U.S. Army Public Health Center (APHC)

Mission
Enhance Army readiness by identifying and assessing current and emerging health threats, developing and communicating public health solutions, and assuring the quality and effectiveness of the Army’s Public Health Enterprise.

APHC Vision
World-class provider of public health services across the Department of the Army and the Department of Defense.

Health Effects Research Division (HEF)

Objectives
To provide Toxicity Assessment (TA) reports (required by AR 40-5 and AR 70-1) to inform the research, development, testing, and fielding of new chemicals and materiel.
To develop safe exposure criteria for military-unique and military-relevant substances.

HEF Guiding Principles
Perform all testing in compliance with U.S. Food and Drug Administration and U.S. Environmental Protection Agency Good Laboratory Practice (GLP) regulations.
Utilize state-of-the-science in silico and in vitro assays to determine toxicity associated with chemicals of military interest, particularly of those released to the environment.

Toxicity Assessment and Testing
Health Effects Research Division - Toxicology Directorate

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Toxicity Testing at the U.S. Army Public Health Center (APHC)

Health Effects Research Division (HEF) within the Toxicology Directorate (TOX) at the APHC develops toxicity assessments (TAs) essential to the research, development, testing, and fielding of new compounds and materiel for military use. The HEF provides direct support to the APHC and Department of Defense (DOD) public health missions in the conduct of human and environmental TAs, providing data and reports on the toxicity of military-unique and military-relevant compounds, and the risks they pose to Soldiers, civilians, and the environment.

Toxicity Assessments (TAs)

Toxicity assessments (TAs) provide the technical foundation for toxicity clearances of chemicals and materiel for military use. TAs interpret toxicity, bioaccumulation, persistence, and fate and transport data to understand potential health and environmental hazards associated with new, emerging, or replacement technologies to inform product life-cycle decisions. The HEF utilizes the following in silico, in vitro, and in vivo assessment tools to produce formal TAs for Army decisionmakers and other customers.

Ex Vivo Assessment Tools

Precision-Cut Tissue Slices: Cost-effective, animal-reducing approach to test chemicals and/or mixtures for multiple physiological and biochemical endpoints to determine toxicity at the tissue and/or organ level.

In Vitro Assessment Tools

Cardiotoxicity: Cultured human cardiac cells to assess chemical-induced proarrhythmia and identify compounds that may damage the heart.

Dermal Irritation and Corrosion: Reconstructed human epidermal tissue to assess localized reversible (irritation) and irreversible (corrosion) damage responses to direct chemical exposure of the skin (OECD 439 and 431).

Endocrine System Effects: Engineered cell lines for functional assessment of stimulation or inhibition of estrogen, androgen, and thyroid activity in response to chemical exposure.

Environmental Water Toxicity: Bacterial bioluminescence and other†† assays to measure chemical toxicity and/or the presence of toxicants in test samples for determining toxicity potential in drinking water, groundwater, and effluents.

Genotoxicity: Bacteria-based modified Ames assay for high-throughput mutagenicity testing (OECD 471).

Neurotoxicity††: Cell- and enzyme-based assays for neurite outgrowth, acetylcholinesterase activity, calcium ion efflux, and neurotransmitter transporter uptake.

Phototoxicity/Cytotoxicity††: Neutral Red Uptake assay for quantitative estimation of cultured mammalian cell viability following chemical exposure with and without ultraviolet light exposure for phototoxicity and cytotoxicity, respectively (OECD 432).

Skin Sensitization: Cellular activation- and biochemistry-based 3-part series of tests that measure critical, defined steps in the adverse outcome pathways for dermal sensitization (OECD 442 C-E).

In Vivo Animal Models

Models for oral toxicity evaluation include a variety of lab and wild species that span multiple animal classes, as appropriate for each study. Toxicity tests range from acute exposures to reproductive and developmental assessments.

In Silico Assessment Tools

Literature Review: Information compiled from peer-reviewed literature, government research, curated toxicity databases, and safety data sheets.


PBPK/ADMET Assessment: Physiologically-Based Pharmacokinetic (PBPK) computational assessment for absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles and pharmacokinetic/pharmacodynamic (PK/PD) analysis.

Various toxicology assays, cell culture methods, computational approaches, and/or animal models following Good Laboratory Practice (GLP) are used to determine the potential toxicity of compounds of interest. A suite of in silico assessments and in vitro and ex vivo assays are used to address knowledge gaps in TAs. Using regulatory accepted methods, HEF scientists also develop, validate, and implement new assays to expand predictive toxicology capabilities. Using these rapid, accurate, and cost-effective approaches, HEF produces the data needed to develop health-based exposure criteria for military-relevant compounds.