

CPCSEA Inspections: Can it be done the AAALAC way?

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Background

India is one of the countries which have oldest regulations for animal welfare and experimentation. The Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) was constituted by the Government of India, way back in 1968 under chapter IV of the Prevention of Cruelty to Animals (PCA) Act, 1960 to oversee the animal experiments and welfare.

Indian National Science Academy (INSA) has published a "Guidelines for Care and Use of Animals in Scientific Research" in 1992. Subsequently, INSA constituted a committee under the Chairmanship of Dr. P.N Tandon to revise these guidelines. These guidelines were published in the year 2000. These two guidelines formed the basis for adopting and functioning by most of the Animal Facilities in India. In addition, internationally there were University Federation for Animal Welfare (UFAW) Handbook on Care and Management of Laboratory Animals. Based on the INSA and CPCSEA Guidelines, Indian Council of Medical Research, New Delhi has published the "Guidelines for Use of Animals in Medical Colleges" in 2001 with addition of small aspect of budget for starting and running a new Animal Facility for breeding and or experimentation.

Ministry of Agriculture constituted the CPCSEA in 1968. In the year 1998, the rules were re-notified in the Gazette of India as a "Breeding of and Experiment on Animals (Control and Supervision) Rules, 1998. The rules have conferred powers to the CPCSEA, Ministry of Environment and Forests and Climate Change, to execute the Breeding of and Experiments on Animals (Control and Supervision) Rules. These rules were subsequently amended in the year 2001 and 2006. The CPCSEA initially published the 'CPCSEA Guidelines for Laboratory Animal Facility' which were revised and published in 2007. CPCSEA published the Standard Operating Procedure (SOP) for Institutional Animal Ethics Committee (IAEC) in January 2010 which is compilation

of all earlier guidelines with addition of specific guidelines; PCA Act, 1960; and other forms related to animal study protocol, record maintenance and format of animal facility inspection report etc.

Prior to 1998, the responsibility for animals used in research in India was controlled directly by the researchers and the quality of animal care and animal welfare varied significantly among research institutions. Even within the same organization or university, research laboratories had inconsistent animal care policies and standards of care and management.

IAEC/ Institutional Animal Care & Use Committee (IACUC) History

International

New USDA regulations based on the 1985 amendment to the Animal Welfare Act became effective between October 1989 and August 1991. These regulations require each registered research institution to appoint an Institutional Animal Care and Use Committee (IACUC) of not less than three members, including a veterinarian, which "serves as the agent of the research facility that assures that the facility is in full compliance with the Act". The regulations also require a member not affiliated with the institution representing community interests in the proper care and treatment of animals.

National

As per the "Breeding of and Experiment on Animals (Control and Supervision) Rules, 1998, every establishment carrying breeding of and experiments on animals shall apply for permission to do so and seek registration from the CPCSEA; form an Institutional Animal Ethics Committee (IAEC); and maintain various records related to breeding, experiment and animal import. It is mandatory that no breeder shall transfer/ procure any animal by sale or otherwise to/from an

establishment, which is not registered under these rules.

As per the rules, the IAEC should have eight members as follows- A biological scientist, two scientist from different biological discipline, A veterinarian involved in care of animals, scientist In-charge of the Animal Facility, a scientist from outside the institute, a non-scientific socially aware member and a CPCSEA Nominee. The first five internal members are nominated by the head of the establishment. In its first meeting, these members have to pass the resolution to register the Animal Facility under the CPCSEA for breeding and/or experimentation using animals. Once the application is made to CPCSEA in Form 'A' format, the CPCSEA nominate a Nominee for inspection and after receiving the inspection report provide the registration number to the organization and also nominate Main CPCSEA Nominee, Scientist from Outside the Institute and Non-scientific Socially Aware Member on the IAEC to represent the CPCSEA. The CPCSEA also nominate a Link Nominee in case the Main Nominee is unavailable for any reason to attend the IAEC meeting.

The Member Secretary of the IAEC is responsible to see that the notifications are timely sent to the researchers to receive the animal study proposals; to forward them to the IAEC; to communicate the date of the IAEC meeting to the researchers who have submitted the new proposals; to communicate the decisions of the IAEC to the researchers; to write draft of the minutes of the IAEC meetings, communicate it to the IAEC members and finalize them; to obtain signature of all members on the minute; and to submit a copy of the IAEC minutes to the CPCSEA, New Delhi within 15 days of the meeting. The Scientist In- charge of the Animal Facility has to breed and/or make available the animals to the researchers as per the approval in the IAEC meeting; to receive the duly filled and signed Form 'D' from the researchers and maintain all necessary records of the IAEC proceedings and animal experiments.

Responsibility of the IAEC

It is the responsibility of the Chairman, IAEC, to conduct the proceedings of the meetings of the IAEC strictly as per the guidelines of the CPCSEA. The CPCSEA registration has to be renewed every three years by paying the stipulated fees. After reconstitution, duration of the nominated members of the IAEC is generally for three years. The IAEC is expected to be reconstituted every three years along with the renewal of the CPCSEA registration. As per the CPCSEA guidelines, the IAEC is required to meet twice a year irrespective of whether there are animal study proposals for discussion or not. IAEC is also responsible for monitoring the functioning of the Animal Facility, to ensure that the experimentation complies the rules and regulations of the CPCSEA and ethical animal care and welfare is practiced.

Submission of the animal study proposal seems to be easy but a complicate task. Since the IAEC has wide range of members in it, all animal study proposals are expected to be written in layman's language enabling all members of the IAEC to properly understand them. All experiments involving the

use of laboratory animals up to the phylogenetic level of rodents (mice, rat, hamster and rabbits) can be reviewed and approved by the IAEC. Animal use above than the rabbits is to be recommended by the IAEC and to be forwarded to the CPCSEA, New Delhi for approval of animal use.

It is expected that the IAEC should not limit themselves to the role of conducting the IAEC meetings and approving/recommending the animal study proposals and forwarding them to the CPCSEA, New Delhi, but it must supervise the entire programme. AAALAC put the onus of executing the entire program of the Animal Facility including breeding, experimentation as well as approval of protocols by the IACUC/IAEC.

CPCSEA inspection and AAALAC Site visit

CPCSEA inspections are one of the requirements for obtaining the CPCSEA registration or its renewal. CPCSEA inspections are also held in cases where complaints are received by the CPCSEA for violation of any of the guidelines set by the CPCSEA. CPCSEA has designed the inspection report based on the Guide for the Care and Use of Laboratory Animals (Guide) published by the National Research Council. The inspection report of the CPCSEA is a miniature form of the "Program Description" (PD) of the AAALAC which is also largely inherited from the Guide. However, there are basic differences in both the reports. AAALAC calls it the 'Site Visit' by the site visitors and CPCSEA calls it as an 'Inspection' by the inspecting team. CPCSEA requires the CPCSEA inspector/s to write the inspection report and submit it to the CPCSEA, New Delhi whereas AAALAC insist the participating organization to write entire information of the Animal Facility in the form of 'Program Description' and submit it to them. CPCSEA may ask the single member to inspect the Animal Facility and submit the report or a team of 2-3 members nominated by the CPCSEA to inspect the Animal Facility and submit the report. An *ad-hoc* consultant who is a local member and Council member/s from other countries constitute the 'Site Visit Team' who visits the participating organization. AAALAC does not have a fixed format for the site visits. The team of 'Site Visitors' go through the information in the report of the PD and tries to ascertain whether the information provided in the PD is really practiced or not. AAALAC site visitors go through each and everything mentioned in the PD and points out the shortfalls on the same day during the 'Exit Briefing' there and there only. CPCSEA has no mention of clear provision to report the discrepancies to the host organization. On the contrary the inspection report is submitted by the team to the CPCSEA, New Delhi and in turn the CPCSEA communicates the shortfalls and instructs the host organization to comply it within stipulated time period, if any. AAALAC expect the participating organization to submit the compliance reply within stipulated time with documented/photographic proofs of compliance before the AAALAC Council meeting which can be incorporated in the site visit report and accepted by the council for accreditation/renewal of the term. The CPCSEA

expect the participating organization to submit the compliance report within stipulated time and may again request the same or different inspection team to inspect and re-submit the report which is placed before the committee for the approval of the CPCSEA new registration/renewal of the registration.

Three primary standards adopted by AAALAC to evaluate the animal care and use program are 'the Guide for the Care and Use of Laboratory Animals' (Guide) published by the National Research Council, 2011 <http://www.nap.edu/catalog/12910/guide-for-the-care-and-use-of-laboratory-animals-eighth>; 'Guide for the Care and Use of Agricultural Animals in Research and Teaching' http://www.fass.org/docs/agguide3rd/Ag_Guide_3rd_ed.pdf; and 'European Convention for the Protection of Vertebrate Animals used for Experiments and Other Scientific Purposes' <http://conventions.coe.int/treaty/en/treaties/html/123.htm>.

AAALAC requires the participating organization to take care of the pain and distress besides other requirements of the program. CPCSEA too needs to precisely include the pain, distress and humane end point in the inspection report/ animal study proposal. AAALAC affirms social housing as default method for all species unless otherwise justified and approved by the IACUC/IAEC. In case single housing is justified and approved by the IACUC/IAEC, AAALAC requires the enrichments to be provided to all such animals housed singly. However, IAEC may consider any exception on enrichment based on the requirement of the Attending Veterinarian or the Principle Investigator and if approved by the IAEC/IACUC.

Discrepancies reported by the site visitors during the actual site visit are weighed on the scale of 3W's i.e., "What, Why and What". Any adverse finding observed during the site visit is answered considering 'What' is the problem; 'Why' it is a problem' and 'What is to be done to correct the problem'. For better understanding of the 3W's, few examples are felt necessary to explain the finding.

Finding no. 1 - In room no. 1510, SS make cages housing the adult rabbits were small to allow the rabbits to express their normal posture. This finding can be written in the "What, Why and What" format as follows-"Adult rabbits in room no. 1510 are not able to stand in their cages as their head and back touches the cage top" is a problem. "Rabbits must be able to assume their normal postural position in standing position" is 'Why' it is a problem. "Provide a cage of sufficient height to the rabbit as per the 'CPCSEA Guidelines' or 'Guide' "is required to fix it.

Finding no. 2 - While reviewing the animal study protocols, some of the Form 'B's has no mention of humane end points. This finding can be written in the "What, Why and What" format as follows-

"Animal study protocol no. IAEC/1050/2015 was seen lacking the information on humane end point" is a problem. In absence of the defined humane end point "Animals having more than an inch diameter of tumor with a bleeding wound

or a paralysed animal may also be maintained in the Animal Facility" is 'Why' it is a problem. "Clearly define the humane end points in the Form-B in terms of tumor growth/wound mark/bleeding/weight loss/paralysis/inability to walk etc" is required to fix it.

Finding no. 3 - While reviewing the program description, it was observed that the minutes of the IACUC/IAEC meeting has no deliberations on review of the protocols recorded in the minutes. This finding can be written in the "What, Why and What" format as follows:

"IAEC minutes did not reflect the deliberation by the committee reviewing new as well as on-going protocols" is a problem. "The IACUC/IAEC is responsible for review of the protocols submitted by the researchers on following points but not limited to- rationale and purpose of animal usage, description of the procedure, options available for alternatives, appropriateness of the model, housing and husbandry requirements, animal welfare, appropriate analgesia, anesthesia, surgical procedures, postoperative care, humane endpoints, euthanasia, expertise of the personnel, occupational health and safety. In many of the animal study protocols, the IACUC/IAEC may overlook one or the other aspect which may compromise the animal welfare and results of the experiments" is 'Why' it is a problem. "IACUC/IAEC need to be more critical on reviewing the animal study protocols on line with the points mentioned above while discussing each protocol in the IACUC/IAEC meeting and also minute the deliberations in the minutes" is required to fix the finding.

Finding no. 4 - During the facility site visit, it was noticed that there was a minimum of 1 inch gap between the bottom of doors and floor of some of the animal rooms.

"Room nos. 009, 013, 025 and 116 has gap of minimum of one inch between the bottom of doors and floor" is a problem. The gap would not prevent entry of vermin, escape/entry by mice, and may affect air balancing in the animal rooms" is 'Why' it is a problem. "A means of closing this gap should be considered" is required to fix the finding.

Finding no. 5 -While reviewing the program description, it was observed that the anesthesia and analgesic is not mentioned in some of the Form 'B's.

"Animal study proposals nos. IAEC/ABC/010, 014 and 026 lack the vital information with respect to name of the anesthetic(s)/analgesic(s), their dosage and route of administration of injections" is a problem. "Alleviation of pain and distress in laboratory animals is achieved by the use of anesthetic (s)/analgesic(s). If not relieved, pain may cause unaccepted level of stress and distress in laboratory animals which may in turn lead to pain response to otherwise non-painful stimuli" is 'Why' it is a problem. Name of appropriate anaesthetic(s)/analgesic(s), their dosage and route of administration must be mentioned in all the animal study protocols." is required to fix it.

Summary

CPCSEA which is a regulatory body who controls the animal experimentation in India regulate and implement the 'Breeding of and Experiment on Animals' (Control and Supervision) Rules, 1998. Adherence to the rules is mandatory on every establishment who wish to breed/and or conduct experiments on animals. An inspection of the Animal Houses is one of the major responsibilities of the CPCSEA for fresh registration/renewal of the existing registrations of the establishments for this purpose. Representative from the regulatory authority with the help of experienced professional in this field are making the inspections possible for this purpose. AAALAC International has set a standard for welfare and humane treatment of animals in science worldwide. In order to upgrade the reviewing the protocol forms and also the animal facilities *per se*, CPCSEA need to revisit on the protocol form, inspection report formats as well as strategy for timely registration or renewal of the registration of the organisations.

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