

Humane endpoints in generating and breeding genetically modified animals

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Many genetically modified animals (GMA) such as transgenic, knockout, and knock-in animals are used in the biomedical research nowadays. These animals are very useful to investigate the function of specific genes as well as useful for disease animal model. However, inheritable malfunction by genetic modification causes serious impact on animal well-being in many cases. Therefore, investigators must consider animal welfare to mitigate pain and distress of GMA. Investigators who will generate a new GMA as well as will breed a GMA provided from other investigators must determine humane endpoints prior to start research. Symptoms of GMA may be available from information reported previously. Investigators must determine humane endpoints from such information, describe them in their animal use protocol, and be approved by IACUC. If investigators intend to generate a GMA by modifying a new gene and have no previous information on this gene, they should predict symptoms by colligating scientific evidence and then determine humane endpoints. During generating or breeding GMA, careful at least daily or more frequent observation is necessary. If unexpected outcomes are identified, investigators should report it to Attending Veterinarian and IACUC and revise their animal use protocol with adequate new humane endpoints.

Investigators in the countries that ratified Cartagena Protocol should follow the municipal law. For example, investigators in Japan must follow the ordinance issued from the Ministry of Education, Culture, Sports, Science and Technology. Main items in this ordinance are prevention of escape of GMA and restriction and indication of rooms where GMA are bred and used. Recently, genome-editing technologies such as using CRISPR-CAS system has taken place of classical method of generation of knockout animals. Because genome-editing technologies may be different from the definition of gene recombination, the management of animals generated by genome-editing technologies may differ in the institutions in Japan. However, considered the aim of the law, animals generated by genome-editing technologies should be managed in the same way as classical GMA.