Risk assessment for nanomaterials

Risk is defined as the probability of harm occurring and is a function of both hazard and exposure. A robust risk assessment for nanomaterials requires detailed information across several key areas.

1. Hazard identification

This involves characterizing the adverse health effects associated with a nanomaterial, typically through *in vivo* (animal) and *in vitro* (cell-based) studies. Given the diversity of nanomaterials, a comprehensive understanding of their effects on the respiratory, cardiovascular, and nervous systems is crucial.

2. Exposure assessment

This is the qualitative and/or quantitative evaluation of likely exposure to nanomaterials.

- **Routes of entry:** Primary routes include inhalation, ingestion, and dermal contact, as well as injection for medical applications. Nanomaterials' small size allows them to cross biological barriers, such as the blood-brain barrier and placenta, and reach secondary organs.
- **Environmental fate and transport:** The assessment must consider how nanomaterials behave in various media (e.g., water, soil), including their tendency to aggregate or form a protein "corona" in biological fluids, which can alter their properties and toxicity.

3. Risk characterization

This final step synthesizes the hazard and exposure data to estimate the nature and magnitude of the health risk. Because of the extreme uncertainties surrounding nanomaterials, qualitative or semi-quantitative risk ranking is often used, relying on expert judgment when data are limited.

Risk management for nanomaterials

Risk management involves selecting and implementing appropriate controls to protect human health and the environment from unacceptable risks.

- **Hierarchy of controls:** The standard hierarchy of controls is applied to nanomaterials, prioritizing the most effective measures:
- **Elimination/substitution:** Using a safer alternative nanomaterial or a non-nano form.
- **Engineering controls:** Implementing local exhaust ventilation, enclosed systems, and glove boxes to prevent aerosol release.
- **Administrative controls:** Establishing safe work practices, hygiene protocols, and proper waste disposal.

    - **Personal protective equipment (PPE):** Providing respirators, gloves, and lab coats as a last line of defense.
    - **Control banding:** This approach assigns materials to hazard "bands" based on toxicity and exposure potential, providing a structured way to determine control measures for low-data materials.

- **Safe-by-Design (SbD):** This proactive strategy integrates health and safety considerations into the earliest stages of nanomaterial design to mitigate risks before they emerge.

- **Medical surveillance:** Programs can help monitor workers for potential health effects and verify the effectiveness of risk management measures.

<u>Factors affecting nanotoxicity</u>

The toxicity of nanomaterials is highly dependent on their physicochemical properties and their interaction with biological systems.

Physical characteristics

- **Size:** As particle size decreases, the surface area-to-volume ratio increases, enhancing reactivity and the ability to generate reactive oxygen species (ROS). Smaller particles also have an easier time penetrating cell membranes and translocating to organs.
- **Shape:** The shape of a nanomaterial can significantly influence its biological activity. For example, fibrous nanoparticles like carbon nanotubes can elicit asbestos-like inflammatory and carcinogenic responses, while spherical particles may show less potency.
- **Aggregation/agglomeration:** Nanoparticles tend to clump together in biological and environmental media. The resulting aggregate's size, shape, and stability influence its transport, deposition, and toxic potential.
- **Chemical characteristics**
- **Composition:** The intrinsic chemical properties of a nanomaterial's core and surface are a primary determinant of its toxicity. For example, some metal oxides may be more toxic than others.
- **Surface chemistry and coatings:** The surface charge (e.g., positive vs. negative) and chemical functionalization dramatically impact cellular uptake, protein corona formation, and overall toxicity. Surface coatings are a key strategy for mitigating nanotoxicity.
- **Solubility:** For soluble nanomaterials, toxicity may be largely driven by the release of toxic ions. The rate of ion release can be influenced by the material's size and surface properties.

Exposure and host factors

- **Route of exposure:** Inhalation, ingestion, and dermal contact can lead to different toxicokinetics and target organs. For example, inhaled nanomaterials often target the lungs and cardiovascular system, while ingested particles affect the gastrointestinal tract.
- **Dose:** The dose of nanomaterials is complex and cannot be based solely on mass concentration. Metrics like surface area or particle number may better correlate with toxicological responses.
- **Host response:** Biological factors in the host, such as the immune system and genetic predisposition, can modulate the toxic effects of nanomaterials.