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MCB 406- MICROBIAL QUALITY ASSURANCE

DEPARTMENT OF BIOLOGICAL SCIENCES

Question: Using the protocol or study plan of GLP requirements, what are the points that are likely to be important in the experimental design for a typical animal toxicity study?

For a study on animal toxicity, the following points are important to be noted based on Organization for Economic Cooperation and Development (OECD) GLP requirements:

* False negatives: A false negative for a toxicity study is a set of results that falsely reports that a test item is not toxic when in reality it is toxic. False negative results are costly, time consuming and present ethical problems (e.g. animals used to no good purpose). They should, therefore, be avoided.
* Buildings: The infrastructure in which an animal toxicity study is carried on should have the following properties:

1. The facility should be designed and operated to control selected parameters (such as temperature, humidity and light), to minimize the effect of environmental variables on the animals.
2. The facility should be organized in a way that prevents the animals from coming into contact with disease, or with a test item other than the one under investigation.
3. A typical animal house should have separations maintained by provision of areas for:

* different species
* different studies
* quarantine
* changing rooms
* receipt of materials
* storage of materials

– bedding and diet

– test doses

– cages

– cleaning equipment

* necropsy
* waste disposal.

1. The building and rooms should provide sufficient space for animals and studies, allowing the operators to work efficiently.
2. Design should allow easy and thorough cleaning of surfaces of walls, doors, floors and ceilings. There should be no gaps or ledges where dirt and dust can accumulate. Water should not accumulate on uneven floors i.e. floors should be smooth and even and without crevices.
3. Whatever the capabilities or needs of the laboratory, sensible working procedures can reduce the damage from outside influences. Such procedures may include:
   * minimising the number of staff allowed to enter the building;
   * restricting entry into animal rooms;
   * organising work flow so that clean and dirty materials are moved around the facility at different times of the day and ensuring that corridors are cleaned between these times;
   * requiring staff to put on different clothing for different zones within the animal facility;
   * ensuring that rooms are cleaned between studies.

* Adequate equipment should be available for study (e.g pH meters), and they should be properly calibrated and in good working conditions to avoid wrong values leading to false negatives. Periodic maintenance should also be carried out, and records of repairs and routine maintenance, and any non-routine work should be kept.

Maintenance may be carried out in two distinct ways:

* preventive or planned, whereby a regular check is made irrespective of the performance of the equipment;
* curative or reparative, when the piece of equipment is not functioning according to specification or when the equipment or system has broken down.
* Proper documentation
* A laboratory used in carrying out the studies may need a stand-by generator capable of maintaining at least the animal room environment to prevent the loss of the animals that would irretrievably affect the study. Meanwhile, samples could be stored for a period until power is restored.
* The test item: In order not to confuse issues and false results, it is very important that the test item be protected from cross contamination from other chemicals (or even the same chemical of a different batch) and from pollution by external factors such as bacteria, dust, water, etc. The GLP Principles therefore require that proper conditions for the receipt and storage of the test item are in place. GLP principles also requires that exact procedures for formulation be implemented each time so that the same method is used, leading to the same concentration each time.

The test container should be strong enough to withstand transportation between sites. The test item should be clearly labelled with sufficient information for identification. A delivery form should ideally contain the following information:

• manufacturer’s name or sponsor’s name

• date of dispatch

• number of containers or items, type of contents and quantity

• identity of the test item

• batch numbers

• identity of the person responsible for the dispatch

• name of the transporter and type of carrier.

Each container should be clearly labelled with sufficient information so that the test facility is able to confirm the test item identity. Ideally labels should contain the following information:

• test item name

• batch number

• expiry date

• storage conditions

• container number

• total weight

• initial gross weight.

These information supplied by the manufacturer or the sponsor should be cross checked by the test facility and records should be kept of each delivery. All deficiencies or problems relating to the receipt of test items should be noted.

* + - Test items should be stored under closely controlled conditions, particularly with respect to access and environment. The stores manager should ensure that only designated staff have access to the material. The stores are kept locked when not in use. Separate areas should be available for storage at different temperatures.
* Disposal: Following the completion of a study, surplus amounts of test item should be disposed of in an environmentally acceptable way.
* Dosing: The dosing procedure should be conducted in a fixed order so as to minimize the possibility of cross contamination and confusion between animals, dose groups and different formulations. When dosing animals orally, most laboratories observe the following precautions:

• The animals are dosed group by group, in ascending dose levels.

• A new catheter and syringe is used for each dose level.

• The used container, catheter and syringe are removed from the dosing station before

the new group is dosed.

• The outside of the catheter is wiped with a clean tissue before each animal is dosed.

This prevents the possibility of test material being drawn into the lungs.

• Only one cage of animals is opened at a time. If the animals are individually housed, they should be returned to the same cage following the dosing. If housed in groups, the animals should be placed in another container until all animals from the cage have been dosed and then returned to their original cage.

• Each animal is identified (e.g. by a tail tattoo), as well as its cage number.

* Acclimatization: For most studies the protocol and SOPs require that animals have a period of acclimatization to laboratory conditions during which time their health status is confirmed and unsuitable individuals are identified/eliminated. The length of this acclimatization period depends upon the species, the supplier and the type of study.

Documentation of room preparation, animal receipt, husbandry, observations, measurements, environmental conditions and any other activities during this period should be maintained.

* Animal identification: Identification of animals must be consistent throughout the study. Most laboratories use a system of cage cards (temporarily before group assignment and permanently afterwards), as described in the protocol.