



# AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

## A Review on Handling of Laboratory Animals

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### ABSTRACT

The aim of the present study was the handling of laboratory animals, their sources, routes of administration. Laboratory animals form the life-line of biomedical research and play a very vital role in the drug development programmes. There is an ever-growing need for better laboratory animal facilities for biomedical research, production of antisera, vaccines and novel drugs, especially to combat the dreadful AIDS and other diseases. The need to maintain the animals under standard animal husbandry conditions, to handle them gently and humanely, and limit unnecessary usage by strictly enforcing ethical considerations demands utmost attention. The present review includes information about housing and environmental condition, feeding techniques, safety handling for animals, routes of administration of drugs, guidelines of animal ethical committee, sources of animals, disposal of animals and also experimentation.

**Key words:** Biomedical Research, Dreadful, AIDS, Antisera, Vaccines.

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Received 14 April 2013, Accepted 29 April 2013

Please cite this article in press as: Patil H. *et al.*, A review on handling of laboratory animals. American Journal of PharmTech Research 2013.

## INTRODUCTION

### **Brief history of animal use:**

Since the beginning of human history man has tried to understand his environment by observation and also by experimenting with animals. It is generally said that first physiological investigations on animals started with observations of **Alcmene of Croton** (550-500 BC) and with **Galen** in Rome (130-201 AD) who performed physiological experiments on pigs, monkeys and dogs. The emergence of **Christian era** stopped any experimental approach in science and animal was then paid very little attention. Animal was considered without soul, sensitivity and consciousness and without interest for increase of knowledge. Consequently animal experimentation was considered no to lead to better knowledge of human body and medicine and investigations on animals were therefore banned for more than a millennium. Experimental medicine and biology recommenced in the 16<sup>th</sup> century with emphasis on anatomy (*Vesalius, Da Vinci*) and during the 17th century when also physiological functions were investigated (Harvey). Animals were considered as unconscious creatures and it was even assumed (Descartes) those animals could not suffer and that living mechanisms could be understood on purely mechanical principles. But it was accepted that animal experiments and their results could contribute to the development of medicine. Animal experimentation as such started in the 19th century with the works of **Claude Bernard** who emphasized the need of animal use to develop experimental medicine and physiology. He stated that animal experimentation was necessary for various scientific aims in fundamental research but also in applied medical research. Using that concept of animal experimentation eminent scientists discovered and tested their concepts in animals. Scientists like **Pasteur and Koch**, for instance stated the evidence of causal relationship between microorganisms and infectious diseases. From the beginning of the 20th century development of biomedical disciplines and the development of pharmaceutical industry caused a rapid increase in animal use in experiment. Animal experimentation was then widely used for multiple scientific aims and not only the total number of animals used in experiments increased but also the number of animal species. Domestic animals were mainly used until the end of the 19th century. From the 20th century rodent are the most used animals but also other mammalians species of birds, reptiles, amphibians and fishes species are being used<sup>1</sup>.

**A. Animal** – Any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes.

**B. Animal Facility** – Any and all buildings, rooms, areas, enclosures, or vehicles, including

satellite facilities, used for animal confinement, transport, maintenance, breeding, or experiments inclusive of surgical manipulation. A satellite facility is any containment outside of a core facility or centrally designated or managed area in which animals are housed for more than 24 hours<sup>2,3</sup>.

### Guiding Principles for the Care and Use of Laboratory Animal:



Fig.1. Mice



Fig.2. Administration of drug by IP route



Fig.3. Hand gloves

#### 1. Facilities for animal experiments:

Animal experiments should be conducted in well-controlled and administered institutions that are furnished with the necessary equipment.



Fig.4. Rabbit



Fig.5. Mice

#### 2. Handling of laboratory animals:

When handling animals, the investigators must have sufficient knowledge concerning maintenance methods and the animals' physiology, ecology, behavior, and breeding.

#### 3. Planning animal experiments:

When the investigators design a plan for animal research, the minimum number of experiments to achieve the purpose of the research should be considered. Sufficient consideration should also be given to the valid selection of animal models and experimental procedures. Moreover, laboratory animals must be treated with appropriate consideration in terms of their environment (cage size, number of animals per cage, temperature, humidity, lighting, etc.).

**4. Attention to animals in experiments:**

From the standpoint of animal welfare, sufficient effort should be made to minimize the anxiety and pain of laboratory animals during experiments.

**5. Care of animals after experiments;**

After an experiment is completed, the animals should be released from pain immediately. Procedures should be carried out in strict accordance with the notification issued from the Prime Minister's Office, No. 6, 1980: "Standards Relating to the Care and Management, etc. of Experimental Animals".

**6. Special attention to hazardous substances:**

Animal experiments using physically and chemically hazardous substances or pathogens should be carried out in strict accordance with appropriate caution, related regulations, etc. Special attention should be given to the maintenance of safety and to the prevention of environmental pollution. In this matter, investigators must work together with the administrative officers of their institutions.

**7. Others:**

Other research procedures should be carried out not only in strict accordance with the guidelines of the investigator's own institution, but also following the guidelines issued by the Science and International Affairs Bureau of the Japanese Ministry of Education, Culture, Sports, Science and Technology, No. 141, 1987: "Animal Experiments in Universities, etc." of the institution that the requirement<sup>3</sup>.

**a. The Need:**

The biomedical scientists generally work to unfold the complicated processes of life and to provide new measures for the health and welfare of the society i.e. the humans, the animals and the environment. There is need to provide them certain degree of freedom and adequate facilities to use animals wherever necessary. It is evident that certain life processes cannot be investigated without involving whole animal system. The in-vitro alternatives can only provide limited information. These cannot totally replace the animals in experiments. This is why the use of animals continues to be mandatory to meet the statutory regulatory requirements. At the same time, it is an obligation of the scientists to ensure that the experiments conducted on animals are rational and unavoidable, and no unnecessary pain or injury is inflicted on them and they are maintained in best possible environmental conditions. It is, therefore, necessary to have well-defined guidelines which will safeguard the pursuit of knowledge, the interest of society and the

welfare of animals<sup>4</sup>.

### **b. The Objectives:**

To provide guidelines for,

1. Housing, care, breeding and maintenance of experimental animals to keep them in physical comfort and good health and to permit them to grow, reproduce and behave normal.
2. Sources of experimental animals of known genetic, health and nutritional status.
3. Development of training facilities for scientists, technicians and other supportive staff for the care of animals and their use in experiments.
4. Acceptable experimental techniques and procedures for anesthesia and euthanasia.
5. Developing alternate in-vitro systems to replace animal experiments.
6. The constitution of institutional ethics committees, their functions and the legal and ethical obligations to ensure minimal and ethical use of animals<sup>3,4</sup>.

### **Current Status:**

The INSA guidelines are the only ones available at the National level and adopted by well established institutions in India for care and use of their laboratory animals. However, there is need to adopt these in all the research animal facilities. It is therefore essential that these guidelines are accepted as the national guidelines.

## **2. SOURCES OF EXPERIMENTAL ANIMALS:**

Animals for experiments should be procured by scientists from recognized animal facilities. The animals trapped from the wild, e.g. the monkeys, feral dogs and cats are also used in research as they are readily available and less expensive compared to colony bred animals. These wild and feral animals are generally quarantined and stabilized in animal facility before use in experiments. The health and genetic status of these animals are not known and therefore a careful screening during quarantine is necessary. The wild and feral animals should be acquired after due clearance from Institutional Animal Ethics Committees and through certified suppliers.

The only authentic source of getting right type of animals for research should be from recognized scientific animal facilities where the animal colonies of known genetic and health status are available. Such animals only can provide reliable results. The scientists should therefore insist upon getting defined animals through organized colonies eliminating unscrupulous traders, which not only supply poor stock of animals but also maintain these animals under most unethical and unhygienic conditions<sup>5</sup>.

### **3. LABORATORY ANIMAL HUSBANDRY AND MANAGEMENT:**

#### **i. Housing and Environment:**

Laboratory animals are very sensitive to their living conditions. It is important that they are housed in an isolated building located as far away from human habitations as possible and not exposed to dust, smoke, noise, wild rodents, insects and birds. The building, cages and environment of animal rooms are the major factors which affect the quality of animals.

In planning an animal facility the space should be well divided for various activities. The animal rooms should occupy about 50-60% of the total constructed area and the remaining area should be utilized for services such as stores (8-10%), washing (8-10%), office and staff (8-10%), machine rooms (4-5%) quarantine and corridors (12-15%).

The cages should be made of suitable metal (stainless steel, galvanized iron sheet/rods) or synthetic material (polypropylene/polycarbonate). They should be of suitable size for each species of animal and should have adequate arrangement for feeding and watering. They must be free from crevices, corners and sharp edges for easy cleaning and to avoid injury. The bedding should be of right material and sterilized before use. Common bedding materials used in India are paddy husk, saw dust, paper curing, dry grass and crushed corn cobs.

The environment of animal room (Macro-environment) and animal cage (Micro-environment) is an important factor on which the production and experimental efficiency of the animal depends. Since animals are very sensitive to environmental changes, sharp fluctuations in temperature, humidity, light, sound and ventilation should be avoided. A constant room temperature is essential, because variation in room temperature causes change in food and water intake. A change in temperature of 4°C can cause 10-fold alteration in biological responses. The temperature also affects fertility and lactation. Coupled with high humidity the increase in temperature causes ammonia built up. If the ventilation is not proper the high ammonia concentration causes respiratory irritation to both animals and attendants, predisposing them to infection by lowering their resistance. An effective ventilation system with 10-12 air changes per hour of 100% fresh air must be provided for animal rooms.

Light and sound are other important factors. The light intensity, the wave length and the photo cycle affect the health and behavior of the animals. Sudden and sharp sounds in the animal rooms disturb the health and behavior of animals and may give rise to ear damage, hypertension, cannibalism, etc<sup>5,6</sup>.

#### **ii. Breeding and Genetics:**

For initiating a colony, the breeding stock must be procured from a reliable/accredited source, ensuring that genetic make-up and health status of animals is known. In case of an inbred strain, the characters of the strain with their gene distribution and the number of inbred generation must be known for further propagation. The health status should indicate their origin, e.g. conventional, specific pathogen free or transgenic gnotobiotic or knock-out stock. The known nutritional status and feeding habits of the stock are also of advantage.

The animal colonies may be inbred or out bred. In case of inbred colonies the number of generation of brother x sister mating and latest genetic monitoring parameters for various markers should be known. Mutations or genetic contamination can be detected by using screening methods, such as histocompatibility (skin grafting), biochemical markers, coat color studies, mandibular biometry or immunological studies. Phenotypic visual characters may also sometime provide clue of genetic contamination<sup>7, 8</sup>.

### **iii. Transgenic/Knock-out Animals:**

Transgenic animals are those animals into whose germ line foreign gene(s) have been engineered, whereas knock-out animals are those whose specific gene(s) have been disrupted leading to loss of function. These animals can be bred to establish transgenic animal strains. Transgenic animals are used to study the biological functions of specific genes, to develop animal models for diseases of humans or animals, to produce therapeutic products, vaccines and for biological screening, etc.

These can be either developed in the laboratory or procured for R&D purpose from scientific/academic institution or commercial firms, generally from abroad<sup>12</sup>.

### **iv. Nutrition and Feeding:**

The results of an experiment are likely to be influenced by co-existence of nutritional deficiencies and imbalance. It is, therefore, essential that laboratory animals are maintained on a balanced diet based on nutritional requirements of each species. Special care is needed on nutritional elements, ingredients used in diet, and feeding practices. A balanced diet should contain protein, carbohydrates, fat, minerals, vitamins, roughage and water in required proportions for each species of animal<sup>6, 9</sup>.

Only quality ingredients should be used in a diet and they should be free from dust, moulds, fungi and other contaminants. Each animal must get required quantity of feed, based on animal maintenance and production requirements.

The feed should be palatable so that it is consumed in adequate quantity by the animals. Any

undesirable odor always causes under consumption resulting in nutritional deficiency in the animals.

No drug, hormone or antibiotic should be added in the feed as these are likely to disturb the normal metabolism of the animals and produce biased results.

The ingredients and the prepared feed must be stored and handled carefully so as to avoid any contamination. The food must be of right consistency and should be presented to animals in proper type of hoppers to avoid wastage. In some cases the feed may be divided in 2-3 meals during the day.

Pelleted feeds balanced for different species of animals are now available commercially. These are easy to procure and use without wastage. However one has to be careful on quality of the feed from batch to batch. It should be obligatory on manufacturer to mark each bag with the type of food, date of manufacture, the batch number, the ingredients used and chemical composition. Random chemical analysis must be carried to for major nutrients to monitor the quality of food from time to time.

Clean, chlorinated water should be available to the animals *ad lib*<sup>6, 12, 20</sup>.

#### **v. Hygiene and Disease Control:**

The building for housing the animals should be provided with barriers to control the entry of contamination into the building through men, material and wild animals. Strict barriers should be provided to avoid the entry of wild rodents, birds, insects and pests. Visitors and service staff should be allowed entry with care and when necessary.

On the exit side an efficient monitoring service should be established to monitor the prevalence of any infection in the colony. A regular medical checkup of the staff, postmortem of dead and sacrificed animals and screening of waste material of the rooms is essential<sup>16</sup>.

#### **vi. Personnel and Training:**

The selection of animal facility staff, particularly the staff working in animal rooms or involved in transportation, is a critical component in the management of an animal facility.

The staff must be provided with all required protective clothing (masks, aprons, gloves, gumboots, etc.) while working in animal rooms. Facilities should be provided for change over with lockers, wash basins, toilets and bathrooms to maintain personal hygiene. It is also important that a regular medical check-up is arranged for the workers to ensure that they have not picked up any zoonotic infection and also that they are not acting as a source of transmission of infection to the animals. He should ensure that persons working in animal house don't eat,

drink, smoke in animal room and have all required vaccination, particularly against tetanus and other zoonoses.

Initial in-house training of staff at all levels is essential. A few weeks must be spent on the training of the newly recruited staff, teaching them the animal handling techniques, cleaning of cages and importance of hygiene, disinfection and sterilization.

A course should address the under mentioned topics:

- a) Biology and husbandry of laboratory animals
- b) Genetic make-up
- c) Microbiology and diseases
- d) Health-hazards in the animal house
- e) Anesthesia, analysis and experimental procedures
- f) Alternatives to animal use
- g) Ethical aspects and legislation

The training courses and workshops may also be organized for the senior level biological scientists to evoke awareness among them about the use of animals in research, alternatives available and the ethical and legal provisions in regard to use of animals. This is particularly important care and management for the supervisory staff and veterinarians exists in the country.

The national level training programmes of following type are essentially required<sup>17,18</sup>.

#### **vii. Records and Evaluation:**

Good quality animals are those which are free from disease. Animal of a specified strain should also have all the characteristics of that strain, i.e. they should be genetically anthesised. The results of regular monitoring of parameters of genetic purity must be scrupulously recorded.

Proper record-keeping is extremely important and vital for an animal facility. The forms should be simple but complete and preferably computer compatible. Too exhaustive and unnecessary recording should be avoided as these are not useful. Records of breeding and experimentation and deaths of all experimental animals at various stages are essential.

Receipt and issue of food and other stores should be recorded. Log books of various machines such as incinerator, boilers, air-conditioning plant should be maintained. Monthly and annual reports of the activities should be prepared and reviewed for evaluation of work and future planning<sup>14</sup>.

#### **viii. Experimentation and Veterinary Care:**

The experimental animal units should generally be looked after by qualified investigators. These

units must have adequate housing and technical facilities for experiment and post-operative care. The equipment provided in the experimental unit should be appropriate for the needs of the experiments. No technique should be used which may cause avoidable discomfort to the animals.

The post-operative holding rooms and cages should be comfortable and such animals should remain under the care and supervision of an experienced scientist or a qualified veterinarian.

The person actually incharge of animal facility should preferably be a veterinarian or a person qualified in laboratory animal science. In any case an experienced veterinarian must be readily available in an animal holding for health care, monitoring, diagnosis and treatment of diseases and injuries. A veterinarian could also be helpful to investigators in animal anaesthesia and surgery<sup>17</sup>.

#### **4. LABORATORY ANIMAL HUSBANDRY AND MANAGEMENT:**

The transport of animals from one place to another is very important and must be undertaken with care. The main considerations for transport of animals are the mode of transport, the containers and the animal density in cages, food and water during transit, protection from transit infections, injuries and stress.

The mode of transport of animals depends on the distance, seasonal and climatic conditions and the species of animals. Animals can be transported by road, rail or air taking into consideration above factors. In any case the transport stress should be avoided and the containers should be of an appropriate size so as to enable these animals to have a comfortable, free movement and protection from possible injuries. The food and water should be provided in suitable containers or in suitable form so as to ensure that they get adequate food and more particularly water during transit. The transport containers (cages or crates) should be of appropriate size and only a permissible number of animals should only be accommodated in each container to avoid overcrowding and infighting<sup>10</sup>.

#### **5. ANAESTHESIA AND EUTHANASIA:**

The scientists should ensure that the procedures which are considered painful are conducted under appropriate anaesthesia as recommended for each species of animals. It must also be ensured that the anaesthesia is given for the full duration of experiment and at no stage the animal is conscious to perceive pain during the experiment. If at any stage during the experiment the investigator feels that he has to abandon the experiment or he has inflicted irreparable injury, the animal should be sacrificed by overdose of anaesthetic. Neuromuscular blocking agents must not be used without adequate general anaesthesia.

In the event of a decision to sacrifice an animal on termination of an experiment or otherwise an approved method of euthanasia should be adopted and the investigator must ensure that the animal is clinically dead before it is sent for disposal.

**a. Anaesthesia:**

Unless contrary to the achievement of the results of study sedatives, analgesics and anaesthetics should be used to control pain or distress under experiment. Anaesthetic agents generally affect cardiovascular, respiratory and thermo-regulatory mechanism in addition to central nervous system.

Before using actual anaesthetic the animal is prepared for anaesthesia by overnight fasting and using pre-anesthetics, which block parasympathetic stimulation of cardio-pulmonary system and reduce salivary secretion. Atropine is most commonly used anti-cholinergic agent. Local or general anaesthesia may be used, depending on the type of surgical procedure.

Local anaesthesia: Local anesthetics are used to block the nerve supply to a limited area and are used only for minor and rapid procedures. This should be carried out under expert supervision for regional infiltration of a surgical site, nerve blocks and for epidural and spinal anaesthesia.

General Anaesthesia: A number of agents are used as inhalants. General anesthetics are also used in the form of intravenous or intra-muscular injections such as barbiturates. Species characteristics and variation must be kept in mind where using an anaesthetic. Side-effects such as excessive salivation, convulsions, excitement and disorientation should be suitably prevented and controlled. The animal should remain under veterinary care till it completely recovers from anaesthesia and post operative stress<sup>10, 15</sup>.

**b. Euthanasia:**

Euthanasia means “easy death” and is resorted to in events where an animal is required to be sacrificed on termination of an experiment or otherwise for ethical reasons. The procedure should be carried out quickly and painlessly in an atmosphere free from fear or anxiety. For accepting of a euthanasia method as humane it should have an initial depressive action on the central nervous system for immediate insensitivity to pain. The choice of a method will depend on the nature of study, the species of animal and number of animals to be sacrificed. The method should in all cases meet the following requirements:-

- (a) Death, without causing anxiety, pain or distress with minimum time lag phase.
- (b) Compatibility with the purpose of study and minimum emotional effect on the observer and operator.

- (c) Location should be separate from animal rooms and free from environmental contaminations.
- (d) Method should be reliable, reproducible and safe to the personnel involved.
- (e) Simple and economical.

It is recommended that tranquilizers be administered to larger species such as monkeys, dogs and cats before a euthanasia procedure.

A number of euthanasia methods have been recognized humane which could be physical, use of inhalant gases, injectable drugs and general anaesthetics in heavy dose<sup>10, 12</sup>

## **6. DISPOSAL OF ANIMAL CARCASSES:**

All animal carcasses whether healthy, infectious or radioactive, must be packed in polythene bags before sending them for disposal. All healthy or infectious animals may be buried deep in the ground covered with lime and disinfectants or burnt in an incinerator. Animals with radioactive material should be packed in double polythene bags and dumped in a special pit meant for this purpose. Details of the pit can be obtained from Bhabha Atomic Research Centre, Mumbai. Strict precautions should be taken to safeguard the health of the personnel handling infectious and radioactive material and in no case these should be brought out in open containers for disposal.

The investigators working with infectious and radioactive material must ensure that the animals are properly disposed off on termination of their experiment and that infection is not transmitted to other animals in the room or to the personnel involved in handling such animals during the experiment and also at the time of disposal. The staff handling such animals for disposal must be apprised of the hazards involved in their job and protective clothing, gloves and mask must be provided to them for their personal safety<sup>13</sup>.

## **7. LABORATORY ANIMAL ETHICS:**

All scientists working with laboratory animals must have a deep ethical consideration for the animals they are dealing with. From the ethical point of view it is important that such considerations are taken care at the individual level, at institutional level and finally at the national level.

Individually each investigator has an obligation to abide by all the ethical guidelines laid down in this regard at institutional level. The Head of the Institution, maintaining animals for scientific experiments, should constitute an Animal Ethics Committee for experimentation to ensure that all experiments conducted on animals are rational, do not cause undue pain or suffering to the animals and only minimum number of animals are used.

Animal Ethics Committee should be well defined,

An Animal Ethics Committee should include: a senior biological scientist of the Institute, two scientists from different biological disciplines, a veterinarian involved in care of animals, the scientist in charge of animal facility, a scientist from outside the institute, a non-scientific socially aware member and a member or nominee of appropriate regulatory authority of Govt. of India. A specialist may be co-opted while reviewing special projects using hazardous agents such as radioactive substance and deadly micro-organisms etc. The investigator may also be called in for any clarification, if required.

The Animal Ethics Committee has to examine all projects involving use of animals before implementation, to ensure that minimum number of animals is used in the project and the ethical guidelines are strictly adhered to. It will also examine that the scientists and technicians handling animals possess adequate skill to perform the experiment. All animals will be maintained under standard living conditions and experiments will be conducted with care. All invasive experiments will be conducted under proper anaesthesia and on termination of an experiment; the animal will be humanely sacrificed under anaesthesia. Before disposal it must be ensured that the animal is clinically dead<sup>3, 14</sup>.

**a. Ethical Guidelines for Use of Animals in Scientific Research:**

1. Animal experiments should be undertaken only after due consideration of their relevance for human or animal health and the advancement of knowledge.
2. The animals selected for an experiment should be of an appropriate species and quality, and minimum number should be used to obtain scientifically and statistically valid results.
3. Investigators and other personnel should treat animals with kindness and should take proper care by avoiding or minimizing discomfort, distress or pain.
4. Investigators should assume that all procedures which would cause pain in human beings may cause pain in other vertebrate species also (although more needs to be known about the perception of pain in animals).
5. Procedures that may cause more than momentary pain or distress should be performed with appropriate sedation, analgesia or anaesthesia in accordance with accepted veterinary practice. Surgical or other painful procedures should not be performed on unanaesthetized animals.
6. At the end of, or when appropriate during an experiment, the animal that would otherwise

suffer severe or chronic pain, distress, discomfort, or disablement that cannot be relieved or repaired should be painlessly killed under anaesthesia.

7. The best possible living condition should be provided to animals used for research purpose. Normally the care of animals should be under the supervision of a veterinarian or a person having adequate experience in laboratory animal care.
8. It is the responsibility of the investigator to ensure that personnel conducting experiment on animals possess appropriate qualifications or experience for conducting the required procedures. Adequate opportunities have to be provided by the institution for in service training for scientific and technical staff in this respect.
9. In-vitro systems to replace the number of animals should be used wherever possible<sup>3, 16</sup>.

## **8. EXPERIMENTATION OF ANIMALS:**

Nothing contained in this Act render unlawful the performance of experiments (including experiments involving operations) on animals for the purpose of advancement by new discovery of physiological knowledge or of knowledge which will be useful for saving or for prolonging life or alleviating suffering or for combating any disease, whether of human beings, animals or plants<sup>16</sup>.

1. If at any time, on the advice of the board, the Central Government is of opinion that it is necessary so to do for the purpose of controlling and supervising experiments on animals, it may, by notification in the official Gazette, constitute a Committee consisting of such number of officials and non-officials, as it may think fit to appoint thereto.
2. The Central Government shall nominate one of the members of the committee to be its Chairman.
3. The Committee shall have power to regulate its own procedure in relation to the performance of its duties.
4. The funds of the committee shall consist of grants made to it from time to time by the Government and of contributions, donations, subscription, bequests, gifts and the like made to it by any person.
6. The committee may constitute as many sub-committees as it thinks fit for exercising any power or discharging any duty of the committee or for inquiring into or reporting and advising on any matter which the committee may refer.
7. A sub-committee shall consist exclusively of the members of the committee. Subject to the control of the Central Government, the committee may appoint such number of officers and

other employees as may be necessary to enable it to exercise its powers and perform its duties, and may determine the remuneration and other terms and conditions of service of such officers and other employees<sup>19, 20</sup>.

It shall be the duty of the committee to take all such measures as may be necessary to ensure that animals are not subjected to unnecessary pain or suffering before, during or after the performances of experiments on them, and for that purpose it may, by notification in the Gazette of India and subject to the condition of previous publication make such rules as it may think fit in relation to the conduct of such experiments.

In particular, and without prejudice to the generality of the foregoing power, such rules may provide for the following matters, namely,

- a. The registration of persons or institutions carrying on experiments on animals.
- b. The reports and other information which shall be forwarded to the committee by persons and institution carrying on experiments on animals<sup>21</sup>.

8. In particular, and without prejudice to the generality the foregoing power, rules made by the committee shall be designed to secure the following objects namely:

That in cases where experiments are performed in any institution, the responsibility therefore is placed on the person in charge of the institution and that, in cases where experiments are performed outside an institution by individuals; the individuals are qualified in that behalf and the experiments are performed on their full responsibility.

That experiments are performed with due care and humanity, and that as far possible experiments involving operations are performed under the influence of some anaesthetic agent of sufficient power to prevent the animals feeling pain.

That animals which, in the course of experiments under the influence of anaesthetics, are so injured that their recovery would involve serious suffering, are ordinarily destroyed while still insensible.

That experiments on animal are avoided wherever it is possible to do so, as for example, in medical schools, hospitals, colleges and the like, if other teaching devices such as books, models, films and the like may equally suffice.

That experiments on larger animals are avoided when it is possible to achieve the same results by experiments upon small laboratory animals like guinea-pigs, rabbits, frogs and rats.

That, as far possible, experiments is not performed merely for the purpose of acquiring manual skill. That animals intended for the performance of experiments are properly looked after both before and after experiments<sup>22</sup>.

9. In making any rules under this section, the Committee shall be guided by such directions as the Central Government (consistently with the objects for which the Committee is set up) may give to it, and the Central Government is hereby authorized to give such directions.
10. All rules made by the committee shall be binding on all individuals performing experiments outside institutions and on persons in charge of institutions in which experiments are performed.
11. For the purpose of ensuring that the rules made by it are being complied with, the committee may authorize any of its officers or any other person in writing to inspect any institution or place where experiments are being carried on and report to it as a result of such inspection and any officer or person so authorized may: Enter at any time considered reasonable by him and inspect any institution or place in which experiments on animals are being carried on, and Require any person to produce any record kept by him with respect to experiments on animals<sup>19</sup>.
12. If the Committee is satisfied, on the report of any officer or other person made to it as a result of any inspection under section 18 or otherwise, that the rules made by it under section 17 are not being complied with by any person or institution carrying on experiments on animals, the committee may, after giving an opportunity to the person or institution of being heard in the matter, by order, prohibit the person or institution from carrying on any such experiments either for a specified period or indefinitely, or may allow the person or institution to carry on such experiments subject to such special conditions as the Committee may think fit to impose.

If any person:

- Contravenes any order made by the committee under section 19, or
- Commits a breach of any condition imposed by the Committee under that section. He shall be punishable with fine which may extend to two hundred rupees, and when the contravention or breach of condition has taken place in any institution, the person in charge of the institution shall be deemed to be guilty of the offence and shall be punishable accordingly<sup>3, 24</sup>.

## **9. Routes of Administration:**

### **Selection of a Route:**

Substances are administered to laboratory animals by a wide variety of routes. A key factor determining the route selected is whether the agent is being administered for a local or systemic

(either enteral [through the digestive tract] or parenteral [outside the digestive tract]) effect. Parenteral administration methods typically produce the highest bioavailability of substances because these methods avoid the first-pass effect of hepatic metabolism, which occurs commonly with orally administered chemicals and therapeutics. Parenteral routes also circumvent some of the unpredictability associated with enteral absorptive processes. Furthermore, regulatory requirements may influence the selection of a particular route, depending on the purpose of the study (for example, nonclinical safety testing, in which the route of delivery to animals should closely resemble the projected route of administration to humans).<sup>18,19</sup>

A substance may be given into the mouth (orally) or delivered directly into the stomach (gastric gavage); delivered into a blood vessel (intravenous); delivered onto, into, under, or across the skin or into a muscle (epicutaneous, intradermal, subcutaneous, transdermal, and intramuscular administration, respectively); instilled onto or into the eye (transcorneal or intraocular, respectively); into the brain (intracerebral) or the space surrounding the dura mater or that surrounding the distal spinal cord (epidural and intrathecal, respectively); administered into the peritoneal cavity (intraperitoneal), directly into the marrow cavity (intraosseous); sprayed into the nose for absorption across the nasal mucous membranes or into the lungs (intranasal) or delivered into the lungs by direct tracheal instillation (intratracheal) or inhalation; or administered by a range of less common routes using other body orifices, surgical exposures, and species-specific anatomic features<sup>21</sup>.

In laboratory species, many of the commonly used methods of delivery require restraint, sedation, or general anesthesia. The use of such manipulations should be considered when selecting the administration route to refine procedures so that they are less invasive or aversive to the animals. In addition, each route has advantages and disadvantages that should be considered depending on the final effect to be achieved, and ultimately the route selected will markedly affect the pharmacokinetics of the substance. This pharmacokinetic effect of route of administration is exemplified by naloxone, a potent opioid antagonist. Given intravenously, naloxone rapidly reverses opioid-induced central nervous system depression but when given enterally, the drug can be used to treat opioid-induced bowel stasis without antagonism of the analgesic effects of systemically administered opioid. Another consideration regarding once-daily administration of substances to animals is their chronobiology or circadian rhythm. Depending on the aims and objectives of the experiment, the timing of substance administration may need to be considered carefully, for example, to administer a therapeutic when an animal's is most or least metabolically active to induce or minimize toxicity<sup>22</sup>.

**Enteral Administration:**

Administration of substances directly into the mouth, admixed in diet or other foodstuffs, or by or gastric or nasogastric gavage is common in laboratory animal medicine and research system<sup>23</sup>.

**Intravenous Administration:**

The intravenous route of delivery is the most efficient means of delivering substances to animals because it bypasses the need for solute absorption<sup>24</sup>.

**Administration to Skin and Muscle**

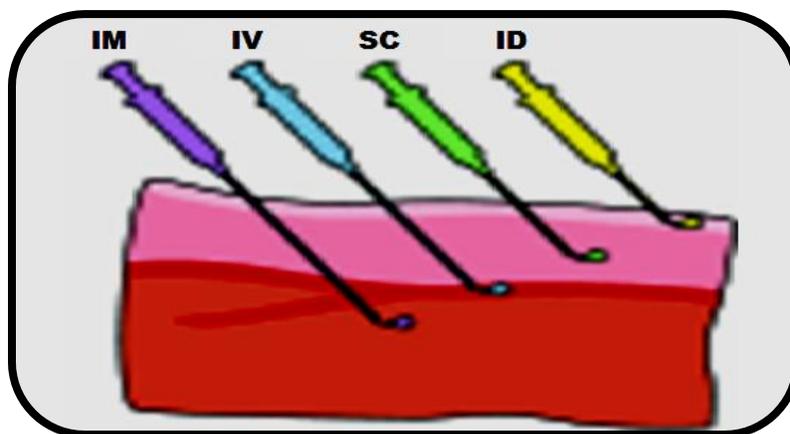
Some substances can be administered directly to the skin surface (epicutaneous administration) for a topical affect<sup>11</sup>.

**Epidural and Intrathecal Administration:**

For rapid effects of substances on cerebrospinal tissues or meninges, substances can be administered into the epidural or subarachnoid (intrathecal) space of the spinal cord<sup>11, 12</sup>.

**Intranasal, Intratracheal, and Inhalational Administration:**

In research settings, animals generally are sedated or anesthetized for the intranasal and intratracheal routes of delivery, to minimize struggling and sneezing. Volumes administered intranasally are small compared with those of other routes to minimize the potential for suffocation and death. The technique may not be useful in animals with signs of rhinitis or conjunctivitis. Intranasal delivery is readily taught and simple to perform in an anesthetized animal. Substances administered by this route should be nonirritating to minimize sneezing, post treatment rhinitis, and epistaxis<sup>24</sup>.



**Fig. 6. Various routes of administration**

**CONCLUSION:**

The present literature is useful tool to study information about housing and environmental condition for various animals, feeding techniques, safety handling for animals, routes of

administration of drugs, guidelines of animal ethical committee, sources of animals, disposal of animals and also experimentation.

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