

## Breakthrough Science and Technology

Battelle offers a strong track record in kinetic studies, biomonitoring, and modeling.

### Virtual Lung to Provide Unprecedented Detail

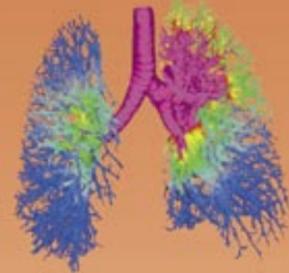
The National Institutes of Health selected us to lead a \$10 million study to devise 3-D imaging and computational models of unsurpassed detail of human and other mammalian respiratory systems. Together with internationally recognized universities and agencies, we will develop full 3-D computational fluid dynamic models for animal and human respiratory tracts.

To do this, the team will adapt magnetic resonance imaging (MRI) to measure structure, airflow dynamics, and particle deposition in the lung. The team will also lay the groundwork for integrating models across the scales of information.

The virtual respiratory tract will provide a better understanding of workplace and environmental exposures to airborne particulates. As the virtual respiratory tract grows in sophistication, it can be used to simulate pulmonary disease states and develop improved treatments for asthma, cystic fibrosis, and other respiratory illnesses. Security-related applications, such as predicting the effects of atmosphere-delivered chemical weapons, are also possible.



*Our model of working rat lungs offers the clearest picture yet of how pollutants enter the respiratory system, how they move, and where they accumulate.*



*Battelle is devising 3-D imaging and computational models of the human respiratory system to improve treatments for asthma and other respiratory ailments.*

### Saliva Provides Quick, Noninvasive Way to Determine Exposure

Using sophisticated mass spectrometry equipment, Battelle is developing a portable microanalytical sensor to quickly diagnose organophosphate pesticide exposure in humans.

The sensor can detect very small concentrations of the pesticide in saliva and then calculate the amount of dose received. The sensor provides immediate results without the need for blood samples.

The biosensor consists of electrodes coated with carbon nanotubes. The carbon nanotubes hold enzymes targeted to the organophosphate chemicals. When electricity is applied and organophosphates are present, there is a decrease in the electrical current that can be correlated to the amount of chemical present.

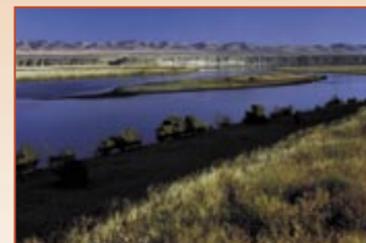
The saliva-monitoring system can detect pesticides, herbicides, chlorophenols, and metals from ongoing occupational exposures, accidents, or terrorist actions.

### Studies Examine Impact of Certain Chemicals at Superfund Sites

With Oregon Health and Science University, we are developing a fundamental understanding of the influence of the exposure route on the total body burden and internal target tissue dosimetry of contaminants commonly encountered at Superfund sites. Chemicals being studied are trichloroethylene, perchloroethylene, 1,1-dichloroethylene, vinyl chloride, toluene, xylene, benzene, diethylbenzene isomers, and chloroform.

Using a novel real-time breath analysis system, exposure assessments are being done with human volunteers to determine contaminant uptake by inhalation, ingestion, and dermal contact. These data are coupled with PBPK modeling to determine the uptake kinetics and brain dosimetry.

The results of this will be applied to developing biomarkers of susceptibility and response. The chemical study and biomarkers studies are sponsored by the National Institute of Environmental Health Sciences.



*Oregon Health and Science University and Battelle are extending existing physiologically based pharmacokinetic models to determine uptake kinetics after chemical exposures.*

## About Battelle

Battelle is a global science and technology enterprise that conducts research, develops and commercializes technology, and manages national laboratories for its customers. As a non-profit corporation, we manage or co-manage five national laboratories: Pacific Northwest, Oak Ridge, Brookhaven, Idaho, and National Renewable Energy. With these laboratories, we oversee 19,000 staff members and conduct \$3 billion in annual research and development.

Battelle provides solutions and helps develop innovative products for commercial customers by leveraging technologies into competitive advantage. We also team with more than 800 federal, state, and local government agencies, providing cost-effective science and technology in the areas of health and life sciences, energy and environment, national security, homeland defense, transportation, and space exploration.

## Bring Us Your Problems

Battelle's contracting method is easy to use and focused on the customers' needs. We routinely establish mutually beneficial collaboration agreements with private industry and academia. With our comprehensive suite of instrumentation and highly talented staff, we can perform all aspects of a toxicological study from in vitro and in vivo experiments to computer modeling based on experimental findings to provide innovative solutions to your problems. Contact us today!



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## Physiologically Based Pharmacokinetic Capabilities



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The Business of Innovation

# Physiologically Based Pharmacokinetic Capabilities

The process of assessing human health risks associated with exposure to an environmental compound relies on a number of assumptions, estimates, and rationalizations. Physiologically based pharmacokinetic (PBPK) modeling is a sophisticated approach to increasing the reliability of these assumptions, providing an important tool for improving the ability to extrapolate across dose, species, and exposure routes. Battelle, Pacific Northwest Division can provide research staff experienced in developing and experimentally validating PBPK models specific to your needs, with capabilities ranging from in vivo and in vitro laboratory studies to development of 3-D models of unsurpassed detail.

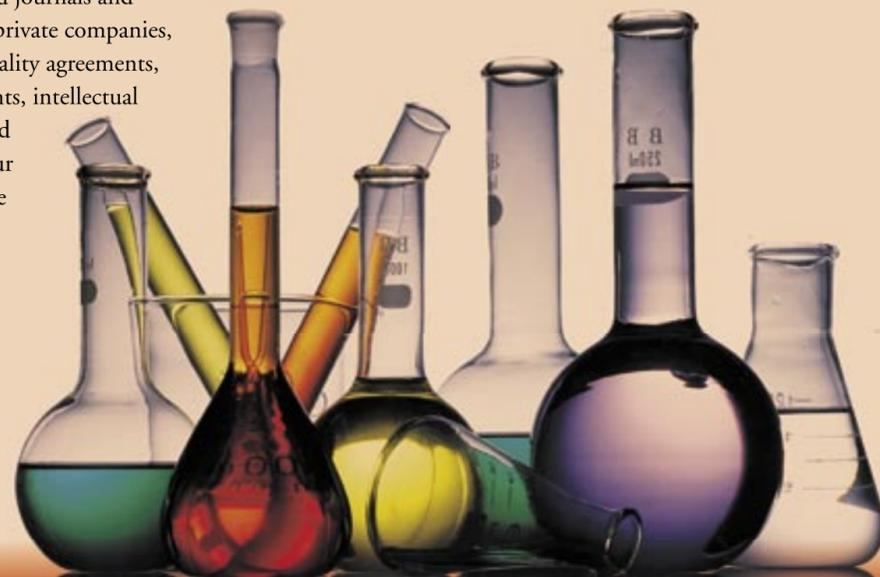
At Battelle's Pacific Northwest Division, we bring together the right expertise to work on your project. We have experts in bioengineering, biology, chemistry, biochemistry, metabolism, computational science, information visualization, statistics, mathematics, physics, and toxicology.

We also have strong relationships with the other Battelle offices, universities, private industry, key government agencies, and national laboratories. These relationships allow us to draw upon experts in other disciplines, such as marine sciences, atmospheric sciences, sensor technologies, microelectromechanics, materials science and biomaterials, and regulatory analysis and compliance.

Our top researchers are "on the ground," conducting research for you. Because research is our main job, the people you read about on the proposal are the ones conducting the experiments, building the models, and managing the project.

For government agencies, we publish our findings in peer-reviewed journals and other publications. For private companies, we customize confidentiality agreements, non-disclosure agreements, intellectual property agreements, and other contracts to fit your needs through our onsite legal office.

*Battelle conducts experiments and develops pharmacokinetic models to determine how chemicals such as organophosphate pesticides and dry cleaning chemicals are absorbed, distributed, metabolized, and eliminated.*

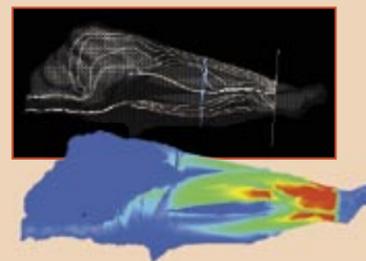


## Leading-Edge Capabilities

### Age, Species, and Gender Specific Kinetic Studies

Battelle conducts studies focused on understanding age, species, and gender dependent kinetics. Our research and modeling capabilities and equipment allow us to provide results beyond typical kinetic studies and focus on the 70-kg adult male. For government agencies, private industry, and others, we are providing detailed information on the human and environmental impacts of a variety of compounds, including

- Glycol ethers, used universally in industry
- Hydroquinone, used in cosmetics, film processing, and homeopathic compounds
- Methanol, used in the production processes of many common industrial items such as plywood, paints, and plastics
- Vinyl acetate, used in the manufacture of glues, paints, and other products
- Styrene, used in the production of plastics and resins
- Bisphenol A, used in the production of plastics and resins.



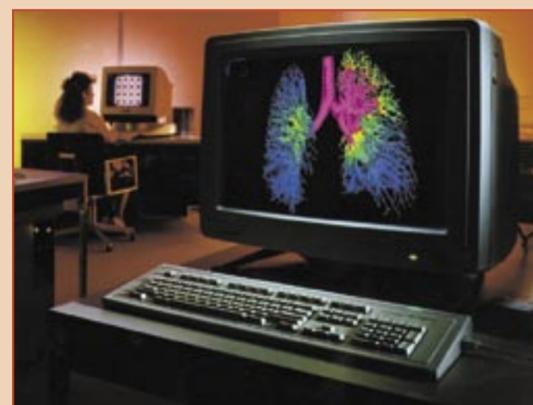
*Using experimental data and advanced modeling systems, including NWPhys and NWGrid, we have developed accurate and reliable models of a rat's nasopharyngeal cavity.*

### Modeling

By developing and using accurate, predictive models, Battelle can determine the internal dose of chemicals and/or their toxic metabolites in target tissues. In addition, we can link the results to realistic environmental exposures with mechanisms of action at the cellular and molecular level.

With expertise in physiology, toxicology, and computational science, we can develop the following models based on your needs:

- 3-D anatomical models
- Classical kinetic models
- Physiological models
- Physiologically based pharmacokinetic models.



*Because our modelers are also our experimental scientists, we can deliver complete, high-quality results that give a comprehensive view of the effects of ag-chemicals, industrial solvents, and other compounds.*

### Noninvasive Biomonitoring

Through our noninvasive biomonitoring, we provide you with detailed data on the uptake of low doses of chemical agents, including halogenated solvents, organics, inorganics, metals, pesticides, antimicrobials, and natural products. Our biomonitoring methods include saliva sampling and breath analysis.



*When people potentially exposed to chemicals breathe into the Exposure-to-Risk Monitor, our scientists can measure the amount of chemicals ingested, absorbed, or inhaled.*

### Internationally Recognized Staff

We are internationally known for our work on chemical studies and risk assessments. Our staff have served on World Health Organization, International Agency for Research on Cancer, International Life Sciences Institute, Society of Toxicology, and panels of the National Academies of Science.

## Available Equipment

With our comprehensive suite of instrumentation, we can perform all aspects of a toxicological study from in vitro and in vivo experiments to computer modeling based on experimental findings to obtain the data needed to make manufacturing and regulatory recommendations to multi-billion dollar industries. Our experimental equipment includes

- Standard analytical equipment (GC, GC/MS, LC, LC/MS, MS/MS)
- Physiology monitoring systems (rhinometry, plethysmography).

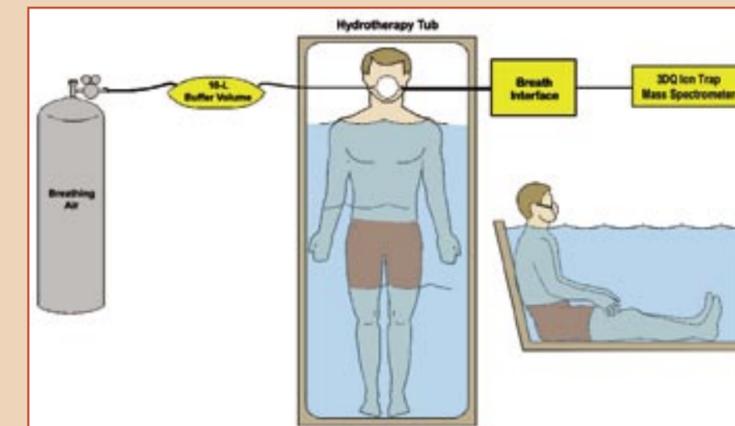
Because we work with engineers and instrumentation specialists, we can design equipment to get the information you need. For example, we have developed innovative, yet simple systems to measure gas uptake, off-gassing, and dermal absorption.

After a rigorous review of our veterinary and animal husbandry practices, the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) has approved all of our animal laboratories. For all of our human studies, we use volunteers and adhere to a strict review process.

Our modeling software and hardware includes

- Mesh generation with NWGrid
- Problem execution with NWPhys
- Visualization and mapping programs
- SimuSolv and ACSL.

Data management and merging along with model development and simulation studies are performed on an array of computing resources, from powerful desktop systems to our 11.8-teraflop supercomputer.



*To understand dermal absorption and metabolism, Battelle has developed a bathwater exposure system. The chemical is introduced into the bathwater and the concentrations of the metabolites in the volunteer's exhaled breath are measured using a 3DQ ion trap mass spectrometer.*



*Our 11.8-teraflop Hewlett-Packard supercomputer has more than 2,000 processors and 6.8 terabytes RAM to conduct modeling studies.*

### Key Collaborators

Oregon State University  
Oregon Health and Science University  
Southern Illinois University  
University of California at Davis  
University of Iowa  
University of Utah  
University of Washington  
CIIT Centers for Health Research of Research Triangle Park  
Mountain-Whisper-Light Statistical Consulting  
Computational Geometry Consulting  
New Mexico Resonance