Evaluation of the Hsd : Sprague Dawley SD rat over 104 weeks

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Abstract

In keeping with our policy of providing clients with flexibility in their choice of strain for all toxicological investigations, supported by extensive background data, Corning Hazleton have undertaken a number of background studies in recent years on different strains of rats and mice.

The greater part of the data produced in toxicological studies is obtained from Sprague Dawley rats. It has been noted that the survival of the Charles River Sprague Dawley (Crl:CDBR) rat routinely used at this and other laboratories is diminishing, with the onset of tumours occurring in younger rats. A background data study was therefore established to investigate background tumour incidence and toxicology data for the Harlan Sprague Dawley (HSD) rat with a view to offering an alternative strain to our clients.

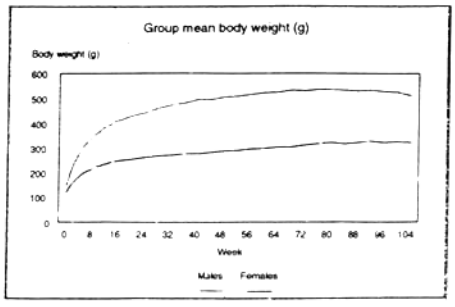
Animals of each sex were obtained from Harlan Olac Ltd in 1994 and allocated to study at approximately 6 weeks of age. Sacrifices were performed after 4, 13, 26, 52 and 104 weeks on study. Animals were housed under our standard conditions and relevant data, as requested by major regulatory authorities, was obtained at regular intervals.

On completion of 104 weeks, survival of the animals was 65% for males and 49% for females. This survival rate is greater than that currently being obtained at this laboratory for the Crl:CDBR rat maintained under the same conditions.

Methods

Four hundred and sixty animals (230 of each sex) were obtained from Harlan Olac Ltd in April 1994. The animals were housed under standard CHE conditions in groups of 5 in stainless steel mesh cages. Throughout the study the animals had access *ad libitum* to SQC Rat and Mouse Maintenance Diet No 1, Expanded, Ground Fine (Special Diets Services Ltd, Witham). Mains water was provided *ad libitum* via an automatic watering system or bottles. Body weight was recorded weekly up to Week 13 and then monthly until the end of the study period. Investigations - clinical observations, palpation, ophthalmoscopy, haematology, clinical chemistry and urine analysis - were performed at intervals commonly requested by the regulatory authorities. Following 4, 13, 26, 52 or 104 weeks on study, groups of animals were sacrificed and a full macroscopic examination performed. At necropsies performed up to and including 52 weeks, organ weights requested by major regulatory authorities were measured. Tissues taken at each necropsy were retained in appropriate fixative, processed to paraffin wax blocks, stained and examined histologically.

Results



Body weight

Sex	Body weight (g) in Week:					
	Start	13	28	52	80	104
Males	152	392	459	507	536	509
Females	128	245	273	284	329	329

Food Consumption

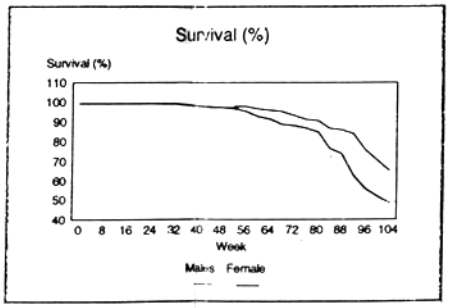
Sex	Grams of food consumed per animal in Week:				
	13	28	52	80	104
Males	153	147	152	149	136
Females	118	111	115	123	134

Condition, Ophthalmoscopy, Clinical Pathology

There was no evidence of change in any parameter that might indicate an undesirable effect of aging within the animals which may affect toxicological interpretation.

Survival

Sex	Survival (expressed as a percentage of the number of animals starting study) in Week:				
	13	28	52	80	104
Males	100	99	98	91	65
Females	100	100	97	86	49



Tumour Incidence

As a measure of the susceptibility of the Hsd rat to early removal from study as a result of the appearance of tumours or on health and welfare grounds, the number of palpable masses were assessed:

	Number of masses observed in Week:				
	13	26	52	80	104
Small moveable					
Males	0	5	14	11	4
Females	0	4	11	13	10
Small stationary					
Males	14	43	36	31	36
Females	4	23	49	28	76
Large movable					
Males	0	0	1	0	5
Females	0	2	8	22	28
Large stationary					
Males	0	1	1	2	2
Females	0	1	2	16	12

Necropsy Findings

The only consistent observation made at any necropsy performed which is considered to be unusual or that could have an effect on the toxicological profile of a test material was a relatively high incidence of kidney abnormalities, for example uneven or mottled surface. There were no other consistent macroscopic abnormalities considered to suggest a possible effect on toxicological interpretation.

Histopathology

At the present time only the histopathological results up to the Week 52 sacrifice are complete. The findings were generally very minor. However, a very minor glomerulonephropathy was noted in animals at the 26 and 52 week sacrifices.

Discussion

The greater part of toxicological data submitted to regulatory authorities is obtained in the Sprague Dawley rat. However, in recent years it has been noted that the survival of the Charles River Sprague Dawley has declined, both at this and at other laboratories. Tumours have been occurring earlier, resulting in the early removal of animals from study. The major contributory factor in this is generally thought to be the high food consumption and body weight of these animals.

By comparison, the data obtained on the Hsd:Sprague Dawley rat maintained under standard CHE housing conditions show this strain to have low body weight and food consumption and high survival. The general condition of the animals remained very good throughout the 104 week study period. It was noted that throughout the study the number of small stationary masses was high. However, these masses were apparent from early in the study period and were generally confined to the ventral hind region. It is considered that the masses were likely to be enlarged preputial/clitoral glands or prominent lymph nodes and that the reason why the incidence was so high is that the thinner nature of these animals allows easier palpation. As with other strains of rat the incidence of palpable masses was greater in females than males, this being the result of the incidence of mammary masses in female animals. However, the incidence or size of large palpable masses did not result in the early removal of animals from the study. These findings are in agreement with other data published on the Hsd:Sprague Dawley [1, 2].

In general there were no findings during the study period to suggest that the use of this strain would adversely affect the toxicological interpretation of results. The only finding of this study which should be considered in selecting the Hsd:Sprague Dawley rat for life span studies is the incidence of macroscopic lesions of the kidney and the minor glomerulonephritis observed in animals after 26 and 52 weeks. However, in the absence of complete histopathological examination the significance of these findings is unknown.

References:

[1]: Body weight and survival of Harlan vs. Charles River Sprague Dawley rats: Implications for carcinogenicity testing. Matray Devoti J, Sharp FF, Davies MH, Schwabenbaur C.

[2]: A comparison study of the Crl:CDBR (CD) and Hsd:Sprague Dawley SD rat. Pettersen JC, Saunders DR, Pavkov KL, Matheson DW, Schwartz DR.

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