

over a period not exceeding 24 h. After the substance has been administered, food may be withheld for a further 3-4 h. Where a dose is administered in fractions over a period it may be necessary to provide the animals with food and water depending on the length of the period. Following administration, observations are made and recorded systematically with individual records being maintained for each animal. The investigation of a second or, in exceptional circumstances, a third dose level is dependent upon the results of the preceding dose level.

Clinical examinations

A careful clinical examination should be made at least once each day. Additional observations should be made during the first few days after dosing so that the test may be terminated if it becomes apparent that the initial dose level chosen was too high. Cage-side observations should include changes in the skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activity and behaviour pattern. Individual weights of animals should be determined shortly before the test substance

is administered, weekly thereafter and at death. Where possible, animals should be weighed daily during the first week. Weight changes should be calculated and recorded. At the end of the test surviving animals are weighed and then humanely killed.

Pathology

All test animals should be subjected to gross necropsy. All gross pathological changes should be recorded. Microscopic examination of organs showing evidence of gross pathology in animals surviving 24 h or more should also be considered.

Treatment of results

Data may be summarised in tabular form showing for each test group the number of animals at the start of the test; the number of animals displaying signs of toxicity; a description of the toxic effects and whether evident toxicity was observed; the time course of any toxic effects; and the necropsy findings. The report should include details of all dose levels investigated, and should provide information on the number of animals which died or were humanely killed.