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Transforming Toxicology:
Advancing Beyond Animal Testing

Innovative technologies are quickly changing how toxicology and safety assessments are conducted in drug development, reducing the reliance on animal testing. These methods include high-throughput screening systems, organ-on-a-chip platforms, induced pluripotent stem cells and *in silico* computational approaches. In concert, they offer more human-relevant results, reduce ethical concerns, and may shorten drug development timelines.

The Tox21 program, a multi-agency partnership among the U.S. National Institutes of Environmental Health Sciences (NIEHS), the Environmental Protection Agency (EPA), National Center for Advancing Translational Sciences (NCATS) and the Food and Drug Administration (FDA) has been valuable. Tox21 focuses on the development of high-throughput screening (HTS) assays using human cells and cell lines to rapidly evaluate the toxicity of thousands of compounds. Unlike traditional animal tests, which can be expensive and time-consuming, these HTS systems allow researchers to evaluate a compound's impact on various biological pathways in a fraction of the time. The data generated support the identification of early toxicity signals, improving the overall predictive power of preclinical toxicological assessment. Over time, the Tox21 has developed hundreds of assays and has generated critical data, which are also publicly available and easily accessible.

Organ-on-a-chip technologies, further advance the replacement of animal testing. These platforms aim to mimic the structural and functional characteristics of human tissues by combining engineered microfluidic devices, tissue-specific cells, and biomimetic environments. For example, a lung-on-a-chip microdevice may be used to reconstruct the critical functional alveolar capillary interface of the human lung and can recreate breathing motions and fluid flow, enabling the study of drug interactions in a more physiologically relevant context than traditional static cell cultures.

These approaches which have now been developed for many other organ systems, allow for more precise control over experimental conditions and facilitate integration with imaging and biosensing technologies. Advances in stem cell biology have also contributed to these developments. Induced pluripotent stem cells (iPSCs) can be derived from patient-specific tissues and then differentiated into various cell types, such as cardiomyocytes or neurons.

These *in vitro* models help predict organ-specific toxicity and study disease pathways in a more personalized manner. These approaches open up possibilities for creating patient-specific drug testing platforms, potentially improving safety evaluations and reducing adverse reactions once the drugs enter clinical trials.

In silico modeling and computational approaches to toxicology likewise bolster efforts to replace animals. By leveraging bioinformatics, machine learning, and systems biology, these methods generate predictions about a compound's toxicity or pharmacokinetics based on its chemical structure or known interactions with biological targets. Such computational tools can streamline decision-making, identifying the most promising drug candidates before committing costly resources to *in vitro* or *in vivo* tests.

As regulatory agencies worldwide develop frameworks to accommodate these alternatives, the promise of replacing animals in routine toxicology studies becomes increasingly attainable. Recently, on April 10, 2025, the FDA also signaled its intention to phase out the animal testing requirement for monoclonal antibodies and other drugs, starting with a pilot program allowing select drug developers to use a non-animal-based testing strategy. Over 300 of these New Approach Methodologies (NAMs) are being currently developed.

At JRF Global, a premier contract research organization for nonclinical research services, we have developed *in-silico* prediction capabilities for toxicology assessments and have several service offerings on this innovative front for our customers in pharmaceutical, agrichemical and cosmetic industries. The shift away from animal models in toxicology is driven by both ethical considerations and scientific advancements. While some challenges remain – such as ensuring robust validation and standardization of some of these new platforms, there is growing consensus that these innovative technologies can offer more human-centric, cost-effective and rapid safety evaluations

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Srinath Rangarajan, Ph.D., serves as Business Manager and Senior Advisor at JRF Global, where he leverages his scientific expertise and strategic insight to support the organization's growth and innovation. With a strong background in research and a passion for advancing health and well-being, he plays a key role in bridging scientific and business objectives to deliver impactful solutions. With over 15 years of experience in the biologics industry, working with global pharma and CRO companies, Dr. Srinath brings a wealth of knowledge and experience to the JRF team.