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## A Review on Drug Testing in Animals

**Bhanu Prasad CH**

Anurag Group of Institutions (CVSR), Lalitha School of Pharmacy, Hyderabad, India

**Corresponding author:** Bhanu Prasad CH, Anurag Group of Institutions (CVSR), Lalitha School of Pharmacy, Hyderabad, Telangana, India, Tel: +917702627935; E-mail: bhanu\_22226@rediffmail.com**Received date:** October 18, 2016; **Accepted date:** November 20, 2016; **Published date:** November 25, 2016**Citation:** Bhanu Prasad CH. A Review on Drug Testing in Animals. Transl Biomed. 2016, 7:4.

### Abstract

An estimated 26 million animals are used every year in the United States for scientific and commercial testing. Animals are used to develop medical treatments, determine the toxicity of medications, check the safety of products destined for human use, and other biomedical, commercial, and health care uses. Research on living animals has been practiced since Ancient times. Researchers will use animal testing to obtain clues to how the disease develops in the body. The purpose of this article is to raise some points for an understanding the ethics of using animals in scientific experiments. I present the various positions from scientific and moral perspectives establishing different ways of viewing animals; the paper aims to analyze the controversial topic i.e. Animal Testing. This paper represents the process of animal testing as well as Alternative Studies to animal Experiments.

**Keywords:** Animal testing; Alternative's to animal studies; Bioethics; Clinical trials; Organs on chip

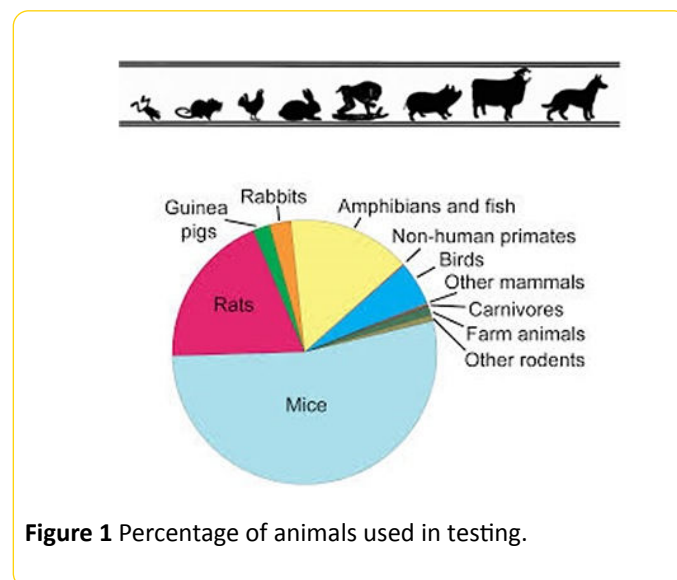
### Introduction

Animals are used to develop medical treatments, determine the toxicity of medications, check the safety of products destined for human use, and other biomedical, commercial, and health care uses. Research on living animals has been practiced since at least 500 BC.

An important area of biomedical research is the use of animal testing helps researchers to study numerous diseases. Animals will be artificially induced with disease's and conducts experiments. These diseases are artificially produced in laboratories in an attempt to mimic the human disease. This allows researchers to develop a new drug by testing on animals [1-4]. Researchers will use animal testing to obtain clues to how the disease develops in the body.

By analyzing animal models, scientists can learn what causes disease as well as how it develops and what aspects of genetics, the environment or diet contribute to the development of disease. For this research many different types of animals are used like mice, rabbit, guinea pig, sheep, albino-

rats, monkeys, primates, frogs etc., but mice is a common animal model. Less frequently, birds and fish are used (Figure 1).

**Figure 1** Percentage of animals used in testing.

The total examination of drug like how drugs are metabolized-including their (absorption, Distribution, metabolism and excretion) and how they affect other body systems and how they are excreted-is vital to ensuring the safety of medications. When drugs are being developed, their safety and efficacy needs to be ensured [5-7].

Supporters of animal testing say that it has enabled the development of numerous life-saving treatments for both humans and animals, that there is no alternative method for researching a complete living organism, and that strict regulations prevent the mistreatment of animals in laboratories [8-11].

Opponents of animal testing say that it is cruel and inhumane to experiment on animals, that alternative methods available to researchers can replace animal testing, and that animals are so different from human beings that research on animals often yields irrelevant results.

## Animal Testing's: How they Conduct?

### Selection of an animal

An animal model is one in which there are one or more observations per animal, and all factors affecting those observations are described including an animal additive genetic effect. During the animal experimentation the animals are often put into restrain tubes or other types of restraints so they have no way of escaping the pain. They generally perform Vivisection (cutting up of a living animal) animals are dissected, infected with diseases.

For practically every known human disease, researchers attempt to induce similar aspects of the disease in animals to create an animal "model" of that disease. Supposedly predictive, animals "are used with the aim of discovering and quantifying the impact of a treatment, whether this is to cure a disease or to assess the toxicity of a chemical compound." This is how animals are "used in the context of drug testing and studying human disease [12-15]. Areas of disease research involving animals include neurological, infectious, digestive, genetic, connective tissue, and chronic diseases. In these areas, animals are used as models of traumatic brain injuries, spinal cord injuries, congenital blindness, Parkinson's, Alzheimer's, AIDS, diabetes, cancer, obesity, and so on (Figure 2).



**Figure 2** Various animal models used in clinical trials.

In order to create these models, animals are subjected to invasive procedures, which can include surgeries, traumatic injuries, burns, force-feeding, blood draws, biopsies, food, water, and social deprivation, dart gun sedation, prolonged restraint, behavioral and environmental manipulations, viral and bacterial infections, and exposure to toxic drugs and chemicals [16-20]. Examples include, "creating heart attacks, heart failure, abnormal heart rhythms, strokes, and other cardiovascular traumas in monkeys, dogs, pigs, and other animals; inducing symptoms of migraines in cats and primates through brain stimulation and manipulation with chemicals; implanting electrodes into the intestines of dogs to induce motion sickness and vomiting; implanting electrodes into the brains and eyes of monkeys and cats to conduct neurological and vision experiments; and dropping weights onto rodents to produce spinal cord injuries and paralysis (Figure 3). Biological

differences between and within species require scientists to proceed with caution when interpreting the results of any experiment. Animals of different ages, sexes, developmental stages, and of different health status can all respond differently to experimental treatments [21-25].



**Figure 3** A mouse with an "ear" seeded from implanted cow cartilage cells growing on its back, the result of a 1997 experiment created by Joseph and Charles Vacant to explore the possibility of fabricating body parts for plastic and reconstructive surgery.

### Types of animals tests currently performed

Eye irritancy, acute toxicity, repeated dose toxicity, skin corrosivity/irritation, skin sensitization, pharmacokinetics/toxic kinetics and metabolism, dermal penetration, mutagenicity, carcinogenicity, reproductive and developmental toxicity, neurotoxicity, ecotoxicity, pyrogenicity.

## Alternatives to Animal Testing

No, there are not good alternatives to animal testing, because alternatives do not do a sufficient job of making sure products and medicines are safe. Not testing products at all will make it next to impossible to develop new products. Testing on humans is also not even testing. There are other things to do, but animal testing is the best way to get new products to markets.

Advanced microchips that use real human cells and tissues to construct fully functioning postage stamp-size organs allow researchers to study diseases and also develop and test new drugs to treat them. Progressive scientists have used human brain cells to develop a model "microbrain," which can be used to study tumors, as well as artificial skin and bone marrow. We can now test skin irritation using reconstructed human tissues (e.g. MatTek's EpiDerm), produce and test vaccines using human tissues, and perform pregnancy tests using blood samples instead of killing rabbits [26,27].

*In vitro* techniques, involving the study of isolated molecules, cells and tissues (which may come from humans, animals, micro-organisms or even plants). This gives useful information about interactions between molecules, within or between cells, or about organ function. In addition, use of computers and other high tech equipment can improve the efficiency of animal, non-animal or human research techniques. Animals are only used when the answers to scientific questions cannot be obtained in any other way. Broadly speaking, animals are used in research and testing

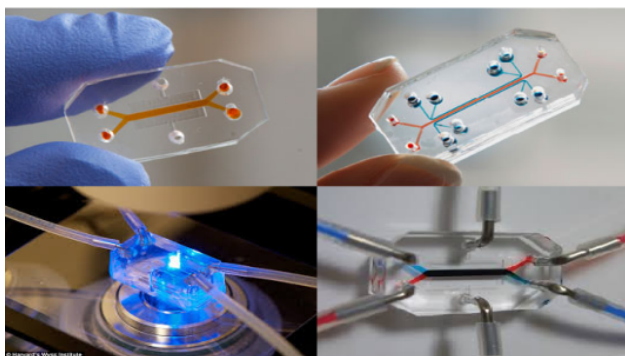
when it is necessary to see what happens in the whole living body. MRI and CAT Scans, DNA sequencing, advanced microscopes and X-rays all enable the medical world to look inside the human body.

Alternatives to animal testing are primarily based on biochemical assays, on experiments in cells that are carried out *in vitro* and on computational models and algorithms. These techniques are typically far more sophisticated and specific than traditional approaches to testing in whole animals, and many *in vitro* tests are capable of producing information about the biological effects of a test compound that are as accurate and in some cases more accurate than information collected from studies in whole animals. In addition, basic research is focusing increasingly on developing models based on organisms that are less expensive and more experimentally efficient than mammals.

Moreover regulators are fast moving towards accepting some of these *in vitro* tests as alternatives to final-stage carcinogenicity (cancer-causing) and genotoxicity (genetically damaging) drug trials. The other major alternative to animal research is computer modelling. Computing power has also opened new windows on the brain, with the advent of neural network modeling and non-invasive imaging. And, more indirectly, the explosion in easily accessible databanks on CD ROM and the Internet has allowed the reduction of duplicate animal testing via the pooling of data.

## Organ on Chip Technology

Institute researchers and a multidisciplinary team of collaborators are engineering microchips that recapitulate the microarchitecture and functions of living organs, such as the lung, heart, and intestine. These microchips, called organs-on-chips, could one day form an accurate alternative to traditional animal testing. Each individual organ-on-chip (**Figure 4**) is composed of a clear flexible polymer about the size of a computer memory stick that contains hollow microfluidic channels lined by living human cells.



**Figure 4** Organ-on-chip technology.

Because the micro devices are translucent, they provide a window into the inner workings of human organs. The Wyss institute team seeks to build ten different human organs-on-chips and link them together on an automated instrument to

mimic whole-body physiology. The instrument will control fluid flow and cell viability while permitting real-time observation of the cultured tissues and analysis of complex biochemical functions. This instrumented "human-on-a-chip" will be used to rapidly assess responses to new drug candidates, providing critical information on their safety and efficacy [28-31].

## Regulations on Animal Testing

New products often have to undergo a range of different tests to meet the requirements of regulatory authorities in different countries. Efforts are being made to harmonize requirements, which should lead to further reductions in laboratory animal use [5-8].

### Animal welfare act (AWA)

A federal law that addresses the standard of care animals receive at research facilities. Yet it excludes roughly 95% of the animals tested upon (such as rats, mice, birds, fish, and reptiles) and provides only minimal protection for the rest [4].

### Public health service (PHS)

The PHS oversees the Food and Drug Administration (FDA) and the centers for disease control and prevention (CDC). The CDC conducts infectious disease research on nonhuman primates, rabbits, mice, and other animals, while FDA requirements mean exploitation of animals in pharmaceutical research. The PHS requires only written assurance of compliance through the office of laboratory welfare (OLAW). When a facility is found deficient, OLAW takes little action, has no mandated follow-up, or on-site inspection.

### United States department of agriculture (USDA)

With only 120 inspectors, the USDA oversees more than 12,000 facilities involved in research, exhibition, breeding, or dealing of animals. Federally-owned facilities, like the department of defense, are not inspected by the USDA-which is the agency charged with enforcing the AWA through the animal and plant health inspection service (APHIS). Penalties for non-compliance are often virtually inconsequential in comparison to massive research revenues.

Other regulatory bodies charged with protecting animals, such as the association for assessment and accreditation of laboratory animal care (AAALAC) and mandatory institutional animal care and use committees (IACUC), are self-chosen, self-policing bodies with little or no punitive power. The IACUC must ensure that alternatives, including non-animal alternatives, have been considered, that the experiments are not unnecessarily duplicative, and that pain relief is given unless it would interfere with the study [11-13].

Today, there are laws which govern the use of animals in research, teaching and product testing in each Australian state. Although there is some variation in the statutory requirements of each state, the Australian code of practice for the care and

use of animals for scientific purposes, sets out the common framework of guiding principles [16].

## Conclusion

Progressive changes have been made in recent years in the principles and practice of animal testing. Although such principles of care and use of animals and alternative propositions to animal research have been welcomed as a step forwards by some animal welfare groups they have also been criticized as both outdated by current research, and of little practical effect in improving animal welfare. Opponents to any kind of animal research-including both animal-rights extremists and anti-vivisectionist groups-believe that animal experimentation is cruel and unnecessary, regardless of its purpose or benefit. There is no middle ground for these groups; they want the immediate and total abolition of all animal research. If they succeed, it would have enormous and severe consequences for scientific research. Animal experimentation is a contentious issue, but it boils down to two essential questions: does it work? and is it ethical? In fact, animal research has contributed to 70% of Nobel prizes for physiology/medicine. Without it, we would-medically speaking-be stuck in the dark ages.

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