ENVIGO

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Beneficial economic impact of using the RccHan®:WIST rat in toxicology studies

Introduction

Achieving regulatory approval of new drugs and chemicals requires substantial preclinical safety assessments that include, where appropriate, short-term toxicological studies and two-year carcinogenicity testing in two rodent species, typically the mouse and rat.

The purpose of this paper is to showcase the results of an analysis that estimates the economic impact of choosing between the RccHan®:WIST and CRL:CD® (SD) rat strains for toxicological and carcinogenicity studies. While these two strains are the most relied upon for safety assessment studies, they have some key differences that researchers should take into consideration prior to choosing a strain for their safety studies. For instance, when compared to the CRL:CD®(SD) rat, the RccHan®:WIST harbors a number of attractive attributes that are advantageous to safety assessment studies, including lower body weight, enhanced survivability, and overall lower tumor burden.

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While the selection of a rat strain for toxicology and carcinogenicity studies is largely based on the availability of robust historical control data (HCD), the intrinsic properties of the strain - such as survivability, body weight, and lesion incidence (neoplastic and non-neoplastic) - should also be considered. Taking into consideration these factors offers researchers the best opportunity for selecting the optimal strain for their study, which can:

+ Maximize the potential success of a study
+ Enhance animal welfare
+ Have a beneficial economic impact

Thus, prior to embarking on a new toxicology or carcinogenicity study, it is important to conduct appropriate due diligence to ensure that all the different variables that can impact a study are taken into consideration. As part of the due diligence process, researchers should consider estimating the economic impact of choosing between the RccHan®:WIST and CRL:CD® (SD) rat strains.

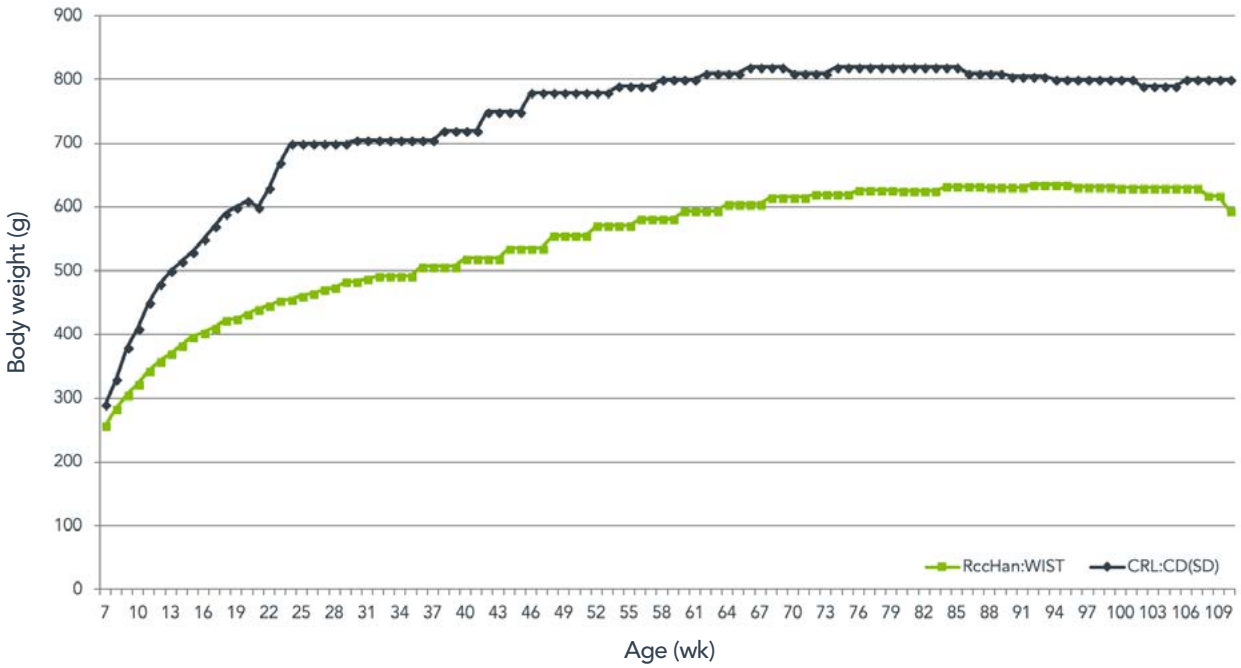
The following section first provides a comparison of the body weight, survival, and incidence of neoplastic lesions between the RccHan®:WIST and CRL:CD®(SD) rat strains, followed by a case study in which an analysis was conducted to model the economic impact of the RccHan®:WIST versus the CRL:CD®(SD) rat for two toxicology study types: 90-day repeated dose toxicity study and a 104-week carcinogenicity study. The per-study cost estimate (in-life study costs only) between these strains was achieved after inputting data from several variables, including technician time, consumables, diet, bedding, overhead, test article cost, vivarium costs, and study type (which incorporates the number of animals and length of study).

Body weight, survival, and incidence of neoplastic lesions

At 104 weeks of age, the CRL:CD®(SD) male rat weighs 35% more than the RccHan®:WIST male rat (800 g compared to 594 g), and the CRL:CD®(SD) female rat weighs 30% more than the RccHan®:WIST female rat (500 g compared to 385 g) (Figures 1 and 2). Body weight begins to diverge at approximately three months of age for both the males and females. Survivability is 32 percentage points lower in the CRL:CD®(SD) male rat compared to the RccHan®:WIST male rat (35% versus 67%) and 33 percentage points lower in the CRL:CD®(SD) female rat compared to the RccHan®:WIST female rat (40% versus 73%) (Figures 3 and 4). Neoplastic lesion incidences are also generally improved at 104 weeks of age in the male and female RccHan®:WIST rats compared to both the male and female CRL:CD®(SD) rats (Figure 5).

Lower body weight in the RccHan®:WIST rat can translate into decreased test article usage, resulting in cost savings. Improved survivability results in fewer animals needed at the study start, allowing for decreased *per diem* and overall housing and husbandry cost savings. Lower overall tumor incidence should result in less time needed per animal for pathology (may also depend on industry being served) and potentially further increase overall cost savings. In conclusion, the lower body weight, robust nature, and improved survival rate of the RccHan®:WIST rat should translate into decreased costs and improved animal welfare for safety assessment studies.

Figure 1: 104-week growth curve for male RccHan®:WIST and CRL:CD®(SD) rats



Body weight, survival, and incidence of neoplastic lesions

Figure 2: 104-week growth curve for female RccHan®:WIST and CRL:CD®(SD) rats

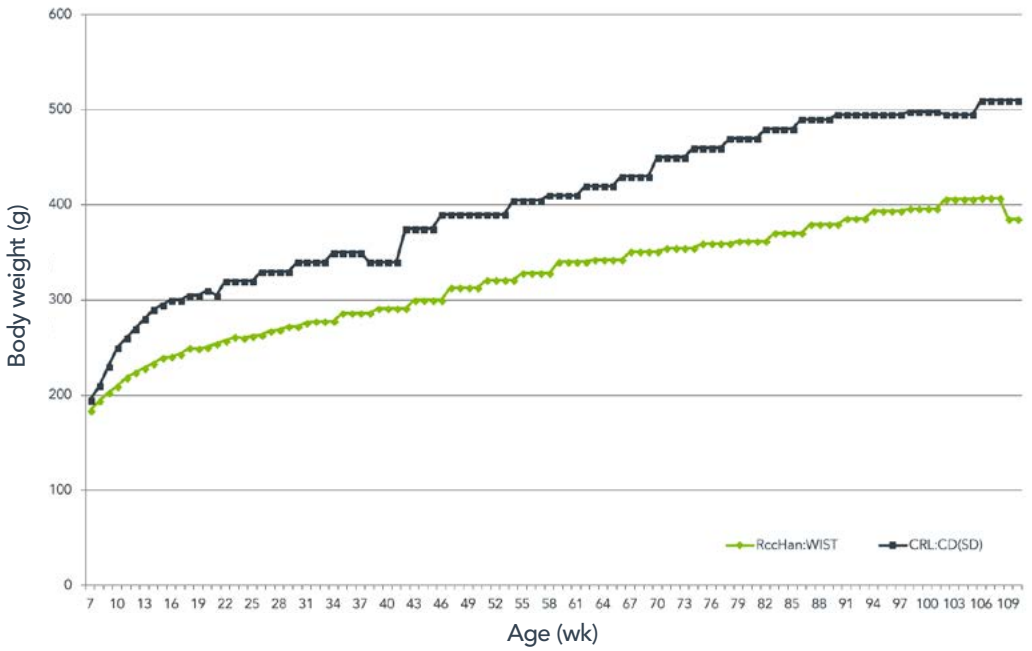
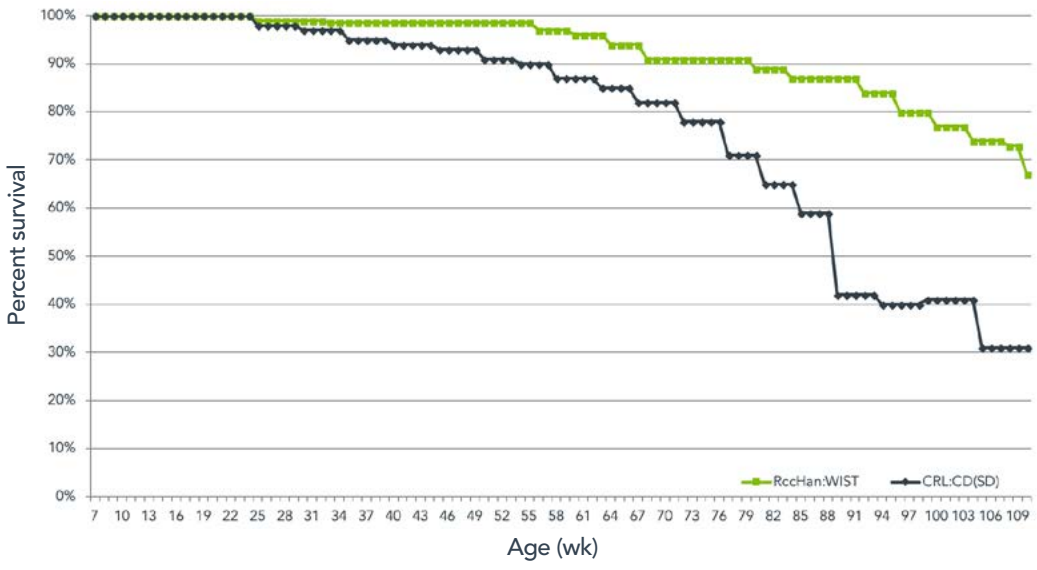


Figure 3: 104-week survival curve for male RccHan®:WIST and CRL:CD®(SD) rats



Body weight, survival, and incidence of neoplastic lesions

Figure 4: 104-week survival curve for female RccHan®:WIST and CRL:CD®(SD) rats

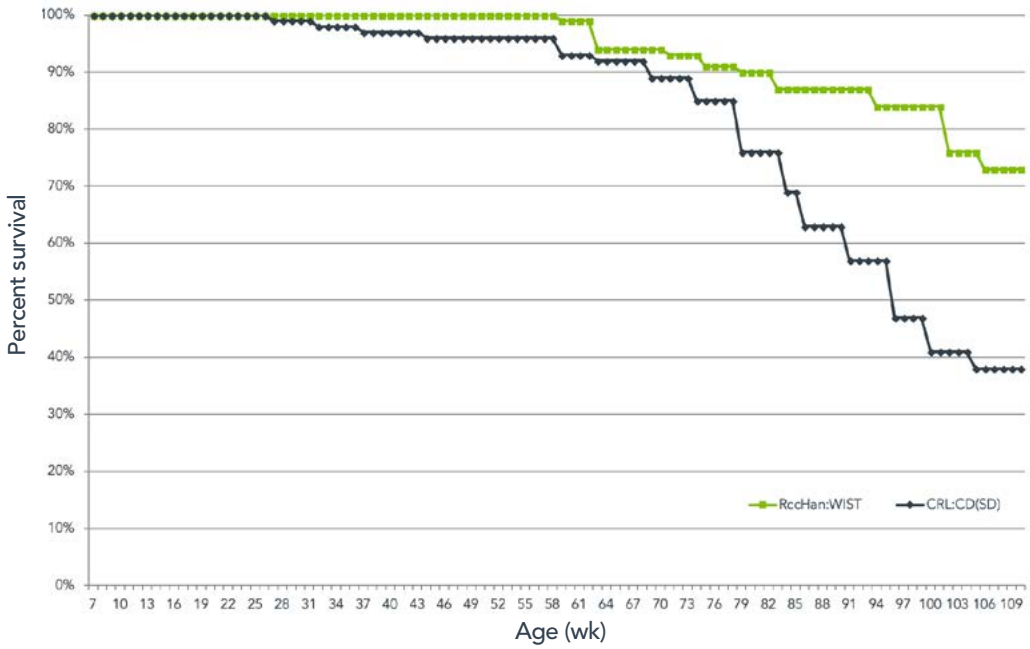
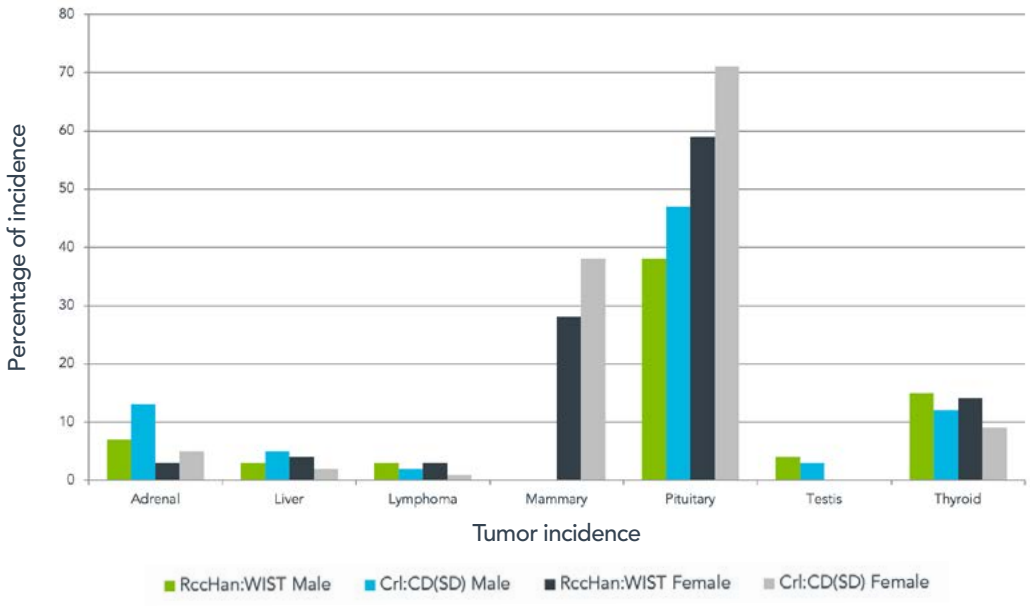


Figure 5: Incidence of neoplastic lesions in RccHan®:WIST and CRL:CD®(SD) rats at 104 weeks



Case study: Comparison of RccHan®:WIST to CRL:CD®(SD) for two toxicology study types

The total study costs were modeled for the RccHan®:WIST versus the CRL:CD®(SD) rat for two example toxicology studies:

1. 90-day repeated dose toxicity study
2. 104-week carcinogenicity study

For the purposes of this case study, several assumptions were made, which are outlined below and where relevant, values can be seen in Tables 1 and 2. For both male and female RccHan®:WIST and CRL:CD®(SD) rats, body weight, survival, and incidence of neoplastic lesions were used for the calculations. It was assumed that all animals were held in a maximum-security barrier facility and housed in solid-bottom, open-top caging with standard paper bedding. The facility was assumed to employ the same number of cages throughout the study and not consolidate cages based on long-term survival.

Further, it was assumed that all animals were maintained on a standard rodent diet (with diet usage equal between rat strains regardless of body weight). Study type, dosing schedule, and study parameters were based on industry standards, with a control group and three dose groups (i.e., low: 100 mg/kg, medium: 300 mg/kg, and high: 1,000 mg/kg). Technician time was assumed at $15.00/hour, animal diet, bedding, and enrichment at $0.10/rat/day, and *per diem* at $1.25/cage/day. As indicated earlier, only in-life study time was considered. For instance, this means that pathologist time was not included, which could further exacerbate the cost difference between the strains based on their different tumor burdens (this can vary depending on the industry being served).

Study type in-life cost assessment

The total study costs were calculated using in-life cost estimates and two test article prices (Scenario A: $0.10/mg, and Scenario B: $10.00/mg) for the 90-day repeated dose toxicity study (Table 1), and the 104-week carcinogenicity study (Table 2).

Overall, cost savings are achieved for the RccHan®:WIST rat for both study types and at both test article prices. Specifically, for the 90-day repeated dose toxicity study, the RccHan®:WIST achieved more than 20% and 22% savings for the $0.10/mg and $10/mg test articles, respectively.

These values translate to savings of more than $60,000 and $6,000,000, for the $0.10/mg and $10/mg test articles, respectively. Meanwhile, the savings achieved for the RccHan®:WIST in the 104-week carcinogenicity study were more than 20% and 22% for the $0.10/mg and $10/mg test articles, respectively. These values translate to absolute savings of more than $269,000 and $20,000,000, for the $0.10/mg and $10/mg test articles, respectively.

Table 1. In-life costs for a 90-day repeated dose toxicity study using three dose groups and two test article costs

	RccHan®:WIST		CRL:CD®(SD)	
	Males	Females	Males	Females
Test Article Dose (mg/kg)	100, 300, 1000		100, 300, 1000	
Total Amount of Test Article Utilized (g)	2,384		2,992	
Number of Animals Required	84	84	84	84
Per Animal Cost	$47.60	$46.50	$51.20	$41.25
Total Animal Cost	$7,904		$7,765	
Technician Time, Housing, Husbandry Cost	$18,554		$18,249	
Results				
Scenario A: Total Study Cost Where Test Article Is $0.10/mg	$264,953		$325,279	
Scenario B: Total Study Cost Where Test Article Is $10.00/mg	$23,875,962		$29,952,415	

Study type in-life cost assessment

Table 2. In-life costs for a 104-week carcinogenicity study using three dose groups and two test article costs

	RccHan®:WIST		CRL:CD®(SD)	
	Males	Females	Males	Females
Test Article Dose (mg/kg)	100, 300, 1000		100, 300, 1000	
Total Amount of Test Article Utilized (g)	7,118		9,119	
Number of Animals Required	241	241	281	281
Per Animal Cost	$47.60	$46.50	$51.20	$41.25
Total Animal Cost	$22,678		$25,978	
Technician Time, Housing, Husbandry Cost	$413,997		$479,860	
Results				
Scenario A: Total Study Cost Where Test Article Is $0.10/mg	$1,148,518		$1,417,778	
Scenario B: Total Study Cost Where Test Article Is $10.00/mg	$71,620,877		$91,699,801	

The findings from the modeled studies are depicted in the following plots (Figure 6 and 7), which offer an immediate sense of the total study costs for each study type and rat strain. While the percent cost savings is 20–25% for both scenarios, as described earlier, the greatest absolute cost savings are achieved for the larger and longer 104-week studies.

Study type in-life cost assessment

Figure 6: Total in-life study costs at $0.10/mg test article

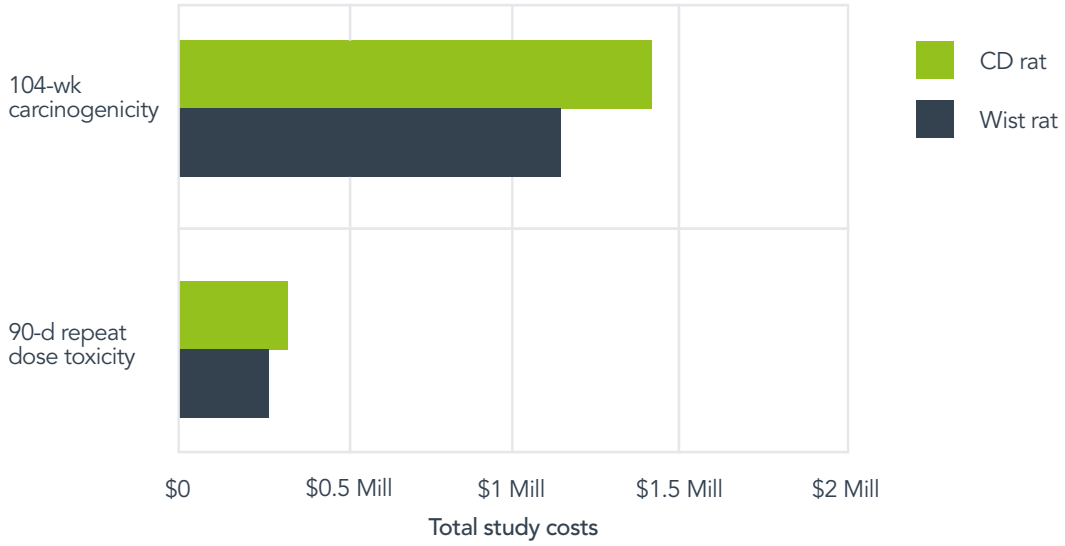
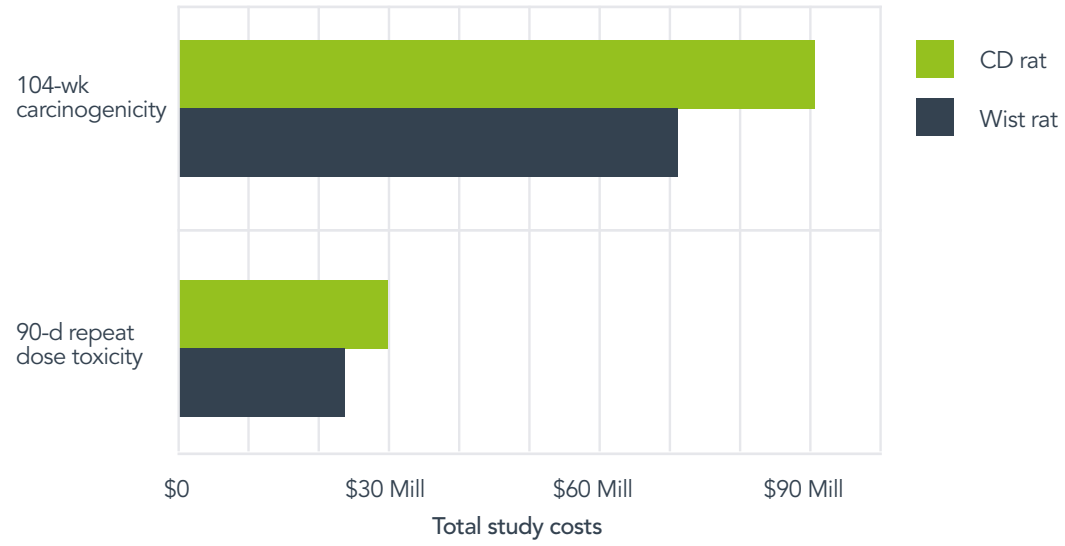


Figure 7: Total in-life study costs at $10.00/mg test article



Conclusions

The RccHan®:WIST and CRL:CD® (SD) rat strains are commonly used for safety assessment studies. While these strains share some similarities, they also harbor key differences, including lower body weight, enhanced survivability, and overall lower tumor burden for the RccHan®:WIST relative to the CRL:CD®(SD) rat. These favorable attributes can result in enhanced animal welfare and cost savings since there is potential for decreased test article usage, fewer animals required at study initiation, and decreased *per diem* and overall housing and husbandry costs.

As demonstrated in the analysis of the two study types, cost savings were achieved for the RccHan®:WIST rat at both test article prices, whereby cost savings ranged between $60,000 and $6,000,000 for the 90-day repeated dose toxicity study, and between $269,000 and $20,000,000 for the 104-week carcinogenicity study.
In summary, it is clear that investigators should carefully consider the potential economic benefits of choosing the RccHan®:WIST rat when planning future studies.