

Occupational Hygiene

Occupational Hygiene - Immunotoxic Chemicals

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What is immunotoxicity?

The World Health Organization's International Programme on Chemical Safety defines immunotoxicity as "any adverse effect on the immune system that can result from exposure to a range of environmental agents, including chemicals. It encompasses studies of various immune pathologies, including allergy, immune dysregulation (suppression or enhancement), autoimmunity, and chronic inflammation."

(Source: World Health Organization's International Programme on Chemical Safety (2012). Harmonization Project Document No. 10: Guidance For Immunotoxicity Risk Assessment For Chemicals)

What is the immune system, and what is its function?

The immune system is a complex system that consists of cells, chemicals, tissues, and organs. The major lymphoid organs are the spleen, thymus, lymph nodes, bone marrow, and areas of the intestine (Peyer's patches).

The function of the immune system is to defend the body from infection, including:

- defence against pathogens or neoplasias (i.e., abnormal growth of cells or tissues in the body)
- response to foreign compounds (e.g., allergens)
- recognition and discrimination of self from foreign components

Can chemicals cause immunotoxicity?

Substances that can affect the immune system can be of synthetic or natural origin. They are referred to as immunotoxicants. Many biological, physical, and chemical substances can disturb the balance of the immune system. Examples of chemicals where there is evidence that they cause immunotoxicity are:

- Airborne pollutants such as nitrogen dioxide, sulphur dioxide, ozone, asbestos, silica, diesel exhaust, and carbon (coal dust)
- Metals and compounds (e.g., mercury, lead, cadmium, organotin compounds such as dioctyltin, gallium arsenide, and beryllium)
- Pesticides (e.g., organochlorine compounds, organophosphate compounds, pyrethroids, carbamates, and dinocap)
- Some organic solvents
- Benzene
- Styrene
- Halogenated aromatic hydrocarbons such as polychlorinated biphenyls (PCBs), 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD), hexachlorobenzene, and polybrominated biphenyls (PBBs)
- Polyaromatic hydrocarbons (e.g., 3-methylcholanthracene and benzo[a]pyrenes)
- Medications such as:
 - Antihypertensive drugs (e.g., hydralazine, methyldopa), anti-arrhythmia drugs (e.g., procainamide, practolol, quinidine), anticonvulsant drugs (e.g., phenytoin, ethosuximide, primidone), antimicrobial drugs (e.g., penicillin, sulfonamides, isoniazid, nitrofurantoin), etc.
 - Immunosuppressive drugs such as azathioprine, glucocorticosteroids, cyclophosphamide, cyclosporin A, etc.

- Substances, such as:
 - Cannabinoids (e.g., marijuana)
 - Phencyclidine (PCP)
 - Opiates (e.g., heroin)
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What industries, manufacturing processes, or occupations use these products?

Many different types of chemicals can cause immunotoxicity. Thus, workers of diverse occupations in various industries may be exposed to them. Examples of industries that may use or produce such products are:

- Chemical industry
- Oil and gas (petroleum) industry
- Companies producing or using pesticides
- Manufacturing companies that use the metals listed above (e.g., use of lead for the production of bullets or lead acid batteries)
- Transportation
- Utilities
- Trade industry
- Pharmaceutical companies that produce therapeutic drugs, such as immunosuppressive drugs
- Healthcare organizations that administer therapeutic drugs or are involved in organ transplantation.

Regardless of the industry, when workers use immunotoxicants, they are at risk of health effects. For example, the following occupations could be exposed to lead, which has been determined to cause adverse health effects to the immune system:

- Firearm instructors
 - Lead smelter workers
 - Lead acid battery workers
 - Silver jewellery workers
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What are the possible health effects and risks from exposure to immunotoxic chemicals?

The type of adverse health effects that workers may have after exposure to immunotoxic chemicals will depend on how the immunotoxic substance affects the immune system, the dose (how much), and the time exposed (how long). The effects may be reversible, delayed, and irreversible. Generally speaking, adverse health effects may include:

- **Suppression** of the normal immune response system, commonly referred to as “immunosuppression”. Effects may vary and include recurrent infections, autoimmune disorders, damage to the heart, lungs, nervous system or digestive tract, increased risk of cancer, or serious infection.
- **Stimulation** of the normal immune response system, or aggravation of autoimmune diseases or allergies. This effect is also known as hypersensitivity. Effects may include worsening of allergic reactions or autoimmune disease and start or increase inflammatory response, possibly causing organ damage. Examples include:
 - Skin disorders: allergic contact dermatitis
 - Immune-mediated respiratory disorders including some types of asthma, hypersensitivity pneumonitis, allergic rhinitis, bronchopulmonary aspergillosis, silicosis, asbestosis, coal workers’ pneumoconiosis, and possibly byssinosis.

Please see the OSH Answers for more information on the following: [Dermatitis, Allergic Contact](#), [Hypersensitivity Pneumonitis \(Extrinsic Allergic Alveolitis\)](#), and [Asthma, Work-related](#)

- **Autoimmunity** – Autoimmunity results from a breakdown in the ability of the immune system to distinguish “self” from “non-self.” Human diseases believed to occur due to autoimmune reactions are:
 - Systemic lupus erythematosus
 - Rheumatoid arthritis
 - Progressive systemic sclerosis (scleroderma)
 - Hashimoto’s thyroiditis
 - Multiple sclerosis
 - Myasthenia gravis
 - Guillan-barré syndrome
 - Diabetes
- Dysfunctional inflammatory responses leading to organ damage or dysfunction

- Adverse health effects on the immune system may also occur in the embryo, fetus, or offspring. Immune dysfunction due to early postnatal exposure or during immune system development may increase the later-life risk of certain autoimmune diseases and other health effects (e.g., decreased defence against infections).
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How does a workplace know if a chemical causes immunotoxicity?

The Workplace Hazardous Materials Information System (WHMIS) provides health and safety information on hazardous products intended for use, handling, or storage in Canadian workplaces.

Immunotoxic substances in the workplace can be identified by:

- Reviewing the Safety Data Sheet (SDS) and label for the product. The immunotoxic health effects (if any) should be reported in the following sections of the SDS:
 - Section 2 Hazard Identification (see the hazard statements)
 - Section 11 Toxicological Information
- Determining if it is identified in the jurisdiction's health and safety occupational exposure limits (OEL) list
- Consulting other exposure limits, such as the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs®) and Biological Exposure Indices (BEIs®) (see TLV® Basis)
- Researching the health hazards associated with ingredients in the product

Depending on the type of immunotoxic health effects a hazardous product poses, it may be classified within the following WHMIS 2015 hazard classes:

- Hypersensitivity/sensitization:
 - Respiratory Sensitizer Category 1, 1A. or 1B
 - Skin Sensitizer Category 1, 1A. or 1B
 - Specific target organ toxicity – single exposure (STOT-SE) Category 1 or 2 (sensitization of other organs such as intestines)
 - Specific target organ toxicity – repeated exposure (STOT-RE) Category 1 or 2 (sensitization of other organs such as intestines)
 - Depending on the type of sensitization, some suppliers may classify under Health Hazards Not Otherwise Classified (HHNOC) - Category 1

- Autoimmunity
 - Specific target organ toxicity – single exposure (STOT-SE) Category 1 or 2 (autoimmunity)
 - Specific target organ toxicity – repeated exposure (STOT-RE) Category 1 or 2 (autoimmunity)
 - Some suppliers may classify under Health Hazards Not Otherwise Classified (HHNOC) - Category 1

- Immunosuppression
 - Specific target organ toxicity – single exposure (STOT-SE) Category 1 or 2 (immunosuppression)
 - Specific target organ toxicity – repeated exposure (STOT-RE) Category 1 or 2 (immunosuppression)
 - Some suppliers may classify under Health Hazards Not Otherwise Classified (HHNOC) - Category 1
 - Health effects due to chronic exposure (more than 3 months) due to effects on the immune system:
 - Carcinogenicity, Category 1, 1A, or 1B, or Category 2
 - Reproductive toxicity, Category 1, 1A, or 1B
 - Hazards Not Otherwise Classified (HHNOC) — Category 1 (autoimmunity or organ damage)

Note that in some cases, there is little information available on the immunotoxic effects of a specific chemical. As such, suppliers or regulators may not be able to identify immunotoxic chemicals. Also, these health effects are not directly addressed by the WHMIS legislation. Consequently, they may not be identified with a WHMIS hazard class.

Are there specific occupational exposure limits for chemicals that cause immunotoxicity?

Most Canadian jurisdictions have adopted the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values® as their occupational exposure limits. Jurisdictions that have not adopted the ACGIH values (e.g., Alberta) specify occupational exposure limits in their health and safety legislation.

Generally, ACGIH will specify if their value considers the chemical's immunotoxicity if such data was available at the time of the ACGIH TLV® publication.

Consult with the jurisdiction to determine if such health effects are considered when establishing the OELs. Please see the OSH Answers [Canadian Government Departments Responsible for Health and Safety](#) for contact information.

What are the employer's responsibilities for protecting workers from immunotoxic chemicals?

Canada's jurisdictions' health and safety legislations require employers to inform workers about known health hazards in their jobs.

Prepare an inventory of chemical products and record information about immunotoxicity from:

- Supplier's SDS (see Sections 2 and 11) and technical literature. As mentioned above, immunotoxic substances may be classified under several WHMIS health hazard classes.
- Measure the amount of airborne immunotoxic contaminants to determine the workers' exposure level.
- Check your jurisdiction's regulatory occupational exposure limits and whether it is based on immunotoxicity effects.
- Without specific information from the manufacturer, search publicly available databases, government publications, and scientific abstracts databases for information on toxicity to the immune system.

Safe work practices include to:

- Carry out a hazard and risk assessment for products used at the workplace that are identified as immunotoxic and for those that have the potential to be immunotoxic based on research data.
- Document and investigate complaints from workers about health effects that may be due to exposure to immunotoxic products. Explore whether exposure to products that cause immunotoxicity is playing a role in worker health complaints.
- Prepare safe operating procedures and safe work practices based on the hazard and risk assessment and literature data.
- Train workers on the procedures and practices and the safe use and maintenance of personal protective equipment (PPE).
- Educate workers about immunotoxicity.
- If the occupational exposure limit for a chemical does not consider immune toxicity, but there is data that indicates it could be immunotoxic, the limit for the chemical should be reduced.

- When exposure to an immunotoxic chemical occurs through dermal exposure (meaning that an air concentration-based occupational exposure limit would not provide adequate protection), biomonitoring should be considered.
- If a worker is immunocompromised, eliminate their exposure to immunotoxic products.
- Implement control measures based on [hazard identification](#) and [risk assessment](#) and follow the [hierarchy of controls](#):
 - Eliminate the use of immunotoxins in the workplace
 - Substitute with a less toxic chemical
 - Implement engineering controls such as:
 - Isolation and enclosures
 - Ventilation - Volatile immunotoxins should be used in chemical fume hoods (i.e., local exhaust) or with other appropriate devices to ensure local capture of any airborne chemical.
 - Implement administrative controls such as:
 - Have a competent person prepare a hazard prevention program
 - Eliminate unnecessary tasks that cause exposure
 - Limit exposure time by rotation
 - Ensure immunocompromised workers or pregnant workers do not handle immunotoxicants or ensure that they are appropriately protected
 - Use Personal Protective Equipment (PPE) – Get information from the manufacturer about how well their PPE performs against the chemicals used at the workplace.
 - Based on the hazard identification and risk assessment, assess and determine the appropriate PPE according to the jurisdiction's health and safety legislation, guidance documents, or adopted standards (if any). Follow industry good practices when no standards are specified or recommended
 - Since many immunotoxic substances can be absorbed through the skin, chemical-protective gloves, arm sleeves, aprons and other appropriate clothing can assist in reducing dermal exposure
 - Head shields, goggles, and glasses will also reduce exposure

What are the worker's responsibilities when working with immunotoxic chemicals?

Worker responsibilities include making sure you have received the appropriate education and training and that you understand:

- How to look up the safe operating or safe work practices (if any) and the SDS for the chemical you are using
- How to follow the instructions in the safe operating or safe work practices that relate to your tasks
- How to use, wear, and maintain any required PPE required
- How to locate information related to WHMIS, emergency response, spill procedures, etc.
- Any warnings in the safe operating or safe work practice, such as early health effects to watch for
- Who to contact when the instructions are not clear or when unsure about any safe handling practices
- The personal hygiene practices that must be followed. Examples of personal hygiene practices are:
 - washing the skin regularly
 - wash contaminated clothing before wearing or wear clothing that is not soaked by chemicals or wear disposal coveralls
 - discarding contaminated clothing that cannot be washed
 - washing chemical-soaked clothing separately from your regular or other household clothing
 - not eating or drinking in work areas
 - cleaning and maintaining PPE according to the employer's safe work practices or safety standards
- When to report health and safety issues or emergencies to your supervisor or employer. For example, if the employer informs you that the substances you are working with are immunotoxic, then inform your supervisor if you are immunocompromised or pregnant.

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