New Drugs and Clinical Trial Rules (2023)

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Why in News: An amendment to the New Drugs and Clinical Trial Rules (2023), recently passed by the Government of India, aims to replace the use of animals in research, especially in drug testing.

Current drug-development pipeline

Every drug in the market goes through a long journey of tests, each designed to check whether it can treat the disease for which it was created and whether it has any unintended harmful effects.

For a long time, the first step of this process has been to test the candidate molecule **in at least two animal species**: a rodent (mouse or rat) and a non-rodent, such as canines and primates.

However, humans are more complex creatures, and biological processes and their responses often vary from person to person as well, based on factors such as age, sex, pre-existing diseases, genetics, diet, etc. – and a lab-bred animal species reared in controlled conditions may not fully capture the human response to a drug.

This ‘mismatch’ between the two species is reflected in the famously high failure-rate of the drug development process.

Despite increasing investment in the pharmaceutical sector, most drugs that cleared the animal-testing stage fail at the stage of human clinical trials, which come towards the end of the pipeline.

Alternative testing modes

The limitations of the conventional testing process, beginning with animals, have led an increasing number of researchers to focus on systems that do a better job of capturing the intricacies of human biology and predicting humans’ responses.

In the last few decades, several technologies have been developed using human cells or stem cells. These include millimetre-sized three-dimensional cellular structures that mimic specific organs of the body, called “organoids” or “mini-organs”.

Another popular technology is the “organ-on-a-chip”: they are AA-battery-sized chips lined with human cells connected to microchannels, to mimic blood flow inside the body. These systems capture several aspects of human physiology, including tissue-tissue interactions and physical and chemical signals inside the body.

Researchers have also used additive manufacturing techniques for more than two decades. In 2003, researchers developed the first inkjet bioprinter by modifying a standard inkjet printer.

Several innovations in the last decade now allow a 3D bioprinter to ‘print’ biological tissues using human cells and fluids as ‘bio-ink’. Such technologies, researchers say, are bringing us closer to recreating a human tissue or organ system in the laboratory.

These systems promise to reshape drug-design and -development. Since they can be built using patient-specific cells, they can also be used to personalise drug-tests.

Status of regulations worldwide

How global regulatory frameworks are designed will play an important role in determining whether researchers will adopt non-animal methods to test the effect and potential side-effects of new drug candidates.

In 2021, the European Union passed a resolution on an action plan to facilitate transition towards technologies that don't use animals in research, regulatory testing, and education.

The U.S. passed the FDA Modernization Act 2.0 in December 2022, allowing researchers to use these systems to test the safety and efficacy of new drugs.

In the same month, South Korea introduced a Bill called 'Vitalization of Development, Dissemination, and Use of Alternatives to Animal Testing Methods'.

In June 2023, Canada amended its Environmental Protection Act to replace, reduce or refine the use of vertebrate animals in toxicity testing.

In March 2023, the Indian government embraced these systems in the drug-development pipeline by amending the New Drugs and Clinical Trials Rules 2019. It did so after inviting comments from the people and in consultation with the Drug Technical Advisory Board, the statutory body that advises Central and State governments on drug-related technical matters.

The recent amendment authorises researchers to instead use non-animal and human-relevant methods, including technologies like 3D organoids, organs-on-chip, and advanced computational methods, to test the safety and efficacy of new drugs.

Challenges with New development methods

One problem is that developing an organ-on-a-chip system typically requires multidisciplinary knowledge. This means

expertise in cell biology to recreate the cellular behaviour in the lab;

materials science to find the right material to ensure that the chip does not interfere with biological processes;

fluid dynamics to mimic blood flow inside the microchannels; electronics to integrate biosensors that can measure pH, oxygen etc.in the chip;

engineering to design the chip; and pharmacology and toxicology to interpret action of the drugs in the chips.

To enable this crosstalk between different disciplines, technology developers in academia and industry have proposed creating a 'Centre for Excellence' in India, akin to the Wyss Institute, to bring together scientists and others with a wide range of expertise to build preclinical human models.

Another important problem concerns the resources needed for research. Most of the reagents, cell-culture related materials and instruments for these technologies are currently imported from the U.S., Europe, and Japan.

Thus, there exists a huge gap and hence opportunity in several diverse areas related to cell culture, material science and electronics, to develop an end-to-end ecosystem in India

To manage the complexity of recreating human tissues and organs in the petri dish, researchers often minimise the number of components required to simulate the disease being investigated. This means, for example, there can be no 'standard' or 'universal' liver-on-a-chip to study all liver diseases.

One lab may create a system with only liver cells, while another lab attempting to study the immune system and liver may also incorporate immune cells in its liver-on-a-chip. So regulators sometimes express concerns about variability in the data arising from differences in lab-to-lab protocols and expertise.

The Way Ahead

It is important to bring out guidelines on the minimal quality criterion and standards for these systems. Also, the current guidelines on animal testing requirements must be re-evaluated and revised, considering newer developments in cell-based and gene-editing based therapeutics