



The National Center for Toxicological Research (NCTR), the primary research arm of the Food and Drug Administration, plays a critical role in the advancement and protection of public health. NCTR's mission is to provide a rigorously scientific basis for the FDA's regulatory actions by exploring subjects such as risk analysis of drugs and food additives or contaminants and by evaluating the effectiveness and standardization of state-of-the-art technologies for measuring the safety and effectiveness of new products.

In 2005, NCTR scientists and their collaborators in academia and industry produced 200 scientific papers and six patents for innovative products. Examples of NCTR's current studies include the toxicity of acrylamide, a food contaminant and animal carcinogen; the toxicity of ketamine, an anesthetic, on the developing brain; the toxicity of modern tattoo inks and permanent cosmetics when exposed to sunlight; methods for rapid detection of antibiotic resistance genes in poultry; and models for the effects of exposing the fetus to life-saving regimens of anti-HIV/AIDS drugs.

To explore these and other scientific problems, NCTR uses emerging technologies—such as genomics, proteomics, metabolomics, and medical imaging—that hold a promise for cost-effective development of personalized drugs. NCTR scientists employ these technologies and traditional safety tests to develop critical risk analyses and regulatory standards. Here are some examples of NCTR's current research agenda.

VALIDATION OF TOOLS FOR SYSTEM TOXICOLOGY

- **Genomics:** NCTR uses commercial and in-house DNA microarrays of rat, mouse, and human genes to develop biomarkers of toxicity in surrogate models and humans. The biomarker patterns link to general mechanisms of toxicity and pathology to provide early recognition of drug safety issues or disease.
- **Proteomics:** NCTR has helped develop a complete mass spectrophotometric infrastructure capable of determining the expression of proteins, the functional units of the genome. Proteomics are being used to explore the function of mitochondria, the energy center of the cell, because energy disruption is a major mechanism of neurotoxicity. The technology also makes possible rapid identification of bacteria affecting the safety of food and drugs.
- **Metabolomics:** NCTR has developed a metabolomic facility, with technology similar to medical Magnetic Resonance Imaging (MRI), for studying the physiology of an organism exposed to chemical, biological, or physical agents. This technology rapidly measures metabolite profiles in the urine, blood, or other bodily fluids of exposed individuals, and is particularly useful for evaluation of both preclinical and clinical samples, and for early detection of disease. NCTR's research in this field is part of an international effort to increase the effectiveness of metabolomics in the study of drug safety.
- **Imaging:** NCTR scientists are evaluating noninvasive medical imaging as a tool to generate both structural and functional data for regulatory use. Imaging is the ideal medium for exploring biomarkers because the methods can be used similarly in humans and animals producing improved drug development decisions.
- **Toxicoinformatics:** NCTR has developed ArrayTrack™ software for management, analysis, integration, and visualization of massive data from emerging technologies. The software provides standard formats for entering microarray data to meet prescribed standards for completeness, accuracy, and ontology, and is being integrated by reviewers to facilitate new drug application data. A DNA microarray database has been constructed and validated. Construction of protein and metabolomic databases and a toxicant library is under way.

NCTR'S COOPERATIVE EFFORTS

NCTR's global scientific contacts are exemplified by its studies on compounds of FDA concern that are being evaluated by the National Toxicology Program (NTP) of the National Institute of Environmental Health Sciences. In addition to all FDA centers and the NTP, these toxicology studies are designed by NCTR scientists in partnership with 10 other government agencies, industry, and more than 25 U.S. or foreign universities and medical centers.