

Animal Experimentation and Ethics in India: The CPCSEA Makes a Difference

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Summary — The Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) is a statutory body formed by the Act of the Indian Parliament under the *Prevention of Cruelty to Animals Act 1960*. Formed in 1964, it was revived in 1998, under the committed chairpersonship of Maneka Gandhi. In the last two years, the CPCSEA has bettered the life of the animals in laboratories across India. This committee is composed of members of the scientific community, regulatory authorities and animal activists. The CPCSEA functions with a brilliant network of volunteers who liaise with the laboratories. For the first time in India: over 665 laboratories are registered with the CPCSEA; Institutional Animal Ethics Committees (IAECs) are constituted in every laboratory, which are only empowered to approve research project proposals that use rats, mice, guinea-pigs or rabbits; every project that uses canines, ovines, bovines or non-human primates can only be conducted if approved by the panel of scientific experts constituted for this purpose; guidelines on laboratory animal care and practice have been formulated and enforced; a protocol for the production of immunobiologicals from equines has been formulated and ratified by the Supreme Court of India; the CPCSEA has been deliberating on alternatives and working out modalities to introduce alternatives in basic/regulatory research and education, in keeping with the international arena; the CPCSEA, to date, has rehabilitated and homed over 300 dogs, 150 equines, 200 non-human primates and several cattle, cats, birds, rabbits and mice; the CPCSEA proactively trains and guides scientific and non-scientific personnel on issues of alternatives and laboratory animal welfare; and the CPCSEA has fought legal issues on laboratory animal care and use and have had verdicts that favoured alternatives and animal welfare.

The greatness of a nation and its moral progress can be judged by the way its animals are treated.
Mahatma Gandhi

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Introduction

Article 51A(g) of the *Constitution of India* reads that it is the fundamental duty of every citizen of India “to protect and improve the natural environment including forests, lakes, rivers and wildlife and to have compassion for living creatures”. In 1960, the *Prevention of Cruelty to Animals Act* was promulgated by an act of the Indian Parliament. Section 15 of the Act provides for constitution, by the Central Government of India, of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), to supervise and control experiments on animals.

Section 17(1) of the *Prevention of Cruelty to Animals Act 1960* lays down as the duty of the committee to take all such measures as may be necessary to ensure that animals are not subject to unnecessary pain or suffering before, during or after the performance of experiments on them. The Act defines that the rules made by the com-

mittee shall be designed to secure the following objectives.

1. That, in cases where experiments are performed in any institution, the responsibility 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 must be qualified, and the experiments are performed under their full responsibility.
2. That experiments are performed with due care and humanity, and that, as far as possible, experiments involving operations are performed under the influence of some anaesthetic of sufficient power to prevent the animals from feeling pain.
3. That, in the course of experiments performed under the influence of anaesthetics, if an animal becomes so injured that recovery would involve serious suffering, it will be euthanised while still anaesthetised.

4. That experiments on animals are avoided wherever it is possible to do so; e.g. in medical schools, hospitals, colleges, etc., if other teaching devices such as books, models, films and the like may equally suffice.
5. That experiments on larger animals are avoided when it is possible to achieve the same results by experiments upon small laboratory animals, such as guinea-pigs, rabbits, frogs and rats.
6. That as far as possible, experiments are not performed merely for the purpose of acquiring manual skill.
7. That animals intended for the performance of experiments are properly looked after both before and after experiments.
8. That suitable records are maintained with respect to experiments performed on animals.

Hence, in 1998, on the initiative of Smt. Maneka Gandhi, Chairperson, CPCSEA (fourth author of this paper), for the first time in India the *Breeding of and Experiments on Animals (Control and Supervision) Rules* were officially notified in the *Gazette of India* by the CPCSEA and they became the first ever effective rules governing experimentation on animals in India.

For over three decades since the first CPCSEA was constituted in 1964, precious little was done to alleviate the suffering of laboratory animals in India, and apparently, the previous committees failed to impose the laws and lacked effective methods for the implementation, and a dismal scenario continued in laboratories across India. Gruesome acts of cruelty in the guise of science and ignorance were perpetrated on animals, during which the degree of sentience, ethics, scientific rationale or purpose were of least concern. A large majority of the animal houses continued to be in an abysmally poor condition. Non-existent animal houses, sheds and store rooms, dark and damp dungeons were referred to as animal houses. Moribund animals were researched upon; old and sick non-human primates were caged in isolation in rusty cages for 20 years or more; animals were regularly picked off the street or from the wild; others were bludgeoned or bled to death; euthanasia and analgesia were scantily practised, good laboratory practices were unknown and neither law nor science were revered.

In the last two years, India has, for the first time, seen an ambitious clean-up mission of laboratories that use animals, due to the efforts of the CPCSEA, under the chairmanship of Smt. Maneka Gandhi. In a country where scientists were looked upon as high priests, and laboratories were considered the *sanc-tum sanctorum* of research, the climb was steep and difficult.

Hundreds of animals, which were found in laboratories in acute stages of physiological and psychological trauma, were rescued and rehabilitated. Laboratories were cleaned, and good laboratory practices are being introduced. The capture and use of domestic, impounded and wild animals has been outlawed and categorically stopped. The wisdom of the alternatives concept has been introduced to a nation ignorant of, and disinterested in, the science of *reduction, refinement* and *replacement*. Careful restrictions were introduced in the use of vertebrates in research and the use of animals in contract research with multinationals outside India. Four-hundred honorary workers throughout the country liaise with the CPCSEA, and they represent the committee in each of the institutes, inspecting, reporting and helping implement the rules governing the use and care of laboratory animals. The success of the CPCSEA in the last two years has been largely due to the efforts of these honorary workers, who have volunteered to work for the cause of animals and have weathered physical assault, lock ups and verbal abuse to carry the mission forward.

The CPCSEA, for the first time in India, has introduced the following changes in laboratory animal use and care.

665 laboratories register with the CPCSEA

It has been made mandatory by law that every institution that uses animals for the purpose of education, biomedical research and/or regulatory purposes, or uses animals for the production of vaccines and immunobiologicals must register with the committee. When registered with the CPCSEA, they are constantly monitored, and their animal housing facilities are inspected. Currently, 86 medical universities, 80 pharmacy colleges, 35 veterinary universities and 464 institutions that use animals for biomedical/regulatory research, have registered with the CPCSEA.

Institutional Animal Ethics Committees (IAECs) constituted in registered laboratories

An eight-member IAEC that includes a nominee of the CPCSEA is constituted in every registered institute as a necessary prerequisite. All research project proposals using small animals, such as rats, mice, rabbits or guinea-pigs, have to be approved by the IAEC before initiation. Every member of the IAEC has the right to question/disapprove of a project; unapproved proposals are referred to a sub-committee of experts for scrutiny and possible approval. The IAEC cannot approve research projects on large animals, such as dogs, cats, non-human primates, cattle, goats, sheep, and so forth, and can only recommend the same to the sub-com-

mittee of the CPCSEA, which, alone, has the power to approve projects on higher vertebrates.

Constitution of an expert sub-committee for scrutiny and approval of research projects on large animals

An expert sub-committee, headed by one of India's most senior and reputed scientists, Dr Ranjit Roy Chaudhury, will scrutinise and study every research project on large animals before consideration for approval. In the last two years, eight meetings of the sub-committee have been held, and less than 30% of the proposals were found to be worthy of approval. Thus, hundreds of animals that would otherwise have been used in futile scientific research have been saved by virtue of the stringent scrutiny and control of this sub-committee.

The observations of this sub-committee of the CPCSEA have been that:

- Due to their high level of sentience, the use of large animals in research requires a deep deliberation. Their use can be justified only if positive results based on the same hypothesis have been obtained using small animals. The CPCSEA has observed that most laboratories in India that use non-human primates do not strictly adhere to this practice and simultaneously work on both small and large animals, despite the fact that Rule 17(e) of the *Prevention of Cruelty to Animals Act 1960* makes mandatory working with small animals first.
- 90% of the large animal laboratories have *ad hoc* arrangements to house non-human primates, canines, sheep, goats, buffaloes, horses and so forth, and do not have scientifically planned animal houses or adhere to scientific/ethical norms of experimentation.
- Several laboratories have been observed to hold surplus animals and to design research projects specifically to use these animals.
- Large animals that carry several zoonotic diseases have been observed being procured by institutes from open markets and small farmers, without knowledge/screening of health status before using them for experiments.
- In several laboratories throughout the country, dogs, horses, sheep and monkeys in states of ill health, as well as geriatric animals, were observed to be subjected to severe and invasive research processes.
- Research project proposals involving large animals do not include expenses for their maintenance,

housing and care; hence, they have been observed to be neglected in terms of their health, hygiene and basic medical attention.

The CPCSEA guidelines for laboratory animal facilities

An expert committee, chaired by the Secretary, Department of Biotechnology, Government of India, and including representatives of the Indian Council of Medical Research, the Indian Council of Agricultural Research, the National Institute of Immunology, the Central Drug Research Institute, the Indian Institute of Science, the All India Institute of Medical Sciences, the Indian Veterinary Research Institute, Ranbaxy Laboratory Ltd. and the CPCSEA, was constituted with the goal of promoting the humane care of animals used in biomedical and behavioural research and testing. The basic objective of the committee is to provide specifications that will enhance animal well-being, as well as quality, in the pursuit of advancement of biological knowledge that is relevant to humans and animals.

These guidelines, referred to as the *CPCSEA Guidelines for Laboratory Animal Facility*, were ratified by the national committee of the CPCSEA in 2002, and they have been made mandatory for all research laboratories that use animals. The guidelines cover aspects of veterinary care, animal procurement, quarantine, stabilisation and separation, surveillance, diagnosis, treatment and control of disease, animal care and technical personnel, durations for which animals can be used in experiments, physical restraint, physical plant, social environment, activity, food, sanitation and cleanliness, waste disposal, pest control, emergency, weekend and holiday care, recordkeeping, Standard Operating Procedures/Guidelines, anaesthesia (including euthanasia), and a section on transgenic animals.

The CPCSEA protocol for the care and management of equines used in the production of immunobiologicals

In India, there are eight institutes that use equines for the production of immunobiologicals, mainly anti-snake venom sera. During the initial visits of the CPCSEA to these institutes, there was shocking and compelling evidence of the most egregious and unscientific methods in practice in terms of animal welfare and care, and it was observed that the ethical issues of animal use were of absolutely no concern to any of these scientific institutes. Blind and lame animals were regularly bled for 12–18 litres of blood at monthly intervals. In the Haffkine Institute, Pune, the authorities have built a memorial for a horse that has donated 5000 litres of blood. Euthanasia was unknown or not practised, and animals were “bled to

death" in the most savage manner. Pregnant mares were injected with venom and bled, and foals were born blind and deformed. Animals died painful deaths in large numbers, due to liver rupture, unnoticed and uncared for. An unscientific and unethical culture reigned in these institutes, and the voiceless animals have languished in pain and died miserable deaths over several decades.

Veterinarians were found to be ignorant of equine care and practice. Bleeding was done in open sheds and stables; bleeding rooms and aseptic conditions were not a part of the bleeding procedure. Oversized, crude, metallic cannulae were unhesitatingly used, leading to open wounds and abscesses.

In this dismal period of July–August 2001, the CPCSEA intervened to introduce scientific and ethical norms of practice. The CPCSEA was forced to issue directives to suspend bleeding to improve the health of the horses used, and to rehabilitate several sick and old equines.

Sensing the need for a standard document on the subject, the CPCSEA has prepared a scientific protocol for animal care and use in the production of biologicals from equines, and this need has been further reinforced by the Supreme Court of India, which led to the Honorable Court's direction that the protocol formulated by the CPCSEA must be followed and must be made mandatory throughout the country in institutes that use equines.

A 19-member committee, headed by Dr Kiran Singh, Deputy Director General (Animal Sciences), was responsible for the formulation of this protocol. The protocol covers aspects of general requirements of equines, selection and quarantine, housing and hygiene, nutrition and feeding, endoparasite control, immunisation and bleeding, maintenance of records and documentation, care of sick and injured equines and a section on common disorders observed in equines.

Alternatives to the use of animals in research and education

The CPCSEA has constituted a sub-committee to recommend the use of alternatives in research and education. On the initiative and the recommendations of this sub-committee, the regulatory authorities and the Ministry of Health of the Government of India have taken steps to introduce the following alternatives.

Tissue culture anti-rabies vaccine (TCARV)

In the last two years, the CPCSEA has repeatedly and persistently reiterated the urgent need to replace the use and production of the neural tissue vaccine with TCARV in several meetings and fora. The CPCSEA finally brought it to court when the Supreme Court of India, in its interim orders dated 15.02.2002 in the

WP.216/2001, asked the Government of India to consider banning the neurogenic anti-rabies vaccine.

After 50 years of the Semple vaccine in India, and 20 years of the World Health Organization (WHO)-recommended ban on neurogenic sheep brain anti-rabies (Semple) vaccine, on the initiative of the CPCSEA, the country will soon finally move into a new era of the safe and painless TCARV.

Discontinuation of the classical LD50 test

On the recommendations made by the CPCSEA Sub-committee for Alternatives, the Registration Committee of the Directorate of Plant Protection, Quarantine and Storage, Ministry of Agriculture, agreed in principle to replace the guidelines as given in the Gaitonde Committee for the acute oral LD50 test in rats and mice with the alternatives as suggested by the OECD, namely test guidelines 420, 423 and 425. An Expert Group has been constituted to examine the alternative methods and to suggest the appropriate amendments in the *Insecticides Rules 1971*. A representative of the CPCSEA will be a member of this group.

Limulus amoebocyte lysate (LAL) assay

The sub-committee for alternatives has submitted a list of 70 biomedical products for the safety testing, for which the LAL assay can be adopted in lieu of the rabbit pyrogen test, to the Chairman, Indian Pharmacopoeia (IP) and Drugs Controller General of India. The committee has been specially constituted by the IP to look into this matter, and it is in the final stage of implementation.

ECVAM and ICCVAM validated alternatives

The alternatives validated by the European Centre for the Validation of Alternative Methods (ECVAM) and the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), such as the EpiDerm™ skin corrosivity test, the rat skin transcutaneous electrical resistance (TER) test, Corrositex®, the 3T3 NRU (neutral red uptake) phototoxicity test and the local lymph node assay (LLNA), have been recommended by the sub-committee to the regulatory authorities for implementation.

In vitro production of monoclonal antibodies

The commercial production of monoclonal antibodies by the ascites method has been banned. However, the production houses have asked for a two-year phase-out period.

Rescue and rehabilitation of laboratory animals

The CPCSEA has also actively rescued and rehabilitated animals that were found in acute conditions of physical and physiological trauma, including cases of non-human primates languishing in cages for 20 years, showing signs of self-mutilation and muscle atrophy; beagles with congenital defects due to inbreeding; and equines that were old, blind and lame, yet being bled 18–20 litres of blood.

The People for Animals (PFA), India's largest animal welfare organisation, with 170 chapters and with animal shelters across the country, has come forward to help the CPCSEA in its rescue endeavours. Other animal welfare organisations have also come forward to extend their local support, as necessary, throughout the country. India's first non-human primate rehabilitation centre, The Hanuman Vatika, was started by the PFA, New Delhi, in 2001.

To date, 277 beagles have been homed, and 53 mixed-breed dogs, 175 equines, 216 non-human primates, 33 sheep, 124 chickens, 110 rabbits, 5 cobras, and several birds, rabbits mice, frogs and rats, have been rescued and rehabilitated.

Training of scientific and non-scientific personnel

In the last two years, the CPCSEA has been proactively training honorary workers of the CPCSEA on issues of laboratory animal care and use, project proposal scrutiny, alternatives, rescue and rehabilitation, and rules and regulations pertaining to animal experimentation in India. Two booklets, *Guidelines for CPCSEA Nominees* and *Guidelines for an Effective Laboratory Check* have been published by the CPCSEA.

Similarly, workshops on issues of animal handling, anaesthesia and euthanasia, good laboratory practices, alternatives, and so on have been conducted across the country, with the help of subject experts.

Legal cases

The CPCSEA, in its efforts to implement good laboratory practices and alternatives to the use of animals in research and education, has been

repeatedly taken to court. The rescue of 227 beagles, ratification of the CPCSEA *Guidelines for the Care and Management of Equines Used in the Production of Biologicals*, and an initiative of the Government of India in the replacement of the Semple Vaccine with TCARV, have been the result of verdicts of the Supreme Court of India.

Conclusion

It is an undeniable fact that some of the research being carried out in Indian laboratories raises numerous ethical questions that need to be debated publicly. The importance of public debate and consensus on the issue of the ethical use of animals for research needs to be stressed, particularly in light of the negligible outcome of scientific research in India, despite huge amounts of publicly funded grants. A glaring example is the fact that from 1956 until the present, only 14 medicines invented by Indian scientists have been approved and released by the Drug Controller of India. Several Chambers of Commerce have even touted India as a cheap testing ground for both preclinical animal trials and human trials.

However, the groundswell of sympathy for animal suffering and the abhorrence of moral double standards are becoming apparent in the country. Concern for animals is overtly evident among the general population. Some scientists today consider it important to look for alternatives to animal experimentation. Animal rights proponents have become vocal in questioning the subsidising of animal experiments from public funds and the taxpayers' money. The conflict between the scientists and animal rights supporters has already been transferred into the political arena, and soon the politicians will have to come clean on their positions on animal rights.

Meanwhile, the CPCSEA continues to press for the implementation of existing rules and to lobby for the constitutional protection for animals, more humane forms of animal experimentation, and the renunciation of non-critical research. At stake, we believe, is the basic regard for life in all its forms, which has been pushed down the list of priorities in the nation's struggle toward progress.