ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

A Unified Organism Exposure and Risk Index (OERI): Integrating Deterministic and Probabilistic Multi-Pathway Assessment of Polycyclic Aromatic Hydrocarbons (PAHs) and Potentially Toxic Elements (PTEs)

Appiah, Mark Kubi[1]

[1]Department of Environmental and Safety Engineering, University of Mines and Technology, Tarkwa

[1]ORCID:https://orcid.org/0009-0006-3044-1255

Publication Date: 2026/03/12

Abstract: Environmental exposure to polycyclic aromatic hydrocarbons (PAHs) and potentially toxic elements (PTEs) presents persistent human health risks due to their carcinogenicity, bioaccumulation potential, and multi-pathway toxicity. Although conventional risk assessment frameworks quantify carcinogenic risk (Incremental Lifetime Cancer Risk, ILCR) and non-carcinogenic hazard (Hazard Quotient, HQ; Hazard Index, HI), they often present outputs separately and rely on deterministic point estimates that obscure uncertainty. This review develops and systematizes a unified Organism Exposure & Risk Index (OERI), a transparent and dimensionless composite screening metric that integrates inhalation, dermal, ingestion, and injection pathways for both PAHs (via benzo[a]pyrene toxic equivalency, BaP-TEQ) and PTEs. The framework synthesizes established chronic daily intake (CDI) equations, slope factor (SF) based carcinogenic modeling under the linear no-threshold assumption, and reference dose (RfD) threshold toxicology into a normalized cumulative index. OERI incorporates regulatory benchmarks to harmonize ILCR and HI scales and allows flexible weighting of carcinogenic and non-carcinogenic endpoints. A probabilistic Monte Carlo extension is presented to propagate variability and uncertainty across exposure factors, generating risk distributions, exceedance probabilities, and sensitivity diagnostics. The approach aligns with contemporary regulatory guidance advocating uncertainty-informed cumulative risk assessment. OERI functions as a screening-level decision-support tool that enhances transparency, comparability, and pathway attribution while preserving component-level regulatory interpretation. This integrative model provides a defensible methodological bridge between environmental monitoring data, toxicological scaling, and risk-informed environmental health decision-making.

Keywords: *Organism Exposure & Risk Index (OERI); Polycyclic Aromatic Hydrocarbons (PAHs); Potentially Toxic Elements (PTEs); Chronic Daily Intake (CDI); Incremental Lifetime Cancer Risk (ILCR); Hazard Quotient (HQ); Monte Carlo Simulation; Cumulative Risk Assessment; Toxic Equivalency Factors (TEFs); Environmental Health Risk Modeling.*

How to Cite: Appiah, Mark Kubi (2026) A Unified Organism Exposure and Risk Index (OERI): Integrating Deterministic and Probabilistic Multi-Pathway Assessment of Polycyclic Aromatic Hydrocarbons (PAHs) and Potentially Toxic Elements (PTEs). *International Journal of Innovative Science and Research Technology*, 11(3), 278-300. https://doi.org/10.38124/ijisrt/26mar037

I. INTRODUCTION

Exposure to environmental pollutants such as polycyclic aromatic hydrocarbons (PAHs) and potentially toxic elements (PTEs) represents a critical concern for both human and ecological health due to their persistence, bioaccumulative potential, and toxicity, including carcinogenicity and mutagenicity across multiple exposure pathways (IARC, 2012; ATSDR, 2022; USEPA, 2023). PAHs, a class of ubiquitous organic contaminants generated primarily through incomplete combustion of organic matter, are widely distributed in air, soil, and water systems and have been extensively associated with carcinogenic risk, cardiovascular dysfunction, and respiratory diseases following inhalation, dermal absorption, and other systemic exposure routes (Boström et al., 2002; Kim et al., 2013; WHO, 2021). Moreover, PTEs such as arsenic (As), cadmium (Cd), chromium (Cr), and lead (Pb) contribute to systemic toxicity, neurotoxicity, nephrotoxicity, and multi-organ damage even at relatively low exposure concentrations,

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

underscoring the necessity of quantitative risk assessment frameworks capable of integrating multiple exposure pathways (ATSDR, 2022; Tchounwou et al., 2012; USEPA, 2023).

Risk assessment, as a structured scientific process, quantifies both the probability and severity of adverse health outcomes following environmental exposure by integrating exposure assessment, dose–response assessment, and risk characterization (NRC, 2009; USEPA, 1989; WHO, 2017). Central to this framework are mathematical expressions that translate environmental contaminant concentrations into biologically relevant exposure doses and corresponding risk probabilities, such as the Hazard Quotient (HQ), Hazard Index (HI), and Incremental Lifetime Cancer Risk (ILCR) (USEPA, 2011; USEPA, 2023). The hazard quotient (HQ), defined as the ratio of the average daily dose (ADD) to the reference dose (RfD), remains a foundational metric in non-carcinogenic risk estimation ($HQ = {}^{D}/_{RfD}$), providing a quantitative benchmark for assessing potential adverse effects via dermal, inhalation, and ingestion or injection routes (USEPA, 2011; ATSDR, 2022). Similarly, carcinogenic risk is typically expressed as the incremental lifetime cancer risk (ILCR), calculated by multiplying chronic daily intake (CDI) by a cancer slope factor (CSF) ($ILCR = CDI \times CSF$), thereby estimating the probability of an additional cancer case over a lifetime of exposure (USEPA, 2005; IARC, 2012). These equations establish the mechanistic link between external exposure concentration, internal absorbed dose, and toxicological response.

The application of these quantitative frameworks enables comparison of exposure scenarios across environmental media and biological routes, identification of dominant exposure pathways, and prioritization of mitigation and regulatory interventions (USEPA, 2011; WHO, 2017). For example, PAH mixture toxicity is commonly standardized using benzo[a]pyrene toxic equivalency factors (BaP-TEQ), allowing consistent estimation of cumulative carcinogenic risk across complex environmental matrices such as air particulates, soil, and water (Nisbet & LaGoy, 1992; USEPA, 2017; Kim et al., 2013). In parallel, PTE risk models incorporate element-specific reference doses, inhalation unit risks, and exposure duration factors tailored to distinct physiological endpoints, thereby generating multidimensional risk profiles for human and ecological receptors (Tchounwou et al., 2012; USEPA, 2023). Such integrated assessments provide a scientifically defensible basis for environmental regulation and public health protection.

Despite their widespread adoption, the reliability of risk assessment equations depends critically on the accuracy of exposure factors, toxicological reference values, and unit harmonization. Variability in assumptions regarding body weight, exposure frequency, bioavailability, and slope factors can significantly influence risk estimates (NRC, 2009; USEPA, 2011). Consequently, contemporary research increasingly advocates the integration of probabilistic techniques such as Monte Carlo simulations to address uncertainty and variability in exposure modeling, thereby enhancing robustness and transparency in environmental risk characterization (WHO, 2017; USEPA, 2014). Standardization of toxic equivalency conversions and calibration of exposure models are similarly emphasized to ensure methodological consistency across studies.

This paper synthesizes the principal risk assessment equations employed for dermal, inhalation, and injection exposure pathways, examine their theoretical underpinnings, and evaluate their applicability to PAHs and PTEs across diverse environmental contexts. Advancing methodological consistency and uncertainty management in these models is essential for strengthening interdisciplinary applications in environmental health risk science.

A single, transparent, reproducible risk-index framework to evaluate an organism's (human) exposure to PAHs (expressed as BaP-TEQ) and PTEs across three pathways: inhalation, dermal, and ingestion.

The output is a dimensionless Organism Exposure & Risk Index (OERI) that combines carcinogenic and non-carcinogenic risks from both chemical classes, interpretable against common benchmarks, and ready for deterministic or probabilistic (Monte-Carlo) implementation.

➢ *Presentation of Equations:*

- the per-pathway dose-risk equations for PAHs and PTEs (metals), then
- the aggregation mathematics and normalization to form OERI.
- the recommended default parameters, interpretation rules, and on Monte-Carlo Simulation

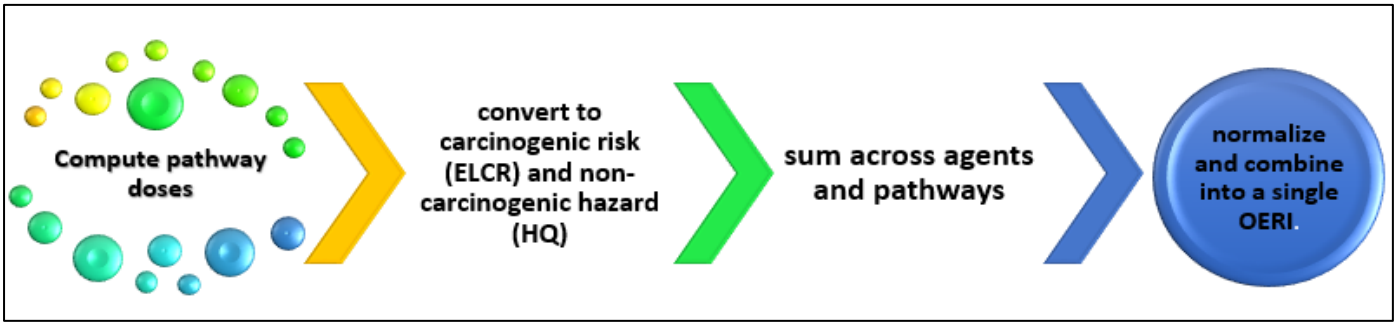

Fig 1 Developmental stages for Organism Exposure & Risk Index (OERI)

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

The schematic (Fig. 1.0) illustrates the conceptual progression from multi-parameter exposure inputs to a unified, normalized risk index represented as the Organism Environmental Risk Index (OERI). The left-most cluster of colored spheres symbolizes heterogeneous contaminant inputs (PAHs and PTEs) and exposure determinants such as concentration (C), ingestion rate (IR), exposure frequency (EF), body weight (BW), and bioavailability (BA). These variables constitute the quantitative exposure domain and are typically integrated through Chronic Daily Intake (CDI) equations as prescribed in the United States Environmental Protection Agency Risk Assessment Guidance for Superfund (RAGS) framework (U.S. EPA, 2009; U.S. EPA, 2011).

The first transition (see Fig 1.0) arrow represents normalization, where contaminant-specific doses are scaled relative to toxicological benchmarks such as Reference Doses ($RfDs$) for non-cancer effects and Cancer Slope Factors (CSFs) for carcinogenic effects. This step produces dimensionless metrics including the Hazard Quotient (HQ) and Incremental Lifetime Cancer Risk (ILCR), enabling comparison across contaminants with different toxicological potencies (U.S. EPA, 2017; ATSDR, 2022).

Fig 1 the second arrow reflects aggregation and weighting. For PAH mixtures, toxicity equivalency factors (TEFs) (using equation 5.6) are applied to convert individual concentrations into benzo[a]pyrene toxic equivalents (BaP-TEQ), thereby addressing mixture toxicity rather than single-compound assessment (Nisbet & LaGoy, 1992; U.S. EPA, 2017). Similarly, cumulative risk principles recommend summing HQs and ILCRs across pathways and contaminants to estimate total risk (WHO, 2017).

The final circular node ("normalize and combine into a single OERI") represents integration into a composite risk index. Such integrative indices are consistent with cumulative risk assessment paradigms that combine multiple stressors, exposure routes, and toxicity endpoints into a unified decision-support metric (U.S. EPA, 2003; WHO, 2017). In the context of thermally modified wood systems, this approach provides a transparent and defensible bridge between contaminant generation, exposure modeling, toxicological scaling, and regulatory risk characterization.

II. THEORETICAL FRAMEWORK FOR MULTI-PATHWAY DOSE AND RISK MODELING

A. The Per-Pathway Dose-Risk Equations for PAHs and PTEs (Metals)

Terms

$$i = chemical\ index\ (PAHs\ congeners\ and\ metal\ species)$$
$$p \in \{inh, Derm, inj\} = pathways\ (inhalation, Dermal, injection)$$

Concentration;

$$C_{i,air}\ in\ ng.m^{-3}\ (air), C_{i,surf}\ in\ mg.kg^{-1}\ (dust/residue)\ or\ mg.cm^{-2}(surface), C_{i,liq} in\ mg.L^{-1}\ (injection)$$

Body parameters;

BW (kg), IR ($m^3.day^{-1}$), SA (cm^2) $skin\ area$,

Toxicity:

SF_i Cancer slope factor $(mg.kg^{-1}.day^{-1})^{-1}$, IUR_i inhalation unit risk (per $.m^{-3}$), $RfD_i\ refernce\ does\ (mg.kg^{-1}.day^{-1})$,

Conversion:

$$BaP - TEQ = \sum_i C_i.TEF_i\ (unit\ same\ as\ C_i)$$

➢ *Conceptual Basis of Environmental Dose Reconstruction*

Modern environmental health risk assessment is grounded in a structured exposure–dose–response paradigm that translates environmental contaminant concentrations into biologically meaningful internal doses and, ultimately, into probability-based risk metrics (USEPA, 1989; NRC, 2009; WHO, 2017; USEPA, 2014). The mathematical formulations used in regulatory science are not arbitrary constructs but operational expressions of toxicokinetic mass balance, chronic exposure integration, and dose–response extrapolation theory, refined over decades of toxicological and epidemiological research (NRC, 2009; Rhomberg & Goodman, 2012).

The chronic daily intake (CDI) and lifetime average daily dose (LADD) equations originate from classical toxicological reasoning in which cumulative absorbed dose, normalized to body mass and biologically relevant time, serves as the predictor of adverse outcome (USEPA, 1989; NRC, 2009). These formulations extend Haber's Law principles by incorporating lifetime averaging and allometric scaling, thereby enabling inter-individual comparability across heterogeneous populations and supporting low-dose extrapolation under regulatory frameworks (NRC, 2009; Rhomberg & Goodman, 2012). The integration of exposure frequency, duration, and averaging time reflects the recognition that chronic disease endpoints, particularly

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

carcinogenesis, are functions of long-term cumulative dose rather than short-term peak exposure (IARC, 2012; WHO, 2017).

For persistent contaminants such as polycyclic aromatic hydrocarbons (PAHs) and potentially toxic elements (PTEs), multi-pathway exposure modeling is essential because inhalation, dermal contact, and incidental ingestion may simultaneously contribute to systemic burden (ATSDR, 2022; Boström et al., 2002; Kim et al., 2013; Tchounwou et al., 2012). PAHs, due to their semi-volatile nature and lipophilicity, partition across air, particulates, soil, and biological tissues, facilitating both inhalation and dermal uptake (Boström et al., 2002; Kim et al., 2013). Similarly, metals such as arsenic, cadmium, chromium, and lead exhibit route-dependent toxicokinetics and target-organ specificity, necessitating pathway-resolved modeling (Tchounwou et al., 2012; ATSDR, 2022). Contemporary cumulative risk frameworks therefore, explicitly recommend integration across exposure routes and chemical classes to reflect realistic environmental scenarios and population heterogeneity (NRC, 2009; USEPA, 2014; WHO, 2017).

➢ *Per-pathway dose equations*

- *Inhalation (PAHs as BaP-TEQ; Metals as Species)*

✓ *For PAHs (use $BaP - TEQ_{air}$ in $mg.m^{-3}$):*

$$LADD_{inh,PAH} = \frac{BaP-TEQ \times IR \times EF \times EDS \times ABS_{inh}}{BW \times AT} \quad (2.1)$$

Convert $BaP - TEQ_{air}$ (ng·m⁻³) → mg·m⁻³ by dividing by 10^6

Equations 2.1 reflects the standard inhalation Chronic Daily Intake (CDI) methodology formalized in regulatory guidance and risk assessment frameworks (USEPA, 1989; USEPA, 2011). The structure operationalizes a toxicokinetic mass-balance model in which airborne concentration is integrated over inhalation rate (IR), exposure frequency (EF), and exposure duration (ED), and subsequently normalized by body weight (BW) and averaging time (AT) to yield a lifetime-adjusted dose metric (NRC, 2009; WHO, 2017). This formulation ensures dimensional consistency (mg·kg⁻¹·day⁻¹) and enables direct linkage to dose–response parameters such as slope factors and reference doses. By incorporating time-weighted exposure parameters, the equation captures chronic cumulative burden rather than transient peak concentrations, consistent with established principles of inhalation toxicology and environmental epidemiology (Rhomberg & Goodman, 2012).

The use of benzo[a]pyrene toxic equivalency (BaP-TEQ) addresses mixture carcinogenicity among PAHs by converting heterogeneous compounds into a common potency-weighted metric. Toxic Equivalency Factors (TEFs), originally proposed for PAHs by Nisbet and LaGoy (1992), allow individual PAH concentrations to be expressed relative to benzo[a]pyrene carcinogenic potency, thereby enabling additive risk estimation under the linear no-threshold (LNT) paradigm (IARC, 2012; Kim et al., 2013). This TEQ-based modeling approach has been extensively adopted in combustion-related exposure assessments and atmospheric particulate studies (Boström et al., 2002; Shen et al., 2013). Reviews published in *Environmental Health Perspectives* and *Science of the Total Environment* affirm that TEQ normalization provides a scientifically defensible and policy-relevant method for integrating PAH mixture toxicity in cumulative cancer risk assessment (Boström et al., 2002; Kim et al., 2013).

Pulmonary absorption fractions are frequently conservatively assumed to approach unity for lipophilic semi-volatile organic compounds during screening-level assessments. This assumption reflects high alveolar surface area, thin respiratory membranes, and efficient gas–particle transfer within the pulmonary region, which together facilitate substantial systemic uptake (WHO, 2017; USEPA, 2011). While compound-specific uptake efficiencies may vary depending on vapor–particle partitioning and respiratory tract deposition patterns, the use of near-complete absorption in preliminary assessments is considered health-protective and consistent with regulatory guidance when empirical bioavailability data are limited (USEPA, 2014; ATSDR, 2022).

✓ *For a certain metal i,*

$$LADD_{inh,i} = \frac{C_{i,air} \times IR \times EF \times EDS \times ABS_{inh,i}}{BW \times AT} \quad (2.2)$$

$C_{i,air}$ in mg·m⁻³ (convert from ng·m⁻³).

For potentially toxic elements (PTEs), species-specific modeling is scientifically indispensable because toxicokinetics, bioavailability, and carcinogenic potency depend strongly on chemical speciation, oxidation state, and compound solubility (ATSDR, 2022; IARC, 2012). The biological reactivity of metals is governed not merely by total elemental concentration but by valence state, ligand association, and redox behavior, all of which influence cellular uptake, oxidative stress generation, DNA interaction, and target-organ toxicity (Tchounwou et al., 2012). For example, chromium(VI) [Cr(VI)] exhibits markedly higher inhalation carcinogenic potency than chromium(III) [Cr(III)] due to its greater membrane permeability, intracellular reduction potential, and ability to generate reactive intermediates capable of inducing DNA damage (IARC, 2012; ATSDR, 2022). This distinction is well documented in mechanistic toxicology and supported by epidemiological evidence from chromate production workers and stainless-steel welding cohorts. Consequently, risk assessment frameworks emphasize that applying a single slope factor to total chromium concentration without speciation analysis may substantially misrepresent true carcinogenic risk (USEPA, 2014; NRC, 2009).

Similar speciation dependence exists for arsenic and cadmium compounds. Inorganic arsenic species (arsenite As^{3+} and arsenate As^{5+}) differ in metabolic transformation, methylation efficiency, and carcinogenic potential, with

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

inorganic forms demonstrating stronger associations with lung, bladder, and skin cancer (IARC, 2012; ATSDR, 2022). Cadmium toxicity varies across oxide, sulfide, and chloride forms, influencing pulmonary deposition and systemic absorption following inhalation exposure (Tchounwou et al., 2012). These examples underscore the necessity of species-resolved exposure modeling where feasible, or alternatively, the transparent adoption of conservative assumptions when speciation data are unavailable.

Experimental validation of inhalation dose reconstruction is supported by multiple lines of evidence. Occupational cohort studies provide real-world exposure–response relationships linking airborne metal concentrations to elevated cancer incidence and organ-specific toxicity (IARC, 2012). Chronic rodent inhalation bioassays establish dose–tumor incidence relationships that underpin slope factor derivation (ATSDR, 2022). In addition, biomonitoring investigations demonstrate correlations between airborne exposure metrics and systemic biomarkers such as blood lead levels, urinary cadmium excretion, or chromium in red blood cells, thereby empirically supporting inhalation CDI modeling assumptions (ATSDR, 2022; Tchounwou et al., 2012). Collectively, these epidemiological, experimental, and biomarker-based data streams provide robust validation for species-specific inhalation dose reconstruction within regulatory risk assessment frameworks (NRC, 2009; USEPA, 2014).

➢ *Dermal (Surface/Dust Contact)*

Use surface concentration, $C_{i,surf}$ in mg·m^{-3} (convert from ng·m^{-3}) or convert mg.kg^{-1} dust to mg.cm^{-2} via dust loading if needed.

$$ADD_{Derm,i} = \frac{C_{i,surf} \times SA \times AF \times EF \times ED \times ABS_{Derm,i}}{BW \times AT} \quad (2.3)$$

SA = exposed skin area (cm²).

AF = adherence factor (mg·cm^{-2}·event^{-1} or mass·area factor).

Dermal exposure modeling is grounded in Fickian diffusion theory, which describes transdermal mass transfer as a function of concentration gradient, exposed surface area, and permeability coefficient (USEPA, 2004; Kissel et al., 2008). In this framework, the absorbed mass is proportional to the contaminant surface concentration, exposed skin area (SA), and adherence factor (AF), while chemical-specific dermal permeability governs the fraction that penetrates the stratum corneum and reaches systemic circulation. The inclusion of an absorption fraction (ABSDerm,i_{Derm,i}Derm,i) operationalizes compound-specific bioavailability and accounts for differences in lipophilicity, molecular size, and partition coefficients that influence skin transport kinetics (USEPA, 2004; WHO, 2017). This parameterization reflects empirical findings from in vitro human skin diffusion assays and in vivo toxicokinetic studies, which demonstrate that dermal uptake varies significantly across chemical classes.

Lipophilic PAHs exhibit measurable dermal penetration due to their high octanol–water partition coefficients (Kow_{ow}ow) and affinity for lipid-rich epidermal layers. Experimental studies and occupational investigations of creosote-exposed workers have documented dermal absorption of benzo[a]pyrene and related PAHs, with subsequent detection of urinary metabolites such as 1-hydroxypyrene, thereby confirming systemic uptake following skin contact (ATSDR, 2022; Boström et al., 2002; Shen et al., 2013). Reviews in *Environmental Health Perspectives* and *Science of the Total Environment* emphasize that dermal exposure may contribute substantially to total PAH body burden in occupational and contaminated-soil scenarios (Boström et al., 2002; Kim et al., 2013).

In contrast, many inorganic metals generally demonstrate lower dermal bioavailability due to limited permeability through intact skin barriers; however, absorption can vary depending on oxidation state, solubility, particle size, and matrix interactions (ATSDR, 2022; Kissel et al., 2008). For instance, hexavalent chromium exhibits greater dermal penetration than trivalent chromium due to its higher solubility and reactivity, while acidic or damaged skin conditions may enhance uptake of certain metal species (ATSDR, 2022). Matrix effects—such as binding to organic matter or particulate carriers—can further influence dermal transport dynamics, underscoring the need for chemical- and context-specific parameterization within risk assessment models (USEPA, 2004; NRC, 2009).

Where bulk dust concentrations are reported (mg·kg^{-1}), conversion to surface loading is required:

If $C_{i,surf}$ is mg·kg^{-1} (dust), use the dust ingestion/transfer pathway or convert via dust loading (DL) (mg·cm^{-2}):

$$C_{i,surf}^{(mg/cm^2)} = C_{i,dust} \times DL \quad (2.4)$$

Dust loading (DL) integrates exposure geometry with mass transfer principles by converting bulk contaminant concentrations (e.g., mg·kg^{-1} in soil or dust) into surface mass per unit area (mg·cm^{-2}) available for dermal contact. This conversion aligns the exposure metric with the physical interface at which contaminant transfer to skin occurs, thereby ensuring mechanistic consistency between environmental measurement and transdermal diffusion modeling (USEPA, 2004; Kissel et al., 2008). By incorporating DL, the model accounts for the thickness and adherence of particulate matter on the skin surface, which directly influences the effective concentration gradient driving dermal absorption under Fickian transport assumptions. Regulatory dermal exposure guidance explicitly recommends the use of dust loading factors to translate environmental contamination levels into biologically relevant contact doses, particularly in soil and occupational exposure scenarios (USEPA, 2004; WHO, 2017).

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

➢ *Ingestion (Accidental Parenteral Exposure)*

Ingestion is uncommon in environmental assessments but can represent accidental contamination (e.g., puncture wounds). Model as a single event systemic dose:

$$Dose_{inj,i} = \frac{C_{i,liq} \times V_{inj} \times F_{sys,i}}{BW} \quad (2.5)$$

where,

$$C_{i,liq} = concentration\ in\ liquid\ (mg \cdot L^{-1}) or\ mg \cdot mL^{-1}$$

$$V_{inj} = injected\ volume\ (mL)$$

$$F_{sys,i} = fraction\ immediately\ bioavailable\ systemically\ (0–1).$$

$$Units\ yield\ mg \cdot kg^{-1}\ (one - time)$$

$$If\ working\ in\ daily\ doses, divide\ by\ appropriate\ averaging\ period\ .$$

$$(AT)\ to\ convert\ to\ mg \cdot kg^{-1} \cdot day^{-1}\ for\ comparison$$

Although uncommon in routine environmental exposure assessments, parenteral modeling represents a direct systemic dose that bypasses physiological absorption barriers such as the respiratory epithelium, gastrointestinal tract, or stratum corneum. In this case, the administered mass is assumed to enter systemic circulation with minimal first-pass loss, subject only to distribution, metabolism, and elimination processes governed by toxicokinetics principles (NRC, 2009; WHO, 2017). The formulation, therefore, aligns with fundamental mass conservation logic, wherein the injected quantity, adjusted for systemic bioavailability (F_{sys}), is normalized to body weight to yield an internal dose metric comparable to CDI-based expressions.

From a toxicological perspective, parenteral exposure modeling is consistent with acute systemic exposure paradigms used in pharmacokinetics and clinical toxicology, where dose is defined as the directly administered mass per unit body weight (mg·kg⁻¹) without intermediate absorption factors (NRC, 2009). Although its application in environmental risk assessment is limited to accidental scenarios (e.g., needlestick injuries, contaminated puncture wounds), the mathematical structure remains compatible with broader risk frameworks by allowing conversion to time-averaged dose (mg·kg⁻¹·day⁻¹) when comparison with chronic reference values is required (USEPA, 2014).

➢ *Convert Doses to Risk Metrics*

- *Carcinogenic Risk (Per Pathway and Chemical)*

Under the Linear No-Threshold (LNT) model, using equation 2.6, incremental lifetime cancer risk (ILCR or $ELCR_{i,p}$) is assumed to be directly proportional to lifetime average dose at low exposure levels, with no biologically safe threshold below which risk is zero (NRC, 2009; Rhomberg & Goodman, 2012). This assumption is grounded in a mechanistic understanding of genotoxic carcinogenesis, where even a single DNA-damaging event has the theoretical potential to initiate tumorigenesis, particularly for mutagenic compounds such as certain PAHs and metal species (IARC, 2012).

Regulatory adoption of the LNT paradigm reflects both experimental and epidemiological evidence demonstrating approximately linear dose–response relationships at environmentally relevant exposure ranges, especially when extrapolated from higher-dose animal bioassays using conservative statistical models (NRC, 2009; USEPA, 2014). Slope factors ($SF_{i,p}$) derived under this framework represent upper-bound estimates of carcinogenic potency, typically corresponding to the 95% confidence limit of the modeled dose–response curve, thereby embedding health-protective conservatism into risk estimation (Rhomberg & Goodman, 2012).

Consequently, within this model structure, $ELCR_{i,p}$ is mathematically expressed as the product of lifetime average daily dose ($LADD_{i,p}$) and the chemical-specific cancer slope factor, operationalizing the proportional relationship between chronic exposure and incremental cancer probability under low-dose linear extrapolation assumptions (USEPA, 1989; WHO, 2017).

✓ *Using Slope Factors:*

SF_i or IUR_i consistent with chemical:

$$ELCR_{i,p} = LADD_{i,p} \times SF_i \quad (2.6)$$

Slope factors represent upper-bound estimates of carcinogenic potency derived from chronic animal bioassays, human epidemiological studies, or a combination of both, using dose–response modeling procedures designed to estimate risk at environmentally relevant exposure levels (IARC, 2012; Tchounwou et al., 2012). In regulatory practice, these values typically correspond to the 95% upper confidence limit of the modeled dose–response curve, thereby incorporating a margin of health-protective

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

conservatism into cancer risk estimation (USEPA, 2014; NRC, 2009). The derivation process involves fitting multistage or other biologically informed models to tumor incidence data observed at higher experimental doses and then extrapolating downward to low-dose regions consistent with environmental exposure scenarios.

High-level methodological reviews published in *Critical Reviews in Toxicology* have examined the statistical and biological foundations of slope factor development, including benchmark dose modeling, model selection uncertainty, interspecies extrapolation, and low-dose linearization assumptions (Rhomberg & Goodman, 2012). These analyses emphasize that slope factors are not empirical constants but modeled parameters influenced by experimental design, background tumor rates, mechanistic evidence of genotoxicity, and assumptions regarding dose scaling. In particular, when mechanistic data support a mutagenic mode of action, low-dose linear extrapolation under the LNT paradigm is considered scientifically justified and precautionary (NRC, 2009).

Thus, cancer slope factors operationalize decades of experimental carcinogenicity research, epidemiological regression analysis, and statistical modeling into a single potency parameter that enables quantitative estimation of incremental lifetime cancer risk from chronic environmental exposure (USEPA, 2014; IARC, 2012).

Alternatively, inhalation unit risk (IUR) provides direct concentration-to-risk translation:

✓ *Using IUR for Inhalation Only:*

$$ELCR_{i,inh} = C_{i,air}(\mu g.m^{-3}) \times IUR_i \quad (2.7)$$

For PAHs, use; BaP-TEQ andSF_{BaP} or IUR_{BaP}:

$$ELCR_{PAH,inh} = LADD_{inh,PAH} \times SF_{BaP} \quad (2.8)$$

$$ELCR_{PAH,inh} = BaP - TEQ_{air}\ (\mu g.m^{-3}) \times IUR_{BaP} \quad (2.9)$$

TEQ-based carcinogenic modeling has been repeatedly validated for combustion-derived PAH mixtures in both environmental monitoring and epidemiological contexts (Boström et al., 2002; Nisbet & LaGoy, 1992; Kim et al., 2013). The toxic equivalency (TEQ) approach enables individual PAHs each with differing carcinogenic potencies—to be normalized relative to benzo[a]pyrene (BaP), thereby permitting additive cancer risk estimation under the linear no-threshold (LNT) framework. This method is particularly appropriate for combustion-related emissions, where complex mixtures of high- and low-molecular-weight PAHs coexist in air particulates, soot, and industrial effluents.

Reviews published in *Environmental Health Perspectives* and *Science of the Total Environment* have demonstrated that BaP-TEQ concentrations correlate more consistently with observed mutagenicity and carcinogenic outcomes than unadjusted total PAH mass, reinforcing the biological plausibility of potency-weighted mixture modeling (Boström et al., 2002; Kim et al., 2013). The TEF methodology, originally proposed by Nisbet and LaGoy (1992), has since been widely adopted in atmospheric risk assessments, soil contamination studies, and occupational exposure evaluations. While uncertainties remain regarding interaction effects among PAHs, additive TEQ modeling remains the most scientifically defensible and policy-aligned approach for estimating cumulative carcinogenic risk from combustion-derived PAH mixtures (IARC, 2012; WHO, 2017).

B. Non-cancer hazard (HQ)

Compute Average Daily Dose, $ADD_{i,p}$ (mg·kg^{-1}·day^{-1}) for pathway p, then:

$$HQ_{i,p} = \frac{ADD_{i,p}}{RfD_i} \quad (2.10)$$

The Hazard Quotient ($HQ_{i,p}$) (see equation 2.10) reflects the principles of threshold toxicology, wherein adverse non-carcinogenic effects are presumed to occur only above a biologically meaningful exposure level. The reference dose (RfD_i) represents an estimate of a daily exposure that is likely to be without appreciable risk of deleterious effects over a lifetime and is typically derived from experimentally identified No-Observed-Adverse-Effect Levels (NOAELs) or Lowest-Observed-Adverse-Effect Levels (LOAELs), adjusted using uncertainty (safety) factors to account for interspecies extrapolation, human variability, database limitations, and subchronic-to-chronic conversion (USEPA, 1989; USEPA, 2014). This framework assumes that non-cancer toxicological endpoints exhibit dose thresholds due to physiological repair mechanisms, homeostatic regulation, and adaptive biological responses (NRC, 2009).

Unlike carcinogenic risk modeling under the linear no-threshold paradigm, non-cancer hazard characterization does not estimate the probability of effect but instead evaluates whether estimated exposure exceeds a protective benchmark (RfD_i). An $HQ_{i,p}$ greater than unity signals potential for concern but does not imply certainty of adverse outcome; rather, it indicates that exposure surpasses a level considered protective for sensitive populations under regulatory assumptions (USEPA, 2014; WHO, 2017).

Metals provide empirically grounded examples of RfD_i - based assessment. Cadmium RfD_is are derived from renal tubular dysfunction endpoints observed in occupational and environmental cohorts, reflecting its well-documented nephrotoxicity (ATSDR, 2022; Tchounwou et al., 2012). Lead exposure is associated with neurodevelopmental deficits, particularly in children, and although modern risk frameworks increasingly employ blood lead modeling rather than traditional RfD_is, the threshold-based paradigm remains conceptually relevant for non-cancer endpoints (ATSDR, 2022). Chromium compounds, depending on oxidation state, demonstrate hepatic and respiratory toxicity in animal and occupational studies, forming the basis for inhalation reference concentrations (RfC_is) and oral RfD_is (IARC, 2012; ATSDR, 2022). These case studies illustrate how experimentally observed organ-specific toxicity is translated

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

into protective exposure benchmarks within the $HQ_{i,p}$ framework, thereby operationalizing threshold toxicology in environmental health risk assessment (NRC, 2009; USEPA, 2014).

III. AGGREGATE RISKS ACROSS CHEMICALS & PATHWAYS

A. Total Carcinogenic Risk ($ELCR_{total}$):

$$ELCR_{total} = \sum_{i \in C} \sum_{p \in \{inh, Derm, Inj\}} ELCR_{i,p} \quad (3.1)$$

C is the set of carcinogenic chemicals (PAHs via BaP-TEQ treated as a single carcinogen term, plus carcinogenic metals like Pb or Cd).

Additivity across carcinogens is based on the assumption that individual agents acting through independent genotoxic mechanisms contribute proportionally and cumulatively to total cancer risk at low exposure levels. Under the linear no-threshold (LNT) framework, each carcinogen is modeled as contributing a small incremental probability of tumor initiation, and these increments are summed to yield total excess lifetime cancer risk (NRC, 2009; USEPA, 2014). This additive formulation reflects the mathematical property of linear dose–response relationships at environmentally relevant exposure levels, where risk is directly proportional to dose and independent across agents when interaction data are absent.

Regulatory cumulative risk guidance endorses this additive approach in the absence of compelling evidence for synergistic or antagonistic interactions (USEPA, 2003; NRC, 2009). The assumption is considered health-protective and scientifically reasonable when chemicals share similar modes of genotoxic action or when mechanistic interaction data are insufficient for more complex modeling. High-level methodological reviews emphasize that additive risk summation under low-dose linearity is a pragmatic extension of single-chemical slope factor methodology, ensuring consistency in regulatory cancer risk estimation across multi-contaminant exposure scenarios (Rhomberg & Goodman, 2012).

While mixture toxicology acknowledges the potential for interaction effects, empirical data for most environmental contaminant combinations remain limited. Consequently, independent additive modeling remains the default and policy-aligned approach for cumulative carcinogenic risk characterization, particularly for complex mixtures such as PAHs and metal co-exposures encountered in ambient air and occupational environments (USEPA, 2014; WHO, 2017).

B. Total Non-Cancer Hazard Index (HI):

$$HI = \sum_{i \in N} \sum_{p} HQ_{i,p} \quad (3.2)$$

N = set of non-cancer relevant chemicals (or all metals for HQ aggregation).

The Hazard Index (HI) approach assumes dose additivity among chemicals that affect the same target organ or share similar toxicodynamics mechanism. Under this framework, individual Hazard Quotients (HQs) are summed across substances and exposure pathways to estimate the cumulative potential for non-carcinogenic effects. This additive principle is grounded in classical mixture toxicology, where compounds producing comparable adverse outcomes such as nephrotoxicity, neurotoxicity, or hepatotoxicity are presumed to contribute collectively to overall organ burden when mechanistic evidence indicates overlapping modes of action (NRC, 2009; WHO, 2017).

International risk assessment frameworks, including those of the World Health Organization (WHO) and the National Research Council (NRC), explicitly support cumulative non-cancer hazard evaluation when chemicals influence the same biological system or endpoint (NRC, 2009; WHO, 2017). The scientific rationale derives from dose-addition theory, which posits that for agents acting on a common pathway, the combined effect can be approximated by summing normalized doses relative to their respective reference values. In practical regulatory application, this is operationalized by aggregating $HQ_{i,p}$ values (using equation 2.10) for chemicals associated with a shared target organ (e.g., renal toxicity for cadmium and lead), provided that interaction data do not demonstrate clear synergism or antagonism.

Although the HI does not quantify probability of effect, it provides a structured screening-level metric for identifying scenarios where cumulative exposures may exceed protective thresholds. When HI > 1 for chemicals affecting a common endpoint, further refined assessment potentially incorporating physiologically based toxicokinetics (PBTK) modeling or mechanistic evaluation is recommended. Thus, the HI framework represents a scientifically grounded and internationally endorsed method for cumulative non-carcinogenic risk characterization under conditions of toxicodynamic overlap (NRC, 2009; USEPA, 2014; WHO, 2017).

The per-pathway dose equations and aggregation framework presented herein represent the codified mathematical infrastructure of contemporary environmental health risk science. These formulations are not merely computational tools but structured representations of established toxicological theory translated into operational quantitative models. At their core, the equations integrate five foundational scientific principles:

- Toxicokinetic mass balance, whereby absorbed contaminant mass is normalized to body weight and biologically relevant averaging time to produce comparable internal dose metrics (e.g., CDI, LADD) (NRC, 2009; USEPA, 2014).
- Fickian dermal diffusion, which governs transdermal transport as a function of concentration gradient, exposed surface area, and permeability characteristics, thereby mechanistically linking environmental contamination to systemic uptake (USEPA, 2004; WHO, 2017).

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

- Linear carcinogenic extrapolation, consistent with the linear no-threshold (LNT) paradigm for genotoxic carcinogens, in which incremental lifetime cancer risk is modeled as proportional to lifetime average dose at environmentally relevant exposure levels (Rhomberg & Goodman, 2012; NRC, 2009).
- Threshold-based non-cancer toxicology, wherein adverse effects are assumed to occur only above protective exposure benchmarks (RfD/RfC) derived from NOAEL/LOAEL data and uncertainty factor adjustments (USEPA, 2014; WHO, 2017).
- Additive mixture assumptions, which permit summation of carcinogenic risks across independent agents and aggregation of hazard quotients for chemicals affecting similar target organs, consistent with international cumulative risk guidance (NRC, 2009; USEPA, 2003).

Collectively, these elements reflect decades of refinement in regulatory toxicology and exposure science. Modernization efforts in risk assessment increasingly emphasize cumulative exposure integration, mechanistic transparency, reproducibility of model structure, and explicit documentation of assumptions—principles strongly advocated in high-level methodological reviews and National Research Council frameworks (NRC, 2009; Rhomberg & Goodman, 2012). The structured nature of the presented equations enhances comparability across studies, facilitates sensitivity and uncertainty analysis, and supports alignment with internationally harmonized risk assessment protocols.

Importantly, this deterministic mathematical integration forms the conceptual and computational foundation upon which probabilistic extensions may be constructed. Monte Carlo simulation frameworks can be layered onto the per-pathway equations to propagate parameter variability and uncertainty, generating exposure distributions rather than point estimates. Similarly, composite indices—such as an Organism Environmental Risk Index (OERI) or related cumulative metrics—can be derived through weighted aggregation of pathway-specific risks. Such extensions advance the framework toward next-generation cumulative environmental health modeling that is quantitatively rigorous, transparent in assumption structure, and adaptable to complex multi-contaminant exposure scenarios (NRC, 2009; WHO, 2017).

C. Theoretical Framework for Integrated Organism Exposure and Risk Assessment

Environmental health risk characterization traditionally reports incremental lifetime cancer risk (ILCR/ELCR) and hazard quotient/index (HQ/HI) separately, reflecting carcinogenic and non-carcinogenic endpoints, respectively (United States Environmental Protection Agency [USEPA], 1989; 2011). While scientifically rigorous, parallel reporting complicates interpretation, communication, and decision prioritization particularly in multi-contaminant, multi-pathway exposure contexts frequently encountered in atmospheric particulate toxicology and thermochemical emission studies (e.g., $PM_{2.5}$-bound PTEs and PAHs).

To address this limitation, introduces a Novel Single-Index Organism Exposure & Risk Index (OERI) a dimensionless, benchmark-referenced metric that integrates carcinogenic and non-carcinogenic risks within a unified, tunable mathematical structure. The framework aligns with cumulative risk assessment principles advanced in contemporary environmental epidemiology and regulatory science (Sexton & Hattis, 2007; NRC, 2009; *Environmental Health Perspectives*; *Science of the Total Environment*).

D. Novel Single Index Organism Exposure & Risk Index (OERI)

ILCR is expressed as a probability, and HQ as a ratio to RfD; direct aggregation is not inherently intuitive. The OERI resolves this by normalizing all risk metrics relative to regulatory benchmarks, making the final value dimensionless.

➢ *Design Goals:*

- Dimensionless, interpretable (OERI = 1 equals 'acceptable benchmark'),
- Combines carcinogenic and non-carcinogenic endpoints,
- Allows adjustable weighting.

➢ *Step A: Normalize component risks*

Choosing normalization benchmarks:

- $ELCR_{ref}$ = $acceptable\ lifetime\ cancer\ risk\ threshold$ ($at\ default$ 1.0×10^{-6} or 1.0×10^{-5})
- Using $ELCR_{ref} = 1.0 \times 10^{-5}$
- $HI_{ref} = 1$ ($standard\ non-cancer\ hazard\ threshold$)

➢ *Now Computing Normalized Components;*

$$R_C = \frac{ELCR_{total}}{ELCR_{ref}} \quad (3.4)$$

$$R_{NC} = \frac{HI}{HI_{ref}} = HI \quad (3.5)$$

Cancer and non-cancer risks are computed under fundamentally different toxicological paradigms:

- Cancer risk (ELCR) is modeled using the linear no-threshold (LNT) assumption, where incremental lifetime cancer risk increases linearly with dose at low exposures (USEPA, 1989; NRC, 2009).
- Non-cancer risk (HQ/HI) is threshold-based, derived from reference doses (RfD) or reference concentrations (RfC) assumed to represent safe exposure levels below which appreciable adverse effects are unlikely (USEPA, 1989; WHO, 2010).

Because ELCR is typically benchmarked against regulatory risk targets (10^{-6}–10^{-4}), while HI is benchmarked against unity (HI = 1), direct summation would be dimensionally inconsistent. Normalization resolves this by

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

expressing both components relative to their regulatory acceptability criteria (Hattis et al., 2001).

Thus:

- $R_C = 1$ Corresponds to ELCR equal to the regulatory benchmark (e.g., 10^{-6}).
- $R_{NC} = 1$ corresponds to HI = 1 (threshold exceedance boundary).

This normalization transforms heterogeneous toxicological endpoints into a dimensionless, comparably scaled decision space, consistent with multi-criteria risk integration frameworks (Linkov et al., 2006; USEPA, 2014).

➢ *Step B Combine into OERI*

$$OERI = W_C \cdot F_C(R_C) + W_{NC} \cdot F_{NC}(R_{NC}) \quad (3.6)$$

The formulation of the OERI equation is grounded in established principles of mixture toxicology, decision theory, and regulatory risk governance. First, it reflects mixture additivity principles, whereby cancer risks from multiple chemicals and exposure pathways are conventionally summed under the assumption of independent action, consistent with the carcinogen risk assessment guidelines of the United States Environmental Protection Agency (2005). Similarly, non-carcinogenic effects are aggregated using the Hazard Index (HI), which is based on dose additivity assumptions for chemicals affecting the same target organ or system, as recognized in cumulative risk assessment frameworks of the World Health Organization (2009).

Beyond toxicological additivity, the equation aligns with multi-attribute utility theory (MAUT), a decision-analytic framework in which heterogeneous outcomes are first normalized and then combined through weighted functions to enable rational comparison and integration of distinct criteria (Keeney & Raiffa, 1993; Linkov et al., 2006). In this context, carcinogenic and non-carcinogenic risks represent separate but relevant health attributes that must be reconciled within a unified evaluative structure.

Furthermore, the model is consistent with broader risk governance principles, as regulatory bodies such as the National Research Council (2009) emphasize the need to balance irreversible carcinogenic outcomes with threshold-based systemic toxicities when establishing environmental health standards. By integrating these components through normalization and weighting, the OERI operates as a composite health risk utility metric that preserves regulatory interpretability while allowing adaptive emphasis on specific health endpoints according to policy priorities or precautionary considerations.

➢ *(C) Weighting Factors (W_C, W_{NC})*

- *Equal weighting:*

W_C, W_{NC} are weights

$$(W_C = W_{NC} = 0.5 \; for \; equal \; emphasis, sum = 1)$$

Assigning equal weights($W_C = W_{NC} = 0.5$) reflects a position of neutral regulatory parity, meaning that carcinogenic and non-carcinogenic health outcomes are treated as equally important within the integrated assessment framework. This approach avoids implicit value judgments and aligns with balanced risk governance, where both probabilistic cancer risks and threshold-based systemic toxicities are considered comparably significant in environmental decision-making.

However, weight tuning (for example,$W_C = 0.7$) is scientifically and policy-justifiable under specific conditions. Greater emphasis on the carcinogenic component may be warranted when exposure involves established genotoxic carcinogens, particularly those classified as Group 1 by the International Agency for Research on Cancer, where the linear no-threshold assumption implies that even minimal exposures contribute incrementally to lifetime cancer risk. In such cases, the irreversible and stochastic nature of carcinogenesis may justify precautionary prioritization.

Similarly, regulatory or institutional policy may explicitly prioritize irreversible endpoints (e.g., cancer, mutagenicity, developmental toxicity) over effects that are potentially reversible upon exposure cessation. Cancer outcomes typically involve long latency periods, cumulative genetic damage, and high societal burden, distinguishing them qualitatively from many non-cancer toxicities that may exhibit recovery below certain exposure levels. From a risk ethics perspective, irreversible and life-shortening effects often receive greater normative weight.

Weight adjustment may also reflect stakeholder-driven precautionary emphasis, particularly in vulnerable populations (children, occupationally exposed workers, immunocompromised groups) or in contexts of elevated public concern. In such scenarios, modifying the weighting coefficients provides a transparent and defensible mechanism for incorporating societal risk preferences into quantitative assessment.

The use of weighted aggregation is well established in integrated environmental health metrics and multi-criteria risk assessment frameworks, where normalization is followed by policy-sensitive weighting to reflect relative importance among endpoints (Linkov et al., 2014). Within this structure, OERI remains methodologically rigorous while retaining the flexibility necessary for context-specific risk governance and adaptive decision-making.

➢ *(D) Scaling Functions ($F_C(R)$): Controlling Nonlinearity and Extreme Values*

Scaling functions prevent dominance of extreme ratios and reflect biological response behavior.

- *For a Linear function;*

$$F_C(R) = R_i F_{NC}(R) = R_{(simple)} \quad (3.7)$$

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

f_C, f_{NC} are scaling functions to control nonlinearity and extreme values.

The adoption of a linear scaling function $F_C(R)$ assumes a proportional response interpretation, meaning that any incremental increase in the normalized risk ratio results in a directly proportional increase in the composite index. In other words, doubling the exceedance of a benchmark (e.g., from R=1 to R=2) leads to a doubling of its contribution to the integrated metric. This preserves intuitive interpretability and ensures that the composite index reflects magnitude differences transparently.

Such linearity is also consistent with regulatory assumptions embedded in carcinogenic risk assessment, particularly under the Linear No-Threshold (LNT) model, where risk is assumed to increase linearly with dose at environmentally relevant exposure levels. Under this paradigm, proportional aggregation does not distort the underlying toxicological inference and remains aligned with the cancer slope factor methodology described by the United States Environmental Protection Agency (2005).

A linear function is most appropriate when normalized cancer and non-cancer risk ratios fall within comparable magnitude ranges and when extreme outliers are absent. In such cases, proportional scaling maintains fidelity to regulatory benchmarks without introducing artificial dampening or amplification effects. However, when risk ratios span several orders of magnitude or exhibit heavy right-skewed distributions, nonlinear transformations (e.g., logarithmic or sigmoid scaling) may be preferable to prevent dominance by extreme values and to improve stability of the composite index.

- *For Log-Damped (Reduces Influence of Outliers);*

$$f(R) = \frac{\ln(1+R)}{\ln(1+R_{max})} \; with\ chosen\ R_{max}\ (assuming, 1000) \quad (3.8)$$

Environmental exposure concentrations and derived risk metrics frequently exhibit log-normal distributions, characterized by right-skewness and occasional extreme values, particularly in occupational and microenvironmental settings (Ott, 1990). In such distributions, arithmetic scaling can cause a small number of high observations to dominate composite indices disproportionately. Applying a logarithmic transformation stabilizes variance, compresses extreme upper-tail values, and produces a more symmetric analytical space, thereby improving statistical robustness and interpretability.

Within the OERI framework, log-damped scaling reflects this statistical reality by moderating the influence of extreme exceedances while preserving rank order. Conceptually, this transformation also aligns with diminishing marginal response behavior: as normalized risk ratios become very large, each additional unit increase contributes progressively less to the composite metric. This does not imply reduced toxicological severity, but rather prevents numerical distortion of the integrated index by outliers.

The approach parallels observations in toxicodynamics where certain biological responses exhibit logarithmic or saturable patterns at higher doses (Calabrese, 2008). Similarly, behavioral and risk perception research suggests that incremental increases in already high risks often produce smaller marginal changes in perceived concern compared to equivalent increases near regulatory thresholds. Thus, logarithmic scaling mirrors both biological response moderation and cognitive response saturation.

Introducing a bounding parameter R_{max} (e.g., 1000) further ensures mathematical stability and comparability across scenarios. By normalizing the log-transformed ratio against $\ln(1 + R_{max})$, the function constrains outputs to a finite and interpretable range (e.g., 0–1), preventing unbounded growth of the composite metric under extreme conditions. This bounded transformation enhances numerical stability, facilitates comparison across studies or exposure scenarios, and maintains regulatory coherence within integrated risk evaluation.

- *For Sigmoid to be Bounded between 0 and 1;*

$$f(R) = \frac{1}{1+ e^{-\propto(R-1)}} \quad (3.9)$$

Biological systems frequently display threshold-like, adaptive, or saturable responses, particularly in non-cancer toxicodynamics where homeostatic control mechanisms buffer low-level exposures and adverse effects intensify only after compensatory capacity is exceeded (World Health Organization, 2009; National Research Council, 2009). Such nonlinear behavior is widely recognized in environmental health sciences, where many physiological systems hepatic detoxification pathways, endocrine signaling networks, and immune responses exhibit adaptive ranges followed by accelerated response once biological thresholds are surpassed. Even in broader population health modeling, exposure–response relationships commonly follow sigmoidal rather than purely linear forms, reflecting gradual onset at low exposure, rapid transition near critical effect levels, and plateauing at high doses due to system saturation or maximal effect constraints (Ritz et al., 2015).

Logistic (sigmoid) functions are therefore extensively applied in toxicological dose–response modeling and epidemiological exposure effect analyses because their mathematical structure captures three biologically plausible phases: minimal response at very low exposure, accelerated change near an inflection point, and asymptotic stabilization at high exposure levels (Ritz et al., 2015; United States Environmental Protection Agency, 2005). Embedding a sigmoid transformation within the OERI framework introduces this biologically grounded nonlinearity into the composite index, improving realism compared with purely linear aggregation.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

A principal advantage of the logistic formulation is that it is bounded between 0 and 1, ensuring that transformed risk contributions remain numerically stable and directly interpretable within a finite decision space. Unlike linear scaling, which increases indefinitely with larger exceedances, the sigmoid function asymptotically approaches an upper bound, preventing extreme values from disproportionately dominating the integrated metric. This boundedness is consistent with best practices in cumulative risk characterization, where preventing mathematical dominance by outliers enhances comparability across scenarios (United States Environmental Protection Agency, 2014).

Centering the sigmoid at R=1 is conceptually significant because this value corresponds to the regulatory benchmark exceedance boundary. At this pivot point, the function passes through its inflection region, meaning that marginal increases above the benchmark generate proportionally greater changes in the composite score. This mirrors regulatory practice, where exceeding established safety thresholds often triggers intensified monitoring, mitigation, or policy intervention (National Research Council, 2009).

The parameter α\alphaα governs the steepness of the transition. A high α\alphaα produces a sharp inflection, approximating a quasi-threshold regulatory trigger in which the integrated index escalates rapidly once the benchmark is surpassed. Conversely, a lower α\alphaα generates a more gradual escalation, suitable in governance contexts emphasizing proportionality and graded response rather than abrupt action. This tunable steepness enables alignment with varying precautionary philosophies, from conservative threshold-based environmental health protection to smoother gradient-based risk management approaches (Linkov et al., 2006).

Accordingly, the sigmoid scaling approach integrates biological realism, regulatory interpretability, and precautionary flexibility within the OERI framework, making it particularly appropriate in contexts where exceedance of health benchmarks warrants nonlinear prioritization of risk mitigation efforts.

- *Deterministic Function (Simple Linear);*

$$OERI = 0.5 \times \frac{ELCR_{total}}{ELCR_{ref}} + 0.5 \times HI \quad (3.10)$$

- ✓ OERI ≤ 1 → combined risk at or below benchmark (acceptable under default assumptions).
- ✓ OERI > 1 → combined risk exceeds benchmark; this investigate mitigation.

Tuning W_C to emphasize cancer ($W_C = 0.7$) or HI to emphasize non-cancer.

This deterministic linear formulation of the OERI preserves regulatory interpretability by maintaining a direct and transparent relationship between normalized risk components and the final composite index. Because both carcinogenic and non-carcinogenic risks are expressed relative to their respective regulatory benchmarks prior to aggregation, the resulting OERI value retains clear policy meaning rather than becoming an abstract mathematical construct.

The structure also maintains proportional contribution, meaning that each unit increase in either normalized cancer risk or hazard index contributes linearly to the overall score according to its assigned weight. This proportionality ensures that the integrated metric reflects the actual magnitude of exceedance without artificial amplification or dampening, consistent with linear additivity principles embedded in cumulative risk assessment frameworks (United States Environmental Protection Agency, 2014).

Importantly, the formulation ensures that OERI = 1 corresponds precisely to benchmark equivalence that is, the point at which the combined normalized cancer and non-cancer risks collectively align with their respective regulatory thresholds. This creates a unified decision pivot analogous to the conventional interpretation of ELCR relative to target risk levels and HI relative to unity.

Accordingly, interpretation follows a clear regulatory logic:

- ✓ OERI ≤ 1 indicates that the integrated health risk remains at or below benchmark levels under default regulatory assumptions and is therefore generally considered acceptable within established risk management frameworks (World Health Organization, 2010).
- ✓ OERI > 1 indicates integrated exceedance of benchmark conditions, signaling the need for further investigation, risk management intervention, or mitigation measures.

This benchmark-centered interpretation mirrors integrated index approaches used in environmental health risk ranking and cumulative assessment systems, where composite indicators are designed to preserve alignment with regulatory decision thresholds while enabling comparison across multiple hazards and exposure pathways (United States Environmental Protection Agency, 2014; World Health Organization, 2010).

E. Pathway Contribution Diagnostics

Calculate the fractional contribution of each pathway and chemical to the index for targeted mitigation:

- ➢ *Pathway Fraction for Carcinogenic Risk:*

$$P_p^C = \frac{\sum_i ELCR_{i,p}}{ELCR_{total}} \quad (3.11)$$

The pathway contribution metric identifies whether inhalation, dermal contact, or ingestion constitutes the dominant driver of the total carcinogenic burden by decomposing total excess lifetime cancer risk (ELCR) into pathway-specific fractions. This structured decomposition is consistent with established cumulative risk assessment methodology, where total risk is expressed as the sum of

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

route-specific exposures (United States Environmental Protection Agency, 2005). The conceptual basis aligns directly with the classical source–pathway–receptor framework articulated by the National Research Council (1983), which defines risk as a function of contaminant release (source), transport and exposure medium (pathway), and the exposed population (receptor).

Within this framework, identifying the dominant exposure pathway is essential for effective and proportionate risk management. If inhalation accounts for the largest fraction of carcinogenic risk, mitigation strategies should prioritize engineering controls such as local exhaust ventilation, emission capture, enclosure systems, and air filtration technologies, consistent with occupational and environmental exposure control hierarchies (World Health Organization, 2010; United States Environmental Protection Agency, 2014). Conversely, if dermal exposure is the principal contributor, risk reduction should emphasize personal protective equipment (PPE), surface decontamination, barrier methods, and minimization of skin contact, in accordance with established exposure pathway intervention strategies (United States Environmental Protection Agency, 2005). Where ingestion dominates, interventions should focus on hygiene practices, contamination prevention, hand-to-mouth exposure control, and environmental sanitation measures (World Health Organization, 2009).

Accordingly, pathway fraction diagnostics transform the composite OERI from a purely evaluative index into a decision-support instrument, enabling targeted mitigation consistent with cumulative risk assessment principles and regulatory risk management frameworks (National Research Council, 1983; United States Environmental Protection Agency, 2014).

- *Chemical Fraction:*

$$Q_i^C = \frac{\sum_p ELCR_{i,p}}{ELCR_{total}} \quad (3.12)$$

Similarly for HQ/HI contributions.

The chemical contribution fraction (Q_i^C) reflects toxicological dominance by quantifying the proportion of total carcinogenic risk attributable to a specific chemical across all exposure pathways. Expressing each contaminant's contribution relative to total ELCR enables identification of the principal risk drivers within a mixture, consistent with cumulative risk assessment frameworks that emphasize characterization of dominant stressors (United States Environmental Protection Agency, 2003; National Research Council, 2009).

A high Q_i^C value indicates that a particular chemical disproportionately contributes to overall risk and therefore warrants priority attention. This supports chemical-specific mitigation, such as emission reduction, source control, engineering modification, or exposure pathway interruption, consistent with hierarchical risk management principles (United States Environmental Protection Agency, 2014). It also informs regulatory substitution evaluation, particularly where safer alternatives exist or where substitution aligns with pollution prevention strategies and sustainable chemical management approaches (United States Environmental Protection Agency, 2003). Additionally, identifying dominant contributors enables focused toxicological monitoring and surveillance, ensuring analytical and biomonitoring resources are directed toward substances with the greatest health significance (World Health Organization, 2009).

Parallel diagnostics apply to non-cancer risk assessment through decomposition of the Hazard Quotient (HQ) and Hazard Index (HI). By evaluating each chemical's fractional contribution to cumulative non-carcinogenic hazard particularly for substances affecting common target organs risk assessors can identify priority toxicants under dose additivity assumptions (United States Environmental Protection Agency, 1989; World Health Organization, 2009). Collectively, these chemical-level diagnostics transform the OERI framework from a summary indicator into a structured prioritization tool aligned with established cumulative and mixture risk assessment practice. These guide whether inhalation, dermal or injection drives OERI and which chemicals are dominant.

IV. PROBABILISTIC RISK ASSESSMENT FRAMEWORK (MONTE-CARLO SIMULATION)

Deterministic risk assessment produces single-point estimates that do not capture environmental variability and parameter uncertainty. To address this limitation, input variables such as contaminant concentration ($C_{i,air}$, IR, EF, ABS), inhalation rate (IR), exposure frequency (EF), dermal absorption fraction (ABS), and other pathway parameters are treated as probabilistic distributions.

Treating inputs ($C_{i,air}$, IR, EF, ABS) as probabilistic distributions (lognormal, normal, triangular). For several (N) iterations:

Sample all inputs → compute; ($ELCR_{total}^K, HI^K, OERI^K$; for K= 1)

- Median, 5th/95th percentiles, probability, P (OERI>1).
- Sensitivity: correlations or rank-order sensitivity (Spearman) between input variables and OERI.

A. Probability Distributions to Inputs

Each exposure variable is modeled using an appropriate statistical distribution based on empirical data or regulatory guidance:

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

Table 1 Statistical Distribution Based on Empirical Data or Regulatory Guidance

Variable	Typical Distribution	Rationale
Concentration (C)	Lognormal	Environmental contaminant data are right-skewed
Inhalation rate (IR)	Normal or lognormal	Physiological variability
Exposure frequency (EF)	Triangular or uniform	Scenario-based bounds
Dermal absorption (ABS)	Triangular or beta	Bounded between 0–1
Body weight (BW)	Normal	Population variability

Presented in Table 1, these distributional assignments ensure that uncertainty and variability are represented in a statistically defensible manner, improving the robustness and realism of probabilistic OERI estimation.

The selection of probability distributions for exposure variables is scientifically justified using either site-specific empirical data or authoritative exposure factor databases (see Table 1). Arbitrary assignment of distributions can introduce systematic bias and distort probabilistic risk outputs. Regulatory guidance consistently emphasizes that distributional assumptions should reflect measured variability, mechanistic plausibility, and documented population behavior patterns (USEPA, 2014; NRC, 2009; WHO, 2017).

Environmental contaminant concentrations (for example $C_{i,air}$, soil PAHs, metal concentrations) are commonly modeled using lognormal distributions because empirical monitoring data frequently exhibit right-skewed behavior arising from heterogeneous emission sources, meteorological influences, and episodic contamination events (Limpert et al., 2001; Ott, 1995). The lognormal assumption is particularly appropriate where multiplicative environmental processes govern contaminant dispersion and deposition. However, goodness-of-fit testing (for example using, Kolmogorov–Smirnov, Anderson–Darling) should be performed when sufficient site data are available to confirm distributional suitability (USEPA, 2014).

From Table 1, physiological parameters such as inhalation rate (IR), body weight (BW), and skin surface area are typically derived from nationally representative exposure factor handbooks, which provide empirically derived percentile distributions for different demographic groups (USEPA, 2011; USEPA, 2019). These variables are often modeled using normal or lognormal distributions depending on skewness and truncation requirements. For example, inhalation rates may follow lognormal distributions due to activity-level variability, whereas body weight in adult populations is frequently approximated by a truncated normal distribution to avoid biologically implausible negative values (USEPA, 2011).

Scenario-based exposure variables such as exposure frequency (EF) or dermal adherence factor (AF) are often characterized using triangular or uniform distributions when only minimum, most-likely, and maximum values are available. This approach is recommended where empirical variance data are limited but bounding estimates are defensible (USEPA, 2014). The triangular distribution is particularly appropriate in screening-level assessments where expert judgment supplements sparse site measurements.

For dermal absorption fraction (ABS), bounded distributions such as beta or triangular are preferred because the parameter is constrained between 0 and 1. In cases involving metals or PAHs, chemical-specific absorption fractions should be sourced from toxicological databases or peer-reviewed literature, and variability should reflect documented inter-individual differences (ATSDR, 2022; WHO, 2017).

Importantly, distribution selection must distinguish between variability (true heterogeneity across individuals or environments) and uncertainty (lack of knowledge regarding parameter values). Failure to separate these components can inflate risk variance or obscure dominant drivers of exposure (NRC, 2009). When sufficient site data are unavailable, hierarchical approaches incorporating literature-derived priors, Bayesian updating, or conservative bounding distributions may be employed to maintain transparency in model assumptions.

In all cases, the chosen distribution, parameterization method (e.g., mean and standard deviation, geometric mean and geometric standard deviation), truncation limits, and data source must be explicitly reported to ensure reproducibility and regulatory defensibility (USEPA, 2014; WHO, 2017). Sensitivity analysis should accompany probabilistic modeling to evaluate the influence of distributional assumptions on final risk metrics such as ELCR, HI, and OERI.

B. Monte Carlo Simulation Procedure

For N iterations (50,000):

➢ *For Each Iteration K;*

Randomly sample all inputs from their respective distributions.

- Compute pathway-specific doses (PSD) using equation (4.1);

$$PSD = CDI_{i,p}^{K} \tag{4.1}$$

- Carcinogenic risk computation using equation (4.2);

$$ELCR_{i,p}^{K} = CDI_{i,p}^{K} \times CSF_i \tag{4.2}$$

- Non-Carcinogenic Hazard computation using equation (4.3);

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

$$HQ_{i,p}^{K} = \frac{CDI_{i,p}^{K}}{RfD_i} \quad (4.3)$$

- Aggregate using equations (4.4 and 4.5);

$$ELCR_{total}^{K} = \sum_i \sum_p ELCR_{i,p}^{K} \quad (4.4)$$

$$HI^{K} = \sum_i \sum_p HQ_{i,p}^{K} \quad (4.5)$$

- Now normalization of composite index in OERI using equation (4.6);

$$OERI^{K} = w_{nc}\left(\frac{HI^{K}}{1}\right) + w_{c}\left(\frac{ELCR_{total}^{K}}{10^{-5}}\right) \quad (4.6)$$

The probabilistic Monte Carlo framework produces a distribution of risk outcomes rather than a single deterministic value, thereby capturing both variability and uncertainty inherent in environmental exposure assessment. Instead of generating one-point estimate for ELCR, HI, or OERI, the simulation yields a full probability distribution that reflects the combined influence of stochastic inputs such as contaminant concentration, exposure frequency, inhalation rate, and absorption factors. This approach aligns with modern risk assessment guidance, which emphasizes characterization of risk as a range of plausible outcomes rather than a single conservative or average estimate (NRC, 2009; USEPA, 2014).

Deterministic models typically depend on point values, often upper-bound or central tendency parameters, which in probability either overestimate or underestimate true risk depending on the environmental setting. In contrast, probabilistic simulation propagates uncertainty and population variability through repeated sampling across thousands of iterations, allowing risk metrics such as ELCR, HI, and OERI to be expressed in terms of percentiles (for instance, median, 95th percentile) and exceedance probabilities (for example, $P\ (OERI\ > 1)$. This probabilistic characterization enhances transparency and improves decision support by quantifying not only the magnitude of risk but also its likelihood (WHO, 2017).

➢ *Importantly, the Resulting Risk Distribution Distinguishes Between:*

- Central tendency risk (for instance, median exposure scenario),
- Upper-bound risk (for example, 95th percentile representing reasonably maximum exposure), and
- Probability of regulatory exceedance, which provides a more policy-relevant metric than a single binary comparison.

➢ *From Data Analytical Point, Producing a Risk Distribution, the Model Enables:*

- Identification of high-end exposure scenarios,
- Evaluation of uncertainty bounds,
- Sensitivity analysis of dominant risk drivers,
- More nuanced regulatory decision-making.

This approach is consistent with recommendations from the National Research Council advocating for risk assessment frameworks that incorporate uncertainty analysis and probabilistic characterization to improve scientific robustness and policy relevance (NRC, 2009). Furthermore, regulatory agencies increasingly encourage probabilistic methods in screening and site-specific assessments when sufficient data are available to justify distributional modeling (USEPA, 2014).

Therefore, the probabilistic framework does not merely refine the numerical output it fundamentally shifts risk interpretation from a deterministic threshold comparison to a distribution-based evaluation of environmental health risk.

Table 2 Comparison of Deterministic and Probabilistic Risk Assessment Approaches

Criterion	Deterministic Risk Assessment	Probabilistic Risk Assessment (Monte Carlo)
Input parameters	Single-point estimates (mean, upper-bound, or conservative default values)	Probability distributions (lognormal, normal, triangular, beta, etc.)
Treatment of variability	Not explicitly represented; often embedded in conservative assumptions	Explicitly represented through stochastic sampling
Treatment of uncertainty	Implicit; typically addressed through safety factors	Explicitly propagated through repeated simulation
Output format	Single value (e.g., ELCR = 2.3×10^{-6}; HI = 0.8; OERI = 1.2)	Distribution of values (median, 5th–95th percentile, full probability density)
Risk interpretation	Binary comparison to the regulatory threshold	Probability of exceedance (e.g., P(OERI > 1) = 0.32)
Captures population heterogeneity?	Limited	Yes
Sensitivity analysis	Often qualitative or scenario-based	Quantitative (Spearman rank, PRCC, regression-based)
Decision-making utility	Screening-level, conservative	Risk-informed, policy-relevant
Transparency of assumptions	Moderate; relies on selected “reasonable maximum exposure.”	High; assumptions explicitly encoded in distributions
Computational demand	Low	Moderate to high (10,000–100,000 iterations)
Regulatory acceptance	Widely accepted for screening	Increasingly recommended when data permit

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

Best suited for	Initial site screening, limited datasets	Site-specific assessment, uncertainty quantification, research applications

Table 2 presents a structured comparison between deterministic and probabilistic (Monte Carlo–based) risk assessment frameworks, highlighting their conceptual, methodological, and decision-analytic differences. In deterministic risk assessment, exposure and toxicity parameters are represented using single-point estimates typically mean values, upper-bound concentrations, or conservative default assumptionsresulting in a single risk metric such as Excess Lifetime Cancer Risk (ELCR), Hazard Index (HI), or Organism Exposure Risk Index (OERI). This approach does not explicitly characterize variability or uncertainty; instead, these components are implicitly incorporated through safety factors and conservative exposure assumptions (U.S. EPA, 1989; U.S. EPA, 2001). Consequently, deterministic assessments are computationally straightforward, widely accepted for regulatory screening, and particularly suitable for preliminary site evaluations or datasets with limited statistical resolution (WHO, 2009; U.S. EPA, 2014) (Table 2).

In contrast, probabilistic risk assessment (PRA) employs probability distributions (e.g., lognormal, normal, triangular, beta) to represent input parameters, thereby explicitly capturing both population variability and parameter uncertainty through stochastic sampling techniques such as Monte Carlo simulation (Vose, 2008; Cullen & Frey, 1999). Rather than producing a single risk value, PRA generates a full distribution of possible outcomes including median, percentile ranges (e.g., 5th–95th), and probability density functions allowing probability-of-exceedance analysis such as P(OERI > 1) (U.S. EPA, 2001; WHO, 2009). This quantitative framework supports formal sensitivity analysis using statistical techniques such as Spearman rank correlation, partial rank correlation coefficients (PRCC), and regression-based methods, thereby enhancing transparency and policy relevance (Saltelli et al., 2008) (Table 2).

Furthermore, while deterministic approaches remain valuable for conservative screening-level decision-making, probabilistic frameworks provide enhanced analytical power for site-specific assessments, research applications, and regulatory contexts requiring explicit uncertainty quantification (U.S. EPA, 2014). Although computationally more demanding typically involving 10,000–100,000 simulation iterations PRA improves transparency because assumptions are explicitly encoded within defined statistical distributions rather than embedded within fixed safety margins (Vose, 2008). Therefore, as shown in Table 2, deterministic and probabilistic methods should be considered complementary: deterministic assessment serves as an initial protective screening tool, whereas Monte Carlo–based probabilistic assessment refines risk characterization when sufficient data are available to support distribution-based modeling.

Table 3 Conceptual Contrast

Criteria	**Deterministic**	**Probabilistic**
Question answered	“Is risk above threshold?”	“How likely is risk above threshold?”
Output type	Point estimate	Risk distribution
Communication style	Conservative screening	Likelihood-based risk communication

Table 3 further distills the conceptual distinction between deterministic and probabilistic risk assessment by clarifying the type of decision question each framework is designed to answer.

In the deterministic approach, the central question is: *“Is the estimated risk above the regulatory threshold?”* This framework generates a single point estimate (e.g., Excess Lifetime Cancer Risk (ELCR), Hazard Index (HI), or Organism Exposure Risk Index (OERI)), which is directly compared to a regulatory benchmark to determine compliance or non-compliance (U.S. EPA, 1989; WHO, 2009). Because variability and uncertainty are not explicitly modeled, conservative exposure assumptions and default safety factors are typically applied to ensure protective decision-making (U.S. EPA, 2001). Consequently, the communication style is screening-oriented and precautionary, focusing on whether the calculated value exceeds an established threshold (Table 3).

By contrast, the probabilistic (Monte Carlo–based) approach addresses a more informative question: *“How likely is the risk to exceed the regulatory threshold?”* Rather than producing a single estimate, probabilistic risk assessment (PRA) generates a full risk distribution through stochastic sampling of input parameter distributions (Cullen & Frey, 1999; Vose, 2008). This enables calculation of exceedance probabilities such as P(HI > 1) or P(OERI > 1), as well as percentile-based risk descriptors (e.g., median, 95th percentile), thereby explicitly characterizing population heterogeneity and uncertainty (U.S. EPA, 2001; Saltelli et al., 2008). Such outputs facilitate likelihood-based risk communication, allowing decision-makers to evaluate not only whether exceedance may occur, but also its probability and magnitude across exposed populations (Table 3).

Thus, as shown in Table 3, deterministic assessment primarily supports conservative screening-level decisions, whereas probabilistic assessment enhances transparency and supports risk-informed policy communication by explicitly quantifying variability, uncertainty, and exceedance likelihood within a structured statistical framework.

Furthermore, from Table 2 and Table 3, deterministic methods are valuable for rapid screening and regulatory compliance evaluations, particularly when site-specific data are limited or when conservative default assumptions are required to ensure public health protection (USEPA, 1989;

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

USEPA, 2011). Screening-level assessments commonly rely on upper-bound or reasonable maximum exposure (RME) parameter values to provide health-protective estimates for regulatory decision-making (USEPA, 1989; WHO, 2017). However, deterministic approaches obscure the full range of plausible risk outcomes because they collapse parameter variability into single-point estimates. Depending on the choice of input values (for example, mean versus upper percentile concentration), such models can either overestimate risk, leading to unnecessary remediation, or underestimate exposure if selected parameters do not reflect population heterogeneity (NRC, 2009; USEPA, 2014). Consequently, deterministic outputs do not quantify the probability that regulatory thresholds are exceeded but instead provide a binary comparison against benchmark values.

Probabilistic approaches (see Table 2 and Table 3), by contrast, provide a more realistic representation of exposure variability and uncertainty by treating key input parameters as probability distributions and propagating them through Monte Carlo simulation (NRC, 2009; USEPA, 2014). This framework enables estimation of percentile-based risk metrics and exceedance probabilities, thereby improving transparency in risk characterization and decision support (WHO, 2017). Such approaches are particularly important for complex contaminant mixtures, including PAHs and potentially toxic elements (PTEs), where environmental concentrations are often lognormally distributed, exposure behaviors vary across demographic groups, and toxicological potency differs by compound and pathway (Limpert et al., 2001; ATSDR, 2022). For example, PAHs require toxic equivalency adjustments relative to benzo[a]pyrene, while metals exhibit speciation-dependent toxicity, further amplifying uncertainty in cumulative risk estimation (IARC, 2012; ATSDR, 2022). By explicitly modeling variability across individuals, media, and exposure routes, probabilistic methods better capture the multidimensional nature of environmental health risk and align with contemporary recommendations for uncertainty-informed regulatory assessment (NRC, 2009; USEPA, 2014).

C. Probabilistic Formulation of OERI

The Organism Exposure Risk Index (OERI) under uncertainty is expressed as a stochastic model:

OERI ~ MC (g(X); N),
X = {$C_{i,air}$, IR, EF, ABS, SA, AF, …..}

Where;

OERI = Organism Exposure Risk Index (dimensionless screening metric)
MC = Monte Carlo simulation procedure
g (·) = Deterministic risk function mapping exposure inputs to risk outputs
X = Vector of uncertain input variables
N = Number of Monte Carlo iterations

Intrinsically, the input vector of each component of **X** is treated as a probability distribution:

$$X_j \sim f_j(\theta_j)$$

(lognormal for concentration, normal for body weight, triangular for adherence factor)

D. Deterministic Risk Function $g\ (X)$

➢ *Inhalation CDI*

The foundational structure of environmental risk assessment equations derives from classical toxicological principles that link external exposure, internal dose, and adverse biological effect (NRC, 2009). The chronic daily intake (CDI) equation:

$$CDI_{inh} = \frac{C_{air} \cdot IR \cdot EF \cdot ED \cdot ABS_{inh}}{BW \cdot AT} \quad (4.7)$$

Is not arbitrary; it operationalizes mass-balance logic. It translates environmental concentration (C) into normalized systemic dose using physiologically meaningful scaling (body weight and lifetime averaging). This framework reflects:

- Haber's Law extensions (concentration × time relationships),
- Allometric normalization to body mass,
- Chronic exposure integration over biologically relevant timeframes.

These formulations have been institutionalized in regulatory guidance because they allow reproducible translation of environmental monitoring data into health-relevant metrics (USEPA, 1989; WHO, 2017).

➢ *Dermal CDI*

$$CDI_{derm} = \frac{C \cdot SA \cdot AF \cdot EF \cdot ED \cdot ABS_{derm}}{BW \cdot AT} \quad (4.8)$$

Dermal exposure modeling is derived from transdermal diffusion principles described by Fick's Law. The equation accounts for:

- Surface area (SA) available for exposure,
- Adherence factor (AF) representing contaminant loading,
- Absorption fraction (ABS_{derm}) reflecting permeability,
- Time-integrated exposure.

The inclusion of ABS_{derm} ensures chemical-specific realism, recognizing that lipophilic PAHs penetrate skin more readily than many inorganic metals (USEPA, 2004).

Experimental validation includes:

- In vitro skin permeation assays,
- In vivo dermal absorption studies of benzo[a]pyrene,
- Occupational dermal exposure studies (creosote workers),
- Biomonitoring correlations between dermal contact and urinary PAH metabolites.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

Such studies confirm that dermal dose contributes measurably to systemic burden under chronic exposure (ATSDR, 2022).

➢ *Cancer Risk*

$$ELCR = CDI_i \times SF_i \quad (4.9)$$

The ELCR equation is grounded in dose–response modeling under the Linear No-Threshold (LNT) assumption for carcinogens. The slope factor (SF):

- Represents the upper 95% confidence limit of cancer potency,
- Is derived from chronic animal bioassays or human epidemiological data,
- Reflects statistical extrapolation from observed tumor incidence.

The equation embodies the concept that incremental risk is proportional to chronic dose at low exposure levels (NRC, 2009).

Slope factors for PAHs and metals are derived from:

- Long-term rodent carcinogenicity studies,
- Epidemiological studies of arsenic-contaminated drinking water,
- Occupational chromium exposure data,
- Mechanistic evidence linking DNA adduct formation (PAHs) to mutagenesis.

Thus, ELCR is directly traceable to experimental tumor incidence modeling and epidemiological regression analysis (IARC, 2012).

➢ *Non-Cancer Hazard*

$$HQ_i = \frac{CDI_i}{RfD_i} \quad (4.10)$$

The HQ_i equation reflects threshold toxicology. The reference dose (RfD_i):

- Is derived from NOAEL or LOAEL values in animal or human studies,
- Adjusted using uncertainty factors,
- Represents an estimate of daily exposure likely to be without appreciable risk.

$HQ_i > 1$ suggests potential for adverse effects but does not guarantee toxicity; it signals exceedance of a protective threshold (USEPA, 2014).

RfD_i is empirically grounded in:

- Cadmium (Cd) nephrotoxicity studies,
- Lead (Pb) neurodevelopmental toxicity research,
- Chromium-induced (Cr-induced) hepatic and renal damage studies.

These toxicological endpoints are experimentally quantified, then translated into protective exposure limits via uncertainty factor frameworks. The HQ_i formulation reflects the concept that non-carcinogenic toxicity has a threshold below which adverse effects are unlikely (USEPA, 2014). Experimental toxicology, particularly organ toxicity studies for cadmium (Cd) (renal), lead (Pb) (neurodevelopmental), and chromium (Cr) (hepatic) forms the empirical basis for RfD_i derivation.

The Hazard Index ($HI = \sum HQ_i$) extends this principle under the assumption of dose additivity for chemicals affecting similar target organs.

➢ *OERI Composite Function:*

The Organism Exposure Risk Index (OERI) is conceived as a unified, dimensionless screening metric that integrates both carcinogenic and non-carcinogenic risk components across multiple exposure pathways and contaminants. Its formulation extends classical cumulative risk assessment logic (ΣELCR and ΣHQ) into a normalized composite index suitable for probabilistic modeling and pathway-weighted decision analysis.

- *Generalized Deterministic Form*

A flexible integrated expression can be written as:

$$OERI = w_c \left(\frac{\sum_{i=1}^{n} ELCR_i}{ELCR_{ref}}\right) + w_{nc} \left(\sum_{i=1}^{n} HQ_i\right) \quad (4.11)$$

Where the symbols have their usual meaning.

- *Pathway-Expanded Form*

For multiple pathways (inhalation, dermal, ingestion, injection):

$$OERI = w_c \left(\frac{\sum_p \sum_i ELCR_{i,p}}{ELCR_{ref}}\right) + w_{nc} \left(\sum_p \sum_i HQ_{i,p}\right) \quad (4.12)$$

Where:

✓ p indexes exposure pathway
✓ i indexes contaminant

This formulation preserves route-specific resolution while enabling cumulative interpretation.

- *Monte Carlo Propagation*

For $k = 1, 2, 3, 4 \ldots \ldots \ldots N$

Sample:

$$X^{(K)} \sim \prod f_j$$

Compute:

$$OERI^{(K)} = g\,(X^{(K)}) \quad (4.13)$$

This produces a distribution:

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

$$\{OERI^{(1)}, OERI^{(2)}, \ldots\ldots, OERI^{(N)}\}$$

From the simulated distribution:

$$P\ (OERI\ > 1) = \frac{1}{N} \sum_{K=1}^{N} I\ (OERI^{(K)}\ > 1) \qquad (4.14)$$

Where $I\ (\cdot)$ is the indicator function.

E. Probability of Exceedance

The probability that cumulative risk exceeds the benchmark:

$$P\ (OERI\ > 1) = \frac{Number\ of\ iterations\ (OERI^{K} > 1)}{N} \qquad (4.15)$$

Similarly:

$$P\ (ELCR_{total}\ > 10^{6})$$
$$P\ (HI\ > 1)$$

This probability-based metric is more informative than deterministic exceedance because it quantifies the likelihood and distribution of risk rather than presenting a binary "acceptable/unacceptable" outcome relative to a fixed benchmark. Deterministic risk characterization typically compares a single-point estimate (example, HQ or ILCR) against a regulatory threshold, which does not convey the probability that this threshold is exceeded across a population or exposure distribution (USEPA, 2014; NRC, 2009). In contrast, probabilistic approaches generate a distribution of possible risk values, enabling estimation of percentile risks (for instance, 50th, 95th percentile) and exceedance probabilities such as P(HQ > 1) or P(ILCR > 10^{-6}). This probabilistic framing enhances transparency by explicitly distinguishing between variability (true heterogeneity in exposure) and uncertainty (lack of knowledge), both of which are central to modern risk science (NRC, 2009; WHO, 2017).

Moreover, probability-based outputs support risk-informed decision-making by allowing regulators to evaluate the proportion of a population potentially at risk rather than relying solely on conservative point estimates that may over- or under-protect certain subgroups (USEPA, 2014; EFSA, 2012). For complex environmental contaminants such as PAHs and potentially toxic elements, where exposure concentrations often follow skewed distributions and toxic potency varies across compounds and pathways, probabilistic metrics provide a more nuanced and scientifically robust characterization of public health risk (Limpert et al., 2001; ATSDR, 2022). Consequently, probability-based risk metrics align with contemporary regulatory guidance advocating uncertainty-informed, distribution-based assessment frameworks.

F. Sensitivity Analysis

To identify dominant drivers of risk variability, compute rank-order correlation coefficients between inputs and OERI:

$$\rho_s\ (X_j, OERI)$$

Where:

ρ_s = Spearman rank correlation coefficient
X_j = input variable

Sensitivity analysis is a critical component of probabilistic risk modeling because it identifies which input parameters exert the greatest influence on model outputs and therefore drive uncertainty in risk estimates (Saltelli et al., 2008; NRC, 2009). By quantifying the relative contribution of each parameter to the variance of outcomes such as ELCR, HI, or OERI, sensitivity analysis enhances transparency and prioritizes data refinement efforts.

First, sensitivity metrics determine whether concentration uncertainty dominates model variability. Environmental contaminant concentrations, particularly for PAHs and PTEs, often exhibit lognormal distributions with high variance, making them frequent primary drivers of total risk (Limpert et al., 2001; USEPA, 2014). If Spearman rank correlation coefficients or variance-based indices indicate that concentration (C_{air}) explains the largest proportion of output variance, this implies that improved site characterization or analytical precision would most effectively reduce overall uncertainty.

Second, sensitivity analysis reveals whether exposure frequency (EF) or duration (ED) drives variability in cumulative dose. Behavioral exposure factors can differ substantially across demographic groups (children vs. adults, occupational vs. residential settings), and these parameters may dominate risk predictions in scenarios where contaminant concentrations are relatively stable (USEPA, 2011; WHO, 2017). Identifying EF as a key driver underscores the importance of accurate activity-pattern data and population-specific exposure assumptions.

Third, dermal absorption parameters (ABS or dermal permeability coefficients) can significantly influence outcomes, particularly for semi-volatile organic compounds such as PAHs and for metals where bioavailability differs by matrix and speciation (ATSDR, 2022; USEPA, 2004). Sensitivity ranking of dermal absorption factors helps determine whether refined bioavailability or toxicokinetic studies are warranted to reduce model uncertainty.

Finally, pathway-level sensitivity decomposition identifies which exposure route ingestion, inhalation, dermal contact, or injection contributes most to OERI exceedance probability. This pathway apportionment is essential for targeted risk management because it clarifies whether mitigation should focus on air quality control, soil remediation, dermal protection, or behavioral interventions (NRC, 2009; USEPA, 2014). In cumulative frameworks such as OERI, where carcinogenic and non-carcinogenic endpoints are integrated, pathway sensitivity analysis ensures that regulatory decisions are informed by mechanistic dominance rather than aggregate totals alone.

Overall, sensitivity analysis transforms probabilistic modeling from a purely computational exercise into a

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

diagnostic decision-support tool, aligning with contemporary recommendations for uncertainty-informed environmental health assessment (Saltelli et al., 2008; NRC, 2009).

V. DISCUSSION

A. State of the Art

➢ *Carcinogenic Risk Benchmark ($ELCR_{ref}$)*

For cumulative lifetime cancer risk, a midpoint reference of:

$$ELCR_{ref} = 1.0 \times 10^{-5} \ ;$$

The above is adopted as a balance between the more conservative regulatory lower bound (1×10^{-6}) and a more permissive upper bound (1×10^{-4}), consistent with modern guidance that encourages probabilistic interpretation of risk and recognition of population variability in sensitivity (USEPA, 2014; WHO, 2017; NRC, 2009). This intermediate benchmark offers a rational screening threshold for mixed PAHs and PTE exposures where uncertainties exist in dose–response functions.

➢ *Core Exposure Factor (Worker Case Study)*

For inhalation and dermal risk pathway calculations in occupational or semi-chronic scenarios, the following well-accepted default exposure parameters are recommended:

Table 4 Default Exposure Parameters

Parameter	Value	Rationale / Source
Inhalation Rate (IR_{worker})	20 $m^3 \cdot day^{-1}$	Typical adult worker ventilation (USEPA, 2011)
Exposure Frequency (EF)	250 $days \cdot yr^{-1}$	~5 days/week occupational exposure
Exposure Duration (ED)	25 years	Standard working life assumption
Body Weight (BW)	70 kg	Default adult mass (USEPA, 2011)
Averaging Time (AT)	70 × 365 days	Lifetime average for cancer risk

Table 4: These defaults align with exposure factor handbooks and regulatory assessments for adult occupational populations (USEPA, 2011; NRC, 2009), and facilitate transparent comparison across studies.

➢ *Absorption Parameters (ABS)*

Inhalation Absorption (ABS_{inh});

$ABS_{inh} = 1.0$ (When compound-specific uptake fractions are empirically known)

Typically, when compound-specific uptake fractions are empirically known, a default of 1.0 (100% absorption) is applied for inhalation; this is a health-protective assumption that avoids underestimating internal dose when respiratory uptake efficiencies are uncertain. Regulatory frameworks often adopt this conservative default for screening (USEPA, 2014; WHO, 2017).

Dermal Absorption (ABS_{derm});

Dermal uptake is compound-specific:

- Benzo[a]pyrene (BaP) dermal absorption fraction: 0.01–0.10 (1%–10%) reflecting experimental bioavailability data (ATSDR, 2022; USEPA, 2004).
- Metals (PTEs): dermal absorption depends on species and oxidation state. For example:

✓ Chromium(VI) (Cr^{6+}) > dermal penetration than Cr(III) (Cr^{3+}),
✓ Arsenic (As) dermal bioavailability is possibly low but significant,
✓ Lead (Pb) shows poor dermal uptake but high systemic toxicity via ingestion/inhalation.

➢ *Injection Exposure (V_{inj})*

As a hypothetically possible rather than routine environmental route, direct injection (for example, accidental needlestick) is parameterized as:

$$V_{inj} \approx 0.05\ mL$$

This very small volume reflects practical needlestick exposures and is suitable for localized clinical risk estimations rather than general environmental assessment.

➢ *Toxic Equivalency (TEF) for PAH Mixtures*

For exposure to PAH mixtures (common in air particulates, soil, and combustion emissions), individual PAH concentrations are normalized to benzo[a]pyrene potency equivalents using equation **(**5.1**)**:

$$TEQ_{BaP} = \sum_i (C_i \times TEF_i) \qquad (5.1)$$

Where TEF_i are toxic equivalency factors relative to BaP, practice follows:

- Nisbet & LaGoy (1992) scheme for BaP TEFs (widely used),
- Or latest WHO/International Agency guidance when updated TEF values exist.

Using TEQs enables consistent cumulative cancer risk estimation across PAH mixtures with heterogeneous potencies.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

VI. CLARIFICATION OF CRITICAL MODELING ASSUMPTIONS IN MULTI-PATHWAY RISK ASSESSMENT

➢ *Ingestion Pathway*

The ingestion pathway must be explicitly defined because dose modeling differs fundamentally between single-event (acute) and repeated (chronic) exposure cases. Acute ingestion (for example, accidental intake of contaminated dust or solution) is evaluated using short-term exposure duration and acute reference doses (RfD_{acute}), whereas repeated exposure requires chronic daily intake (CDI) calculations averaged over a lifetime ($AT = 70 \times 365$ days for carcinogens) (USEPA, 1989; USEPA, 2011).

Failure to distinguish these scenarios can substantially bias risk estimates. Chronic ingestion modeling assumes repeated contact and steady-state dose accumulation, whereas a single ingestion event does not justify lifetime averaging for carcinogenic endpoints (NRC, 2009). Therefore, manuscripts should explicitly state:

- Whether ingestion represents incidental soil/dust ingestion,
- Accidental workplace contamination,
- Or a one-time clinical or occupational event.

Definite cases improve reproducibility and regulatory interpretability.

➢ *Metal Speciation: Oxidation State Determines Carcinogenic Potency*

For potentially toxic elements (PTEs), carcinogenic potency and toxicity depend strongly on chemical speciation and oxidation state, not merely total concentration. For example:

- Chromium (VI) (Cr^{5+}) is classified as carcinogenic via inhalation, whereas Chromium (III) (Cr^{3+}) has substantially lower toxicity.
- Cadmium (Cd) compounds differ in carcinogenic classification depending on route and compound form.
- Lead (Pb) exhibits complex toxicodynamics; inorganic Pb is not currently assigned a cancer slope factor by some agencies but is recognized for significant non-cancer neurotoxicity, especially in children (ATSDR, 2022; IARC, 2012).

Risk assessment that applies a single slope factor (SF) to total metal concentration without confirming oxidation state may significantly over- or underestimate risk. Best practice requires:

- Chemical speciation analysis, where feasible,
- Or a conservative assumption clearly stated and justified (USEPA, 2014).

Speciation-sensitive modeling aligns with modern toxicological guidance emphasizing biologically relevant dose metrics (NRC, 2009).

➢ *TEFs and Slope Factors (SF)*

Toxic Equivalency Factors (TEFs) for PAHs and Cancer Slope Factors ($^{CSFs}/_{SFs}$) vary across regulatory sources (for example, USEPA IRIS, WHO, regional regulatory agencies). For example:

- BaP TEFs follow Nisbet & LaGoy (1992) or updated WHO recommendations.
- Cancer slope factors may be revised periodically based on new epidemiological data (USEPA IRIS database updates).

Because ELCR (see equation 5.7) is directly proportional to the slope factor:

$$ELCR = CDI \times SF \tag{6.1}$$

Even small differences in SF values can alter risk magnitude by orders of magnitude. Therefore, best practice requires:

- Explicit citation of the source database,
- Version/date of toxicological parameters,
- Consistent application across all modeled compounds.

This ensures transparency and reproducibility (USEPA, 2014; WHO, 2017).

➢ *OERI: Screening Index (Not a Regulatory Endpoint)*

The Organism Exposure Risk Index (OERI) integrates carcinogenic and non-carcinogenic components into a dimensionless screening metric. However:

$$OERI > 1$$

Interpreted as a flag for potential concern, not proof of unacceptable risk.

Screening indices are intended to identify scenarios requiring:

- Refined, site-specific exposure characterization,
- Biomonitoring studies,
- Bioavailability assessment,
- Or physiologically based toxicokinetics (PBTK) modeling (NRC, 2009; USEPA, 2014).

Thus, OERI functions analogously to $HQ > 1$: it signals the need for further evaluation but does not, in isolation, mandate remediation.

➢ *Regulatory Compliance Requires Component-Level Comparison*

While composite metrics (HI, OERI) are useful for integrated assessment, regulatory decisions are typically made at the component level. Therefore:

- Each $ELCR_i$ should be compared to jurisdictional acceptable risk ranges (for instance,$10^{-6} - 10^{-4}$).

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

- Each HQ_i should be compared against unity (HQ ≤ 1) or jurisdiction-specific thresholds.

Many regulatory frameworks (for instance, Superfund, EU chemical risk guidance, and WHO frameworks) require individual contaminant compliance before considering cumulative indices (USEPA, 1989; WHO, 2017). Hence, OERI should complement, not replace, traditional endpoint-specific evaluation.

VII. CONCLUSIONS

This review establishes a coherent mathematical and toxicological foundation for integrating multi-pathway exposure and multi-contaminant risk into a single dimensionless screening index (OERI). The framework extends conventional risk assessment logic by normalizing carcinogenic (ILCR) and non-carcinogenic (HI) outputs relative to regulatory benchmarks, enabling unified interpretation while maintaining mechanistic transparency.

The deterministic formulation preserves compatibility with established USEPA and WHO risk assessment guidance, while the Monte Carlo extension improves scientific robustness by explicitly propagating variability and uncertainty. Sensitivity diagnostics further enhance interpretability by identifying dominant exposure drivers and pathway contributions.

Importantly, OERI does not replace component-level regulatory comparison but complements it by functioning as a cumulative screening and prioritization metric. The model is adaptable across occupational, residential, and environmental contexts and is particularly suitable for complex contaminant mixtures such as PAHs and PTEs where mixture toxicity and multi-route exposure dominate risk characterization.

Overall, OERI provides a reproducible, transparent, and uncertainty-informed bridge between exposure modeling, toxicological scaling, and cumulative environmental health decision-making.

RECOMMENDATIONS

➢ Regulatory Application as Screening Tool

OERI should be applied as a screening-level cumulative risk index to identify scenarios requiring refined site-specific assessment.

➢ Standardized Toxicological Parameter Reporting

Studies should explicitly report slope factor sources, RfD versions, TEF schemes, and database update dates to ensure reproducibility.

➢ Speciation-Based Metal Assessment

Where feasible, oxidation-state–specific modeling (e.g., Cr(VI) vs Cr(III)) should replace total metal concentration assumptions.

➢ Routine Probabilistic Modeling

Monte Carlo simulation should be incorporated where sufficient data exist to improve transparency and policy relevance.

➢ Pathway-Specific Mitigation Design

Sensitivity-based pathway diagnostics should guide targeted interventions (air control, dermal protection, soil remediation).

AREAS FOR FURTHER RESEARCH

- Empirical validation of OERI against biomonitoring datasets (e.g., urinary PAH metabolites, blood metal levels).
- Integration with physiologically based toxicokinetic (PBTK) modeling.
- Development of age-specific OERI variants (children, elderly, occupational groups).
- Bayesian updating approaches for refining exposure distributions.
- Application of OERI to emerging contaminants (e.g., PFAS, microplastics-associated metals).
- Comparative evaluation of OERI against machine-learning–based risk prediction frameworks.
- Incorporation of ecological receptor modeling for ecosystem-level adaptation.

➢ *Author declaration*

The author, Mark Kubi Appiah, declares that this manuscript is an original scholarly work developed independently. All referenced materials have been appropriately cited. The conceptual development of the Organism Exposure & Risk Index (OERI) represents original synthesis based on established regulatory risk assessment frameworks.

➢ *Conflict of interest declaration*

The author declares no conflict of interest. There are no financial, institutional, or personal relationships that could have influenced the development or presentation of this work.

➢ *Similarity report*

This manuscript was developed through an original synthesis of established regulatory frameworks and toxicological principles. Standardized equations (e.g., CDI, HQ, and ILCR) originate from publicly available regulatory guidance (USEPA, WHO, NRC) and are reproduced in conceptual form for scholarly review purposes. The narrative structure, integration into OERI, probabilistic formulation, and composite normalization methodology are original contributions. Any textual similarity with regulatory guidance reflects the necessary use of established terminology in environmental risk assessment. The overall intellectual content is novel and academically synthesized.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar037

REFERENCES

[1]. ATSDR (2022). *Toxicological Profiles for Polycyclic Aromatic Hydrocarbons and Selected Metals*. Agency for Toxic Substances and Disease Registry. Available at: https://www.atsdr.cdc.gov/toxprofiles/

[2]. Cullen, A. C., & Frey, H. C. (1999). *Probabilistic techniques in exposure assessment: A handbook for dealing with variability and uncertainty in models and inputs*. Springer Science & Business Media.

[3]. EFSA (2012). Guidance on uncertainty analysis in scientific assessment. *EFSA Journal*, 10(1), 2555. https://doi.org/10.2903/j.efsa.2012.2555

[4]. IARC (2012). *Monographs on the Evaluation of Carcinogenic Risks to Humans*. Volume 100F. International Agency for Research on Cancer. Available at: https://monographs.iarc.who.int/

[5]. Kim, K.H., Jahan, S.A., & Kabir, E. (2013). A review of diseases associated with polycyclic aromatic hydrocarbons (PAHs). *Environment International*, 60, 71–80. https://doi.org/10.1016/j.envint.2013.07.011

[6]. Limpert, E., Stahel, W.A., & Abbt, M. (2001). Log-normal distributions across the sciences: Keys and clues. *BioScience*, 51(5), 341–352. https://doi.org/10.1641/0006-3568(2001)051[0341:LNDATS]2.0.CO;2

[7]. National Research Council (NRC) (2009). *Science and Decisions: Advancing Risk Assessment*. National Academies Press. https://doi.org/10.17226/12209

[8]. Nisbet, I.C.T., & LaGoy, P.K. (1992). Toxic equivalency factors (TEFs) for polycyclic aromatic hydrocarbons (PAHs). *Regulatory Toxicology and Pharmacology*, 16(3), 290–300. https://doi.org/10.1016/0273-2300(92)90009-X

[9]. Saltelli, A., Ratto, M., Andres, T., Campolongo, F., Cariboni, J., Gatelli, D., Saisana, M., & Tarantola, S. (2008). *Global sensitivity analysis: The primer*. John Wiley & Sons.

[10]. Saltelli, A., Ratto, M., Andres, T., et al. (2008). *Global Sensitivity Analysis: The Primer*. Wiley. https://doi.org/10.1002/9780470725184

[11]. U.S. Environmental Protection Agency (U.S. EPA). (1989). *Risk assessment guidance for Superfund (RAGS), Volume I: Human health evaluation manual (Part A)* (EPA/540/1-89/002). U.S. EPA, Office of Emergency and Remedial Response.

[12]. U.S. Environmental Protection Agency (U.S. EPA). (2001). *Risk assessment guidance for Superfund (RAGS), Volume III: Process for conducting probabilistic risk assessment* (EPA 540-R-02-002). U.S. EPA, Office of Emergency and Remedial Response.

[13]. U.S. Environmental Protection Agency (U.S. EPA). (2014). *Human health evaluation manual, supplemental guidance: Update of standard default exposure factors* (EPA/600/R-09/052F). U.S. EPA, Office of Research and Development.

[14]. U.S. Environmental Protection Agency (USEPA) (1989). *Risk Assessment Guidance for Superfund (RAGS), Volume I.* EPA/540/1-89/002. Available at: https://www.epa.gov/risk

[15]. U.S. Environmental Protection Agency (USEPA) (2004). *Risk Assessment Guidance for Superfund: Dermal Exposure Assessment*. EPA/540/R/99/005. Available at: https://www.epa.gov/risk

[16]. U.S. Environmental Protection Agency (USEPA) (2011). *Exposure Factors Handbook*. EPA/600/R-09/052F. https://doi.org/10.2172/1032049

[17]. U.S. Environmental Protection Agency (USEPA) (2014). *Human Health Risk Assessment Framework*. Available at: https://www.epa.gov/risk

[18]. Vose, D. (2008). *Risk analysis: A quantitative guide* (3rd ed.). John Wiley & Sons.

[19]. World Health Organization (WHO) (2017). *Environmental Health Risk Assessment: A Guide to Identifying Hazards and Estimating Risks*. Available at: https://www.who.int/

[20]. World Health Organization (WHO). (2009). *Principles and methods for the risk assessment of chemicals in food*. Environmental Health Criteria 240. WHO Press.