate adverse health effects in children resulting from inhaling pollutants that occur in indoor air.

The recent study measured the concentrations of fine particulate matter ($PM_{2.5}$) and 11 metals (arsenic, cadmium, chromium, copper, iron, manganese, nickel, lead, antimony, selenium, and zinc) from air samples taken during both winter and spring, and focused on urban and rural area kindergartens in Poland, typified by the use of fossil fuels for power and heat purposes.

The researchers combined related inhalation intake estimates for children and health effects using separate dose-response approaches for $PM_{2.5}$ and metals.

Results show that impacts on children from exposure to $PM_{2.5}$ is approximately 10 times lower than cumulative impacts from exposure to the metal components in the $PM_{2.5}$ fraction of indoor air.

Highest metal-related health impacts were caused by exposure to hexavalent chromium.

The study provides insights into the potential risks of children associated with inhalation exposure to $PM_{2.5}$ and several metals in kindergarten air.

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# Repeated Exposure to Chlorpyrifos and Chronic Neurobehavioral Deficit in Adult Rats

Depression is one of the most prevalent psychiatric disorders worldwide. The etiology of depression is complex and multifactorial, being the cumulative contribution of many genetic and environmental risk factors such as air pollution, noise, trace pharmaceuticals, and pesticides.

Organophosphate (OP) chemicals include commonly used pesticides and chemical warfare agents, and mechanistically they are potent inhibitors of the cholinesterase (ChE) enzyme.

Epidemiological studies report long-term neuropsychiatric issues, including depression and cognitive impairments in OP-exposed individuals.

Amongst the OP pesticides, chlorpyrifos (CPF) is one of the most widely used worldwide. CPF exposures during gestation, adolescence, and adulthood are reported to affect brain morphology and elevate the risk for Attention-Deficit Hyperactivity Disorder (ADHD), autism traits, cognitive disorders and depression.

Multiple laboratory studies have reported on long-term behavioral effects of a single, very high dose CPF exposure, near-term behavioral effects of repeated low-dose CPF exposure, or sub-chronic behavioral effects, particularly the cognitive effects of repeated low-dose CPF exposure.

However, no studies have reported on long-term mood and depression-related behavioral effects of a CPF exposure regimen in adult rats that would mimic occupationally relevant exposures.

In agreement with multiple epidemiological studies, the results provide the first experimental evidence that occupational-like CPF exposures in adult rats were associated with signs of chronic behavioral depression.

In this study, adult male rats were injected with comparatively much lower CPF doses (1 mg/kg/d to 10 mg/kg/d) that were not associated with acute cholinergic toxicity and thus would be considered sub-threshold doses for 21 consecutive days.

This dosing paradigm in rats has been shown to produce ChE inhibitions that mimic ChE activity levels seen following sub-chronic OP exposures in humans.

Finally, to study the latent effects of these repeated low-dose CPF exposures, rats were tested for depression-related and anxiety-related signs at 11-weeks post-exposure.

The approach of combining repeated sub-threshold doses coupled with long-term behavioral assessment provides an experimental paradigm for studying cause and effect relationships between environmental and occupational OP exposures and the development of chronic behavioral deficits.

Dependent on the CPF dose, ChE activity was inhibited approximately 60-80% in the blood and about 20-50% in the hippocampus at 2-days after the end of CPF exposures. Following a 12-week washout period, a complete recovery of ChE activity was noted.

However, CPF-treated rats exhibited a dose-dependent increase in signs related to anhedonia (sucrose preference test), anxiety (open-field and elevated plus-maze), and despair (forced swim test) at this stage.

In summary, this could be the first laboratory study that demonstrates a cause-effect relationship between low-dose, occupational-like OP, CPF exposures in adult rats and the development of long-term depression-related outcomes.

Recently, genetic and epigenetic mechanisms have been highlighted as potential mediators of OP-induced chronic neurotoxicity.

The depressive phenotype following CPF exposures could result from various molecular mechanisms such as changes to second messenger systems, gene expression, epigenetic modifications, or synaptic plasticity.

The CPF exposure paradigm proposed in this study could provide an ideal model system to further study these molecular mechanisms underlying environmental OP exposures and the elevated risk for chronic behavioral deficits.

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***Source:*** NeuroToxicology, Vol. 90, Pages 172-183, May 2022.

## *Children Health Impacts from Indoor Exposure to $PM_{2.5}$ and Metals*

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When combining measured children exposure estimates with health effect information, the results illustrate that exposure to metals in the $PM_{2.5}$ air fraction can be a substantial contributor to overall impacts on children from inhaling kindergarten air. On the other hand, the analysis also suggests that effect estimates for metals show large uncertainties.

These uncertainties emphasize the need for improved dose-response models and underlying data for individual metals, differentiated by cause and between children and adults as well as between exposure routes, in order to derive impact estimates that are better aligned between approaches for $PM_{2.5}$ and approaches for metals.

The present study contributes to a better understanding of exposure and related risk levels of kindergarten children in Poland, but also highlights the need for broader monitoring to allow generalization beyond the studied locations, and the need for improved dose-response modelling, especially across the wider range of relevant metals.

The study provides initial recommendations for policy makers to reduce exposure of children to air pollutants in kindergarten air, and for the research community to improve health impact assessment for children.

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***Source:*** Environment International, Vol. 160, Article 107062, February 2022.

# The Potential Role of COVID-19 in the Induction of DNA Damage

The coronavirus disease-2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is challenging global health and economic systems.

In some individuals, COVID-19 can cause a wide array of symptoms, affecting several organs, such as the lungs, heart, bowels, kidneys and brain, causing multiorgan failure, sepsis and death. These effects are related in part to direct viral infection of these organs, immunological deregulation, a hyper-coagulatory state and the potential for development of cytokine storm syndrome.

There has been an increase in the number of patients who report symptoms for more than 10 months after the original infection, now recognized by the WHO as long-COVID or post-COVID syndrome. Thus, it is relevant to further study the long-term consequences related to the initial viral infection.

Infectious diseases are a well-known to increase the risks of developing some forms of cancer. The International Agency for Research on Cancer (IARC) includes 10 pathogens as group 1 carcinogens that include bacterial, parasitic and viral infections.

It was estimated that 12 % of all human cancers are potentially the result of viral infections. These viral-induced cancers occur principally in immuno-deficient or immunocompromised individuals. Interestingly, risk factors associated with severe COVID-19 patients, such as obesity and type 2 diabetes are often related to an impaired immune system.

The present review focused on current evidence of the mechanisms of DNA damage mediated by coronaviruses and also discussed the recent analysis of protein-protein interactions between the proteins encoded by the SARS-CoV-2 and human proteins relevant to DNA repair mechanisms.

Potential mechanisms triggered DNA damage in the host directly by SARS-CoV-2 proteins and indirectly through the immune system including aberrant inflammation, immune response and oxidative damage.

The mechanisms are based on the knowledge of proteins encoded by the SARS-CoV-2, SARS-CoV, infectious bronchitis virus and the MERS-CoV. Since the orthologous proteins encoded in the SARS-CoV-2 genome share a high percentage of identity/similarity, it is possible that these mechanisms are induced by this newly described virus.

Data supports that these viruses can induce DNA damage, genomic instability, and cell cycle deregulation during their replication in mammalian cells.

It is known that DNA damage and aberrant repair mechanisms are implicated in the pathogenesis of many chronic diseases such as cancer, obesity, diabetes, atherosclerosis and metabolic syndrome.

These potential outcomes highlight the need to evaluate the long-term effects of this novel viral disease in the recovered COVID-19 patients as well as in asymptomatic but infected individuals.

***Source:*** Mutation Research/Reviews in Mutation Research, Vol. 789, Article 108411, January–June 2022.

# WHO: Health Effects of the Use of Non-sugar Sweeteners
## A Systematic Review and Meta-analysis

Non-sugar sweeteners have been developed as an alternative to sugars and are widely used both as an ingredient in pre-packaged foods and beverages and added to food and beverages directly by the consumer.

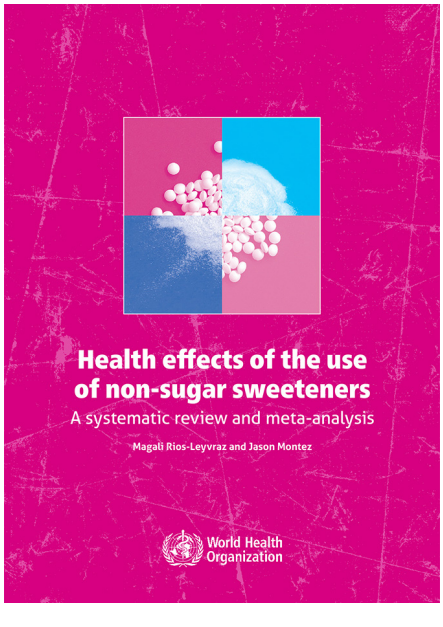
Individual non-sugar sweeteners undergo toxicological assessment by the by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and other authoritative bodies to establish safe levels of intake (i.e. acceptable daily intake or ADI).

While results of randomized controlled trials (RCTs) have generally suggested non-sugar sweeteners may have little impact on glucose metabolism and result in lower body weight when coupled with energy restriction in the short-term.

There is no clear consensus on whether non-sugar sweeteners are effective for long-term weight loss or maintenance, or if they are linked to other long-term health effects at intakes within the ADI. This systematic review brings together the most current scientific evidence on health effects of non-sugar sweetener use.

Further research is needed in children and pregnant women, and for the latter, prospective cohort studies currently suggest possible unfavourable effects of NSS consumption on birthweight and adiposity in offspring later in life.

***Source:*** World Health Organization. Health Effects of the Use of Non-Sugar Aweeteners: A Systematic Review and Meta-analysis. April 2022.



# CALENDAR OF EVENTS

## International Training Courses in Environmental and Health Risk Assessment and Management of Toxic Chemicals Year 2022

| | Training Course | Date | Closing Date |
|---|---|---|---|
| 1 | Environmental and Health Risk Assessment and Management of Toxic Chemicals: Fundamentals of Risk Assessment | November 28 - December 3, 2022 | October 15, 2022 |
| 2 | Applications of the Risk Assessment Paradigm for Solving Real World Problems: Risk Assessment in the 21st Century (RISK21), Dietary Risk Assessment, and Chemical Incident Management | December 6-10, 2022 | October 15, 2022 |

**Course Coordinator:** *Khunying* Mathuros Ruchirawat, Ph.D.

**Background:**

The Chulabhorn Research Institute (CRI) is aware of the importance of providing a training program to assist developing countries with human resource development in the field of environmental toxicology and risk assessment. Through the years, courses on risk assessment have been organized to train personnel to be capable of carrying out risk assessments of toxic chemicals for the protection of human health and the environment, and therefore serve the needs of the governmental, academic, and industrial sectors. In November-December 2022, CRI is organizing a comprehensive training programme on risk assessment, comprising two courses on risk assessment, to be taught (in English) primarily by international experts from the United States and Europe, with a wealth of experience in conducting risk assessments, as well as conducting training courses in developing countries. These courses have been designed to be complementary, with the first course focusing on the fundamentals of risk assessment, including hazard assessment, exposure assessment, risk characterization and issues for special consideration, and the second course focusing on RISK21, dietary risk assessment and the public health management of chemical incidents, with many practical examples of how the risk assessment paradigm is used to solve the real-world problems.

**Training objectives:**

*This series of two back-to-back training courses is designed to:*

- Provide information on basic and advanced principles and concepts of risk assessment and the processes involved, including the well-established risk assessment paradigm and specific issues like chemical-specific adjustment factors, PBPK modeling, mode of action and the human relevance framework.
- Illustrate by using practical examples, i.e. case studies, how risk assessments are conducted and what different and unique issues are involved.

***It is expected that participants who go through both courses will receive training sufficient to allow them to conduct environmental and human health risk assessments in their own countries. Participants who complete the course(s) will receive a Certificate of Completion for their professional portfolio.***

**Course Content:**

***Course 1: Environmental and Health Risk Assessment and Management of Toxic Chemicals***

This fundamental course is an integration of science and policy and covers the principals of human health and environmental risk assessment. Topics include:

- Problem Formulation
- Hazard Identification
- Hazard Characterization
- Risk Characterization
- Ecological Risk Assessment
- Mode of Action
- Human Relevance Framework
- Physiologically-based Pharmacokinetics Modeling
- Chemical-specific Adjustment Factors
- Complex Mixtures
- Integrated Health Impact Assessment
- Risk Perception, Reduction and Management

**Teaching Faculty:**

1. **Herman Autrup, Ph.D.**
   Professor, Institute of Public Health, University of Aarhus, Denmark
2. **Leonard Ritter, Ph.D.**
   Professor, School of Environmental Sciences, University of Guelph, Canada
3. **Martin van den Berg, Ph.D.**
   Professor, Institute for Risk Assessment Sciences, University of Utrecht, The Netherlands

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## *International Training Courses in Environmental and Health Risk Assessment and Management of Toxic Chemicals Year 2022*

*(Continued from page 7)*

***Teaching Faculty:****(continued)*

4. **Bette Meek, Ph.D.**
   Associate Director, Chemical Risk Assessment, McLaughlin Institute, University of Ottawa, Canada
5. **Mathuros Ruchirawat, Ph.D.**
   Vice President for Research and Academic Affairs, Chulabhorn Research Institute, Bangkok, Thailand
6. **Daam Settachan, Ph.D.**
   Research Scientist, Chulabhorn Research Institute, Bangkok, Thailand

***Course 2: Applications of the Risk Assessment Paradigm for Solving Real World Problems***

The practical applications of risk assessment course will utilize practical exercises with guidance from the lecturers so that participants can put their knowledge to use. Topics include:

- Risk Assessment in the 21st Century (RISK21)
- Public Health Management of Chemical Incidents
- Dietary Risk Assessment
- Food Safety

**Teaching Faculty:**

1. **David Russell, Ph.D.**
   Co-director, WHO Collaborating Centre for the Public Health Management of Chemical Exposures, UK Health Security Agency, UK
2. **Maged Younes, Ph.D.**
   Chair, Food Additives and Nutrient Supplements Panel, European Food Safety Agency (EFSA), Italy
3. **Michelle Embry, Ph.D.**
   Associate Director, Environmental Science, Health and Environmental Sciences Institute (HESI), USA

**Applicant Qualifications:**

Applicants must fulfill the following requirements:

1) At least two (2) years work experience related to the use of basic knowledge in chemistry, biological sciences or medicine.
2) Hold a bachelor's degree from a university/technical college.
3) Demonstrate proficiency in English (speaking, reading and writing).
4) Be in good health, both physically and mentally, and have a health certificate provided by an authorized physician. This form is also attached together with the Nomination Form. Pregnancy is regarded as a disqualifying condition for participation in the course.

***Applicants are encouraged to attend both training courses to maximize the usefulness of the training they receive. It is expected that the theoretical aspects of risk assessment from the fundamentals course and the practical aspects of risk assessment in the practical applications course will provide them with well-rounded training and the ability to conduct risk assessments back in their home institutions. While applications to one of the two courses will be considered, applicants who apply to attend both courses will receive special consideration.***

**Fellowships:**

The fellowship will cover course fees, round trip airfare, accommodation allowance, daily stipend, training material, and health insurance.

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Please visit - https://www.cri.or.th/en/academic/actcalendar.php




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