National Library of Medicine

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ICCVAM Public Forum

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U.S. National Library of Medicine (NLM)

NLM’s Mission: Collect, organize, preserve, and disseminate health-related information.

- World’s largest biomedical library
- Services: PubMed, MedlinePlus, and many others
- Research and Development
  - Biomedical informatics and communications
- Quite new focus: Disaster information
PubMed Commons

Developed to allow the sharing of opinions and information about publications in PubMed

All authors in PubMed are eligible to become members

Commons authors can comment on any publication, rate the helpfulness of comments, and invite other eligible authors to join

Includes a Journal Clubs option

ALTBIB® Web portal

- Provides access to information on *in silico, in vitro*, and improved (refined) animal testing methods
- Information on the testing strategies incorporating these methods and other approaches
Searches

News

Organizations

Methods

Guides and other “support”

Search Animal Alternatives Literature

Links to PubMed citations on more than seventeen alternative methods categories

Search PubMed using ALTBIB animal alternatives search strategy

(e.g. Corrositex, “androgen receptor binding assay”)

Limit search:
- Citations from 2000 to present
- Citations with Animal Use Alternatives as the main topic
- Citations from the PubMed Toxicology Subset

View/Edit PubMed Search Strategy

Search ALTBIB 1980-2000

ALTBIB citations have been selected from articles, books, book chapters, and technical reports published from 1980 to 2000. These citations examine methods, tests, assays, and procedures that may be useful in establishing alternatives to the use of intact vertebrates.

ALTBIB Support

- Fact Sheet
- Help
- The Principles of Humane Experimental Technique by W.M.S. Russell and R.L. Burch
- Guide for the Care and Use of Laboratory Animals Eighth Edition (2011)
- Conducting a literature search for alternatives to painful/distressful procedures Animal Welfare Information Center, National Agricultural Library, USDA

Animal Alternatives News

News from...

- ICCVAM/NIEHS: Interagency Coordinating Committee for the Validation of Alternative Methods
- Altweb News: Johns Hopkins University
- US EPA: Computational Exposure Science publication

Additional Resources

- AltTox.org - Non-animal Methods for Toxicity Testing
- Altweb - Alternatives to Animal Testing on the Web
- Animal Welfare Information Center (USDA)
- EURL ECVAM - European Reference Laboratory for Alternatives to Animal Testing
- FRAME - Fund for the Replacement of Animals in Medical Experiments
- NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (HH/S/NIH/NIEHS)
- Center for Alternatives to Animal Testing (Johns Hopkins University)
- Center for Animal Alternatives (UC Davis)
- SOT In Vitro and Alternative Methods Specialty Section (Society of Toxicology)
- U.S. EPA National Center for Computational Toxicology (EPA)
- American Society for Cellular and Computational Toxicology (ASCCT)

Evaluation/Acceptance of Test Methods

- Regulatory Acceptance of Alternative Methods (ICCVAM)
- U.S. and International Milestones in Alternative Test Method Development and Evaluations (ICCVAM)

A new teaching tool is the updated and enhanced Tox Tutor

The latest approaches

Testing for and Assessing Toxicity

Alternatives to animal testing have emerged in recent years. Since about 1990, numerous attempts have been made around the world to reduce the use of and replace laboratory animals in toxicology and other studies. These efforts have involved finding alternatives to animal testing and incorporating the “3Rs” concept (Replacement, Reduction, and Refinement), which means using test methods that:

- replace the use of animals with other types of studies and approaches;
- reduce the number of animals in studies;
- refine the procedures to make studies less painful or stressful to the animals.

Regulatory authorities, companies, and others have endorsed the principle of the 3Rs, and alternative testing methods have been and are being developed. An international group that has played a key role is the International Cooperation on Alternative Test Methods (ICATM). Established in 2009, ICATM includes representatives of organizations from various countries.

Finding Information about Alternatives to Animal Testing

Many countries including the United States, Canada, and the European Union member states require that a comprehensive search for possible alternatives be completed before some or all research involving animals is begun. Because numerous Web resources are now available to provide guidance and other information on in vitro and other alternatives to animal testing, conducting such searches and keeping current with information associated with alternatives to animal testing is much easier than it used to be.

Future Approaches and Methods

In the future, there will likely be additional, and refined in vitro methods, and the emergence of in silico and “chim” approaches. Many current efforts are underway to refine, develop, and evaluate in vitro methods.

In Silico Methods

Also emerging are in silico methods, meaning “performed on computer or as computer simulations.” The term was developed as an analogy to the Latin phrase avianus or viae.

Advanced computer models called “Virtual Tissue Models” are being developed by the U.S. EPA’s National Center for Computational Toxicology (NCTR). The NCTR’s Virtual Tissue Model is described as using “new computational methods to construct advanced computer models that simulate how chemicals affect tissue and organ development, as well as how those effects may influence human development, virtual tissue models are some of the most advanced methods being developed today. These models will help reduce dependence on animal study data and provide much better human chemical risk assessment” (source).

One example is the Virtual Britney (in Britney) approach to research, aimed at developing prediction models to more accurately and efficiently understand how chemical exposure may affect human health. Researchers are leveraging new types of silico, in vitro, and in silico models that simulate virtual aspects in real development, Virtual Britney models are useful biological interactions dynamic during development and predict chemical disruption of key biological events in pathways that is believed to lead to adverse effects.

“Chip” Models

Also emerging are “chip” models, such as an “organ on a chip.” Chip models include human cell cultures that are placed on a computer chip and studied there. The Wyss (pronounced “wess”) Institute for Biologically Inspired Engineering is a helpful resource for more information.

For example, the “Lung on a chip” is described as combining microfabrication techniques with modern tissue engineering, lung-on-a-chip offers a new in vitro approach to drug screening by mimicking the complicated mechanical and biochemical behaviors of a human lung (source). To learn more, watch a video of from the Wyss Institute that uses the chip to mimic fluid accumulation on the lungs (pulmonary edema).

Figure 6. Lung-on-a-chip used to mimic pulmonary edema
(Image Source: The Wyss Institute for Biologically Inspired Engineering)
Toxicology Data Network (TOXNET): One Example

Hazardous Substances Data Bank
Comprehensive toxicological information on almost 6,000 substances (human and animal toxicity, safety and handling, environmental fate, and more). Scientifically peer-reviewed.
Chapter 9  U.S. National Library of Medicine Resources for Computational Toxicology

Chapter Outline:
Summary
1. Introduction
2. Selected NLM Resources for Computational Toxicologists and Others
3. Other NLM Resources to Consider
4. Case Study of NLM Database Results Relevant to PBPK Modeling
5. Recommendations and Future Resources
6. Acknowledgments
7. References

https://www.crcpress.com/Computational-Methods-for-Reproductive-and-Developmental-Toxicology/Mattison/9781439861073
Other Recent NLM Efforts/Support

December 2016 Webinar (Publicker and Hakkinen) with the NN/LM National Training Center on “Using ALTBIB: What, Why and How”

Society of Toxicology (SOT) March 2017 exhibit and talk

NLM (Hakkinen and Fonger) can help with ICCVAM-relevant identification and compilation of information from publications for working groups and others

Ongoing enhancement (Publicker, Hakkinen, and others) of ToxTutor

2016 – 2017 participation (Hakkinen) on JaCVAM peer review panels for eye and embryotoxicity methods
Twitter and email updates

@NLM_SIS – Clinical and non-clinical toxicology, environmental health and disaster information updates

https://service.govdelivery.com/accounts/USNLMTEH/subscriber/new
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Please feel free to stay in touch about anything you want to publish related to NLM resources