New Approach Methodologies (NAMs)

Why Develop New Approaches

The Environmental Protection Agency uses many types of information to evaluate the potential risks of chemicals to human and ecological health. Due to the large number of chemicals regulated by EPA, better, faster and more cost effective methods are needed for chemical evaluation. Associated with this need, is the goal of reducing, refining and replacing the use of animals in testing. The increased application of new approach methodologies (NAMs) holds the promise of meeting both the need and the goal.

New Approach Methodologies (NAMs) refer to any technology, methodology, approach, or combination thereof that can provide information on chemical hazard, exposure, and risk assessment. These include *in vitro* tests, *in chemico* assays and *in silico* models.

NAMs Research Approach

EPA's Office of Research and Develoment (ORD) is actively developing, testing and applying NAMs to improve Agency approachs to evaluate the potential impacts of chemicals on human and ecological health. Working collaboratively with federal partners and other stakeholders, EPA is developing NAMS that will provide data to fill critical information gaps and build confidence for the use of these new approaches in regulatory decisions. EPA has developed a three-part strategy that: 1) characterizes the scientific quality and relevance of existing animal tests, 2) develops recommended reporting requirements, and 3) demonstrates application of the NAMs to regulatory decisions through case studies. These efforts are focused on developing information of "equivalent or better" scientific quality and relevance to animal test-based results.
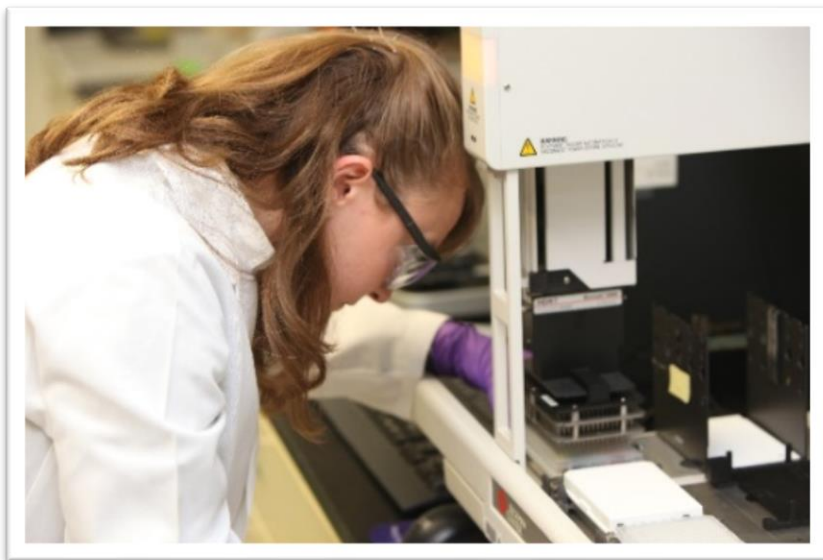
Reduced Use of Animals

A benefit of NAMs is that they can reduce the use of vertebrates in testing. EPA has set a goal to reduce the use of mammals in toxicity testing by 30 percent by 2025 and eliminate all mammals in toxicity testing requested by the Agency by the year 2035.

Progress has been made on several NAMs for chemical properties, pathways, and exposure. For examples, see the reverse side.

More Information

EPA Chemical Safety Research:
http://epa.gov/research/chemicalscience/

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Progress on the Development of NAMs

High-Throughput Toxicology

ORD has developed a computational NAM model to evaluate potential estrogenic activity for the Agency's Endocrine Disruptor Screening Program (EDSP). The model is being used to evaluate the potential estrogenic activity of over 1800 environmental chemicals and will reduce the use of low-throughput *in vitro* and *in vivo* assays. Looking forward, EPA will continue to modernize the EDSP by 1) completion of computational models for estrogen receptor activity, androgen receptor activity, and steroidogenesis; 2) continued development of high-throughput thyroid assays and associated models; 3) development of species extrapolation approaches; and, 4) development of interactive dashboard tools, such as the CompTox Chemicals Dashboard (comptox.epa.gov/dashboard), for data interpretation, translation, and chemical prioritization.

Virtual Tissue Models

Chemical assessments include consideration of risks to vulnerable subpopulations and life stages. NAMs help to address potential adverse developmental outcomes that reflect the best available knowledge of human developmental biology and do so with less reliance on traditional animal testing. EPA is exploring evaluating the effects of chemical exposure during human development on phenotypic responses in human based *in vitro* and virtual tissue model systems to predict chemical hazard. In addition, EPA is developing and applying *in silico* virtual tissue models, agent-based models, and organotypic cell culture models to evaluate and model the effects of chemicals on reproductive and developmental endpoints.

Adverse Outcome Pathways (AOPs)

Successful adoption and use of NAMs in risk assessments and regulatory decision making depends upon developing confidence that new methods and approaches provide equivalent or better scientific quality and relevance compared to existing approaches. To achieve this confidence, an understanding of both chemistry and biology is needed to establish the scientific rationale that support the use of NAMs in evaluating potential chemical impacts. EPA is actively developing AOPs for high-priority pathways and chemicals, designing relevant case studies, and disseminating the results through an AOP knowledgebase. Additionally, EPA is conducting *in vitro* and *in vivo* studies for high-priority AOPs to support predictive model development. EPA's work on AOP will help to understand and define biological points of departure, actionable effect levels, and susceptibility factors for important chemicals of interest.

Informatics, Synthesis, and Integration (ISI)

Chemical curation is the process of validating data sources to increase data quality and is an essential component of EPA's overall approach to understanding the potential impacts of chemicals. EPA continues to invest in the curation and development of mammalian toxicity databases (including new and legacy data) to support regulatory decision making, chemical prioritization efforts, predictive model development, and validation of NAM data.