Comparison of Historical Control Data in Two Strains of Rat in Different Cage Environments Used in Carcinogenicity Studies

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Introduction

Regulatory guidelines necessitate carcinogenicity testing of potential new human therapeutics intended to be administered to humans for longer than six consecutive months. The assessment of a chemical's ability to induce tumor growth in animals helps predict the relative risk in humans. Further evaluations including survivability and body weight are monitored for the entire lifespan of the species. Suitable strains have been previously selected for carcinogenicity testing, namely Sprague Dawley IGS and Wistar (Hannover) and a body of data is available for these strains. Recent changes in housing requirements in part resulting from guidance from the European Union have resulted in changes to the housing environment utilised and more studies are being run using solid bottom bins with bedding material.

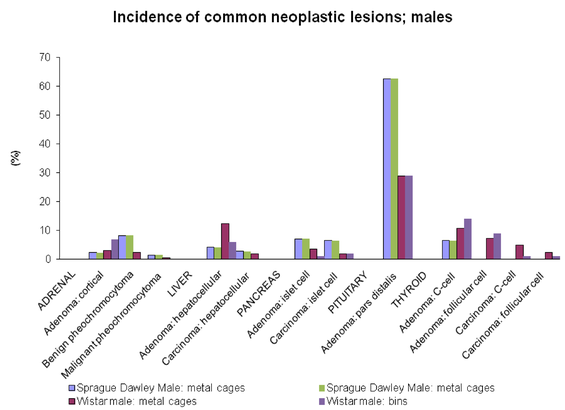
Experimental Procedures

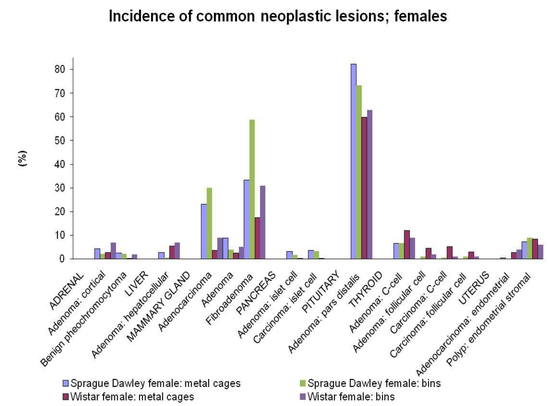
Data collected from 2 year carcinogenicity studies in Sprague Dawley CD® IGS, (Crl: CD [SD]), and Wistar (Han) IGS (Crl: WI [Han]) rats principally from Charles River Laboratories housed in a conventional non-barrier facility, was compared. Rats were group housed and were between six and eight weeks of age at the start of treatment. Primary end points chosen for the comparison included survival, body weight and body weight gain, onset, progression and incidence of common neoplastic lesions. Dosage routes included, oral gavage, subcutaneous injection, and nose only inhalation. Caging systems used were either conventional wire or perforated steel plate floors, and solid bottom polycarbonate bins with bedding material. Appropriate levels of environmental enrichment such as chewing objects and hiding tubes were provided in the majority of studies.

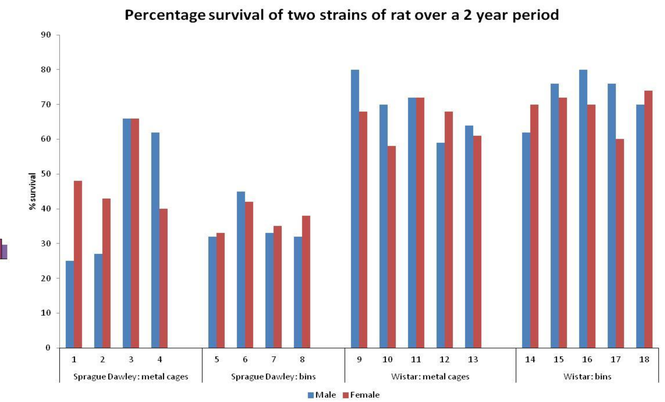
Results

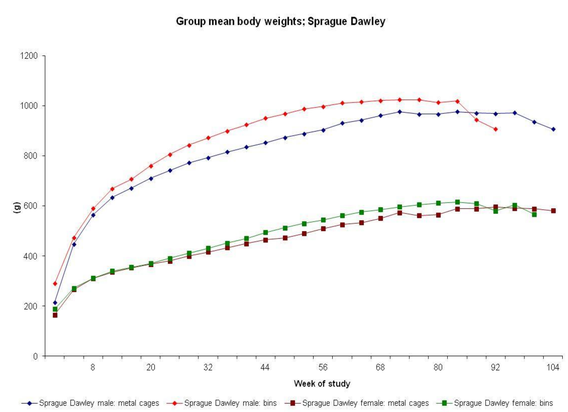
Sprague Dawley rats were noticeably heavier than Wistar rats, where lower bodyweights in Wistar rats were associated with increased survival rates and a lower incidence of spontaneously occurring tumors over a two year period. The incidence of clinical signs associated with foot lesions was higher in Sprague Dawley rats however a general reduction in the incidence and a delay in onset of these clinical signs were noted in rats housed in solid bottom cages, when compared to rats housed in metal bottom cages.

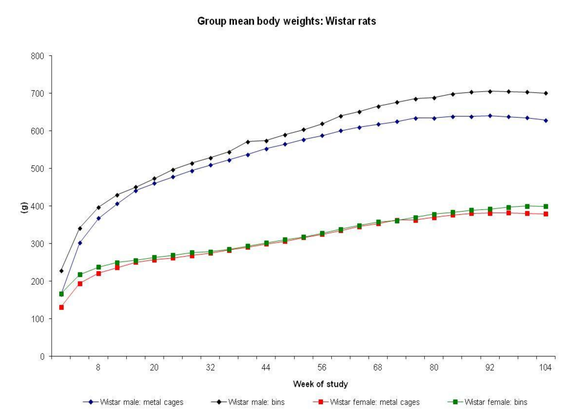
The type of neoplastic and non-neoplastic lesions seen in the two strains differed principally in incidence. Spontaneously occurring tumors were seen in tissues including, pituitary, adrenal, and mammary tissue, there was no evidence of significant changes in incidence patterns in the data evaluated for each respective strain and the type of cage had no apparent influence on this data.











Conclusion

It is concluded that differences in cage environment had minimal effect on the selected parameters examined. Survivability in Wistar rats was greater and associated tumor burden less than that seen in the Sprague Dawley rats.

References

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