

**A Review of the In-life
Parameters and Tumour Data in
Ten Gang-housed Dietary
Tumorigenicity Studies using
the Charles River International
Genetic Standard or Original
Strain Designations of Sprague-
Dawley Rat.**

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ABSTRACT

At Huntingdon Life Sciences, data obtained from the Charles River International Genetic Standard (IGS) strain of Sprague-Dawley rat have been closely monitored since the introduction of this new strain designation in 1996. The in-life and tumour data from the control groups of ten gang-housed dietary tumorigenicity studies (using low protein maintenance diet) have been assessed, with five IGS rat studies (completed 1998-99) compared against five studies (completed 1994-97) using the original strain of Sprague-Dawley rat.

These comparisons have shown that the IGS rat is showing a similarly high mortality pattern to that seen in the original strain studies. The bodyweight growth pattern, and bodyweight gain and food consumption data analysed over the first year, have only shown minor differences between the IGS rat and the original strain of rat. Assessment of the tumour profile (tumour incidence, number of tumour bearing rats and factors contributory to death) has not shown any major differences between the two groups.

From the results available, it can be concluded that the IGS rat is not remarkably different from the original strain of rat.

INTRODUCTION

The Charles River International Genetic Standard (IGS) strain designation of Sprague-Dawley rat CrI:CD[®] BR (VAF) superseded the original strain designation of rat from 1996. At these laboratories, the data obtained from tumorigenicity studies using the IGS rat have been closely monitored and compared with data obtained from the original strain designation of Sprague-Dawley rat [1, 2, 3]. Additionally, a comparison of data obtained from the first 13 weeks of gang housed dietary studies has shown that there were no remarkable differences in the in-life, laboratory and organ weight parameters examined between the IGS and original strain of Sprague-Dawley rat [3, 4]. This review was conducted to assess the data obtained from ten gang-housed dietary tumorigenicity studies. Five IGS rat studies (completed 1998-99) were compared with five studies (completed 1994-97) using the original strain designation of Sprague-Dawley rat. The mortality pattern, bodyweight and food consumption data, tumour profile and pathological factors contributory to death have been assessed.

References

1. Hooks, W.N. and Saunders, M.D. Toxicology Letters 1/85 (1998).
2. Hooks, W.N. Biological Reference Data on CD (SD) IGS Rats 1998, edited by Dr T Matsuzawa, Yamanouchi Pharmaceutical Co. Ltd., Japan.
3. Hooks, W.N. and Hooks, W.N. *et al.* Biological Reference Data on CD (SD) IGS Rats 1999, edited by Dr T Matsuzawa, Yamanouchi Pharmaceutical Co. Ltd., Japan
4. Hooks, W.N. and Harris, B. The Toxicologist, 42: 59 (1998).
5. Hooks, W.N., *et al.* Toxicology Letters 1/74 (1994).

PROCEDURAL DETAILS

Animals

- Sprague-Dawley CrI:CD® BR (VAF) rats obtained from Charles River breeding laboratories in the UK or USA and maintained as control rats for tumorigenicity studies.
- Approximately 6 weeks of age at start of study and housed 5 rats/cage
- Maintained under standard laboratory conditions, with target ranges of 19-23°C for temperature and 40-70% for relative humidity. A 12 hour light and 12 hour dark cycle was maintained.

Study Design

- **Studies reviewed:**
Dietary administered tumorigenicity studies.
- **Number of control groups reviewed:**
Original strain: 5 (completed 1994-97). IGS strain: 5 (completed 1998-99). At least 50 males and 50 females in each control group.
- **Diet (fed *ad libitum*):**
Ground rodent maintenance diet (Special Diets Services Rat and Mouse No. 1: typically 14.5% protein, 3% fat, 4% fibre).
- **Histopathological procedures:**
Tissues fixed in 10% neutral buffered formalin were routinely processed and embedded in paraffin wax. Sections were cut at 4µm and stained with haematoxylin and eosin. The slides were read by a pathologist and subjected to a peer review.

Data presentation and analysis:

- **Mortality:** The mortality pattern is presented in Figures 1 and 2 over the period of Weeks 52 to 104 only, as mortality in the first year is low.
- **Bodyweight:** The bodyweight growth pattern over 104 weeks is presented in Figure 3.
- **Terminal mortality, bodyweight gain and food consumption:** The mean terminal (Week 104) percentage mortality values, the mean bodyweight gain values over Weeks 0 to 52 (the period of maximal growth) and the mean weekly food consumption (g/rat/week) values over the period of Weeks 1 to 52 are presented with standard deviations in Table 1. For these parameters, a comparison based on a 't' distribution was made following analysis of variance to compare differences.
- **Tumour assessment:** An assessment of the tumours present has been performed. Tumour incidences are presented in Figures 4 and 5 (excluding occasions where the incidence for both comparison groups are 0.4% or below). The tumour categories, including the number of tumour bearing animals, are presented in Figures 6 and 7. Tabulated data are available separately.
- **Pathological factors contributory to death:** The major factors are presented in Figures 8 and 9.

RESULTS

Figure 1: Mortality over Weeks 52 to 104 - males

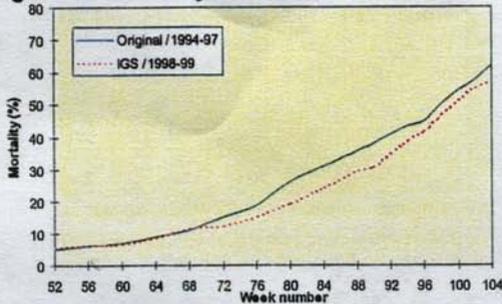
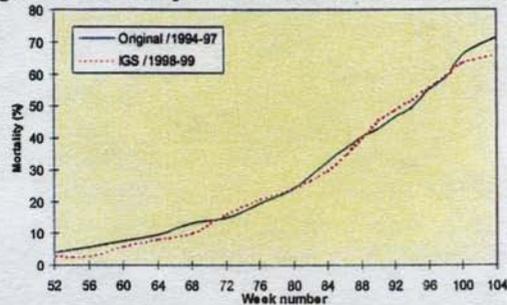


Figure 2: Mortality over Weeks 52 to 104 - females



Figures 1 and 2: The mortality pattern over the period of Weeks 52 to 104 for male and female IGS rat studies was similar to that of studies using the original strain of Sprague-Dawley rat

Figure 4: Tumour incidence - males

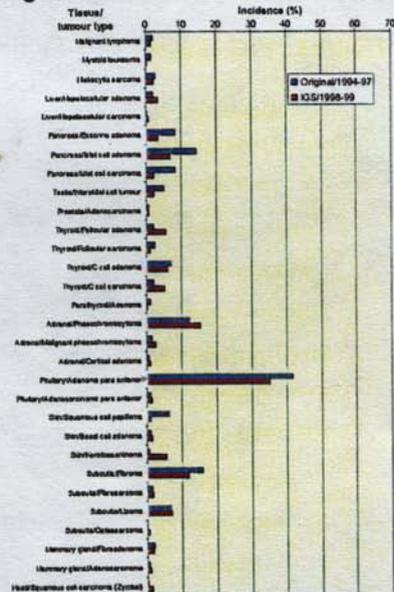
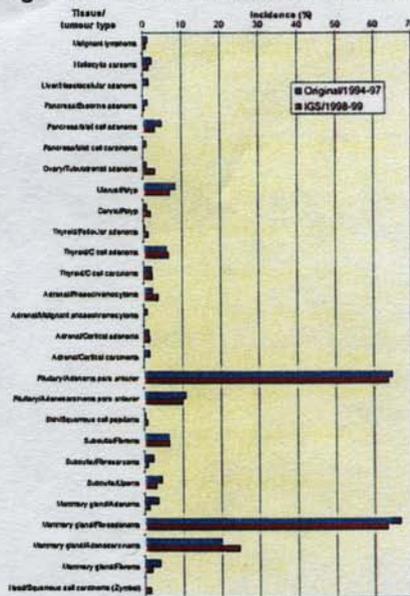


Figure 5: Tumour incidence - females



Figures 4 and 5: The incidence of tumours for both comparison groups is presented in Figure 4 for males and Figure 5 for females. Differences in percentage incidence of 5% or greater between the two comparison groups were only observed for a small number of tumours in male rats only, which included pancreatic islet cell adenoma and carcinoma, and pituitary adenoma (pars anterior).

Figure 6: Tumour categories - males

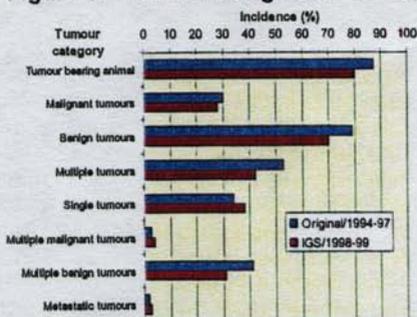
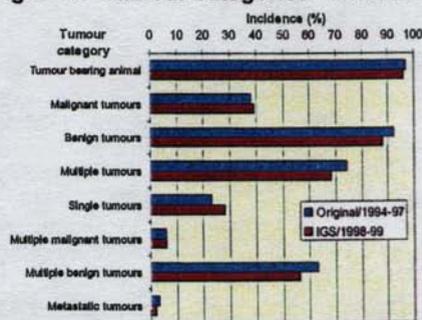


Figure 7: Tumour categories - females



Figures 6 and 7: The categories of tumours, including the number of tumour bearing animals, are presented in Figure 6 for males and Figure 7 for females. Although the results for male rats were comparable, the IGS rats showed slightly lower figures for tumour bearing animals and animals with benign tumours in comparison with the original strain of rat. In females, the results between the original and IGS strain were comparable.