

NTP

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Harlan

Advantages

Inbred Animal Models

- Highly consistent
- Essentially genetically identical - isogenicity
- Highly reproducible across individuals and generations
- Test different chemicals and doses on essentially the same genotype
- Minimize phenotypic variances
- Maximizes sensitivity of toxicological assays [Festing 1987; Festing 1995]
- Use multiple strains to ensure that one of the strains is sensitive to a given toxicant

F1 Hybrids

- Highly reproducible isogenic strains
- Uniformly heterozygous at all loci differing between parental strains
- Uniform genotypes
- Appropriate for single generation toxicology assays
- Not appropriate for multigenerational assays due to increased variability of the F2 and F3 generations

Outbreds

Avoid

- Genetic bottlenecks
- Small numbers of breeders
- Rederivation

Harlan Outbred Rats

- **Primary Source Colony**
supplies breeders for each geographically separate Harlan outbred colonies
- **Multiple international breeding units**
using rotational mating
- **Future Breeders**
Minimal selection pressure
- **Large breeding colonies**
- **International standardized colony management program**
e.g. Same Harlan Teklad diets manufactured in the US and Europe
- **Cryopreservation?**

Outbred Rats

- **Production Performance**

PEI = Production Efficiency Index

number of offspring weaned per female per week

LA = Litter Average

- **Body Weights**

weaning

8-10 weeks of age

growth to 6 months

- **Other characteristics**

- **Health – Pathogen Free / Barrier Raised**

Rat Stocks / Strains

- **Wistar Institute 1906**

- almost ½ of inbreds and many of the outbreds

- LEW
 - WF
 - LE
 - Sprague Dawley

- **Other sources**

- F344
 - AUG
 - COP
 - ACI



Hsd:Sprague Dawley[®]TMSD[®]TM

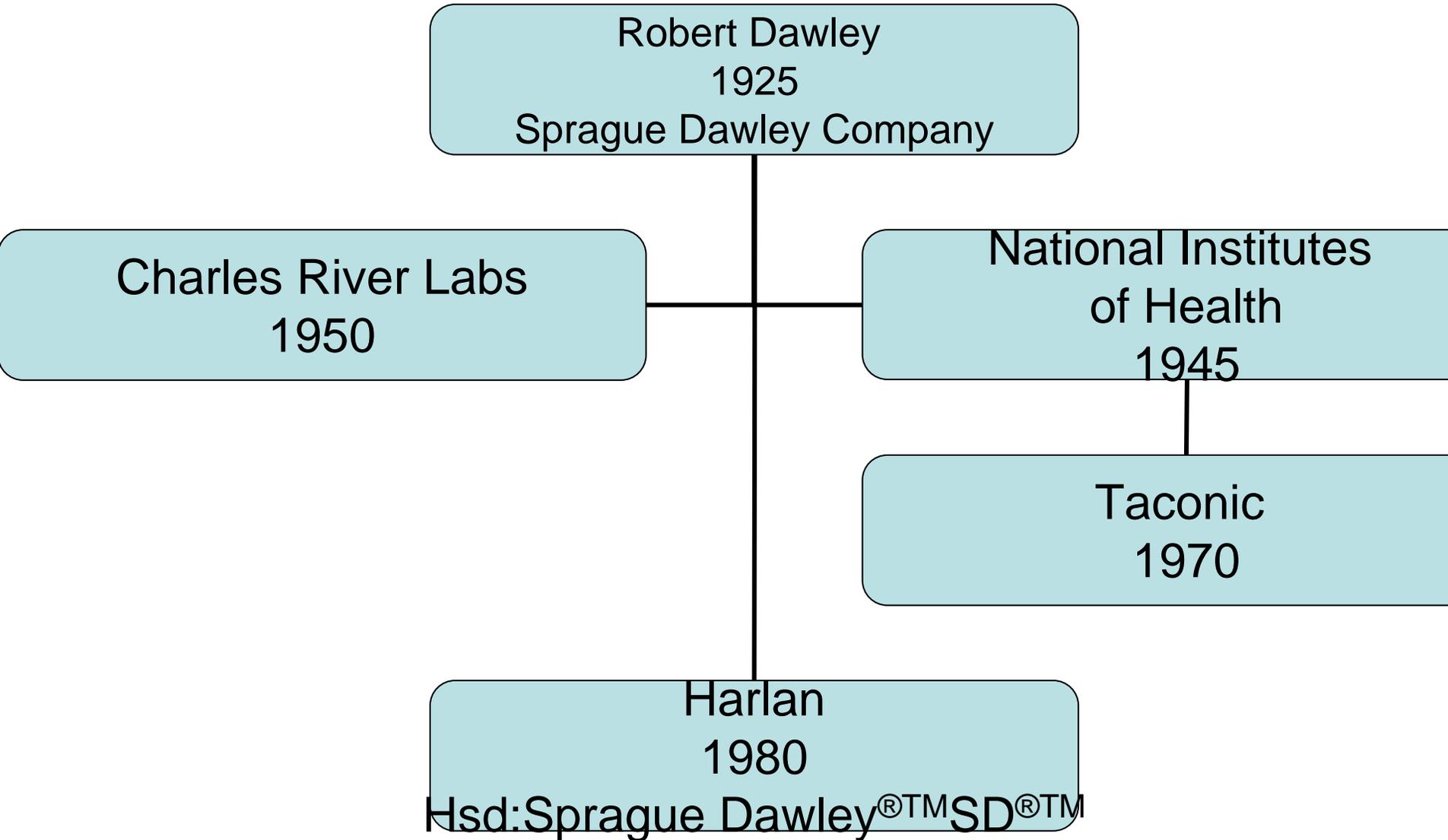
Registered trademarks of Harlan Sprague Dawley, Inc.,
Indianapolis, Indiana
and Harlan Sprague Dawley, Inc., in the United Kingdom

Sprague Dawley Rats

- Originated by Robert W. Dawley in 1925
- Black hooded hybrid male rat of exceptional size and vigor -- genetically half white -- origin unknown [wild?]
- Mated to a white female [probably Wistar] and backcrossed the male to the offspring of the white female for 7 consecutive generations
- Developed inbred lines
- Crossed the best 10 inbred lines to form the Sprague Dawley
- Selected stock for high lactation, rapid growth, vigor, good temperament and high resistance to arsenic trioxide
- Selection methods most likely deleted deleterious recessive genes
- Most genes probably originated from the single male
- Harlan purchased Sprague Dawley Inc in 1980

Hsd:Sprague Dawley[®]TMSD[®]TM

Sprague Dawley Rat



SD[®] Differences from CD[®]

- **Body weights lower**
[Klinger 1996] [Petersen 1996] [Stanhope 2000]
- **Longevity greater**
[Klinger 1996] [Petersen 1996] [Stanhope 2000]
- **Litter average lower**
[Timwell 2002] [Heindel 1994] Daughtrey 1994] [Tyl 2002]
- **Adult onset obesity not seen**
[Stanhope 2000]
- **Nitric oxide synthase inhibition effects on blood pressure and fetal weight differ**
[Pollock 1998] [Turnbull 1999] [Buhinschi 2001]



HsdRccBrIHan:WIST

Hannover Wistar Rat

RCC / BRL

Rederivation

Isolators

HsdRccBrlHan:WIST

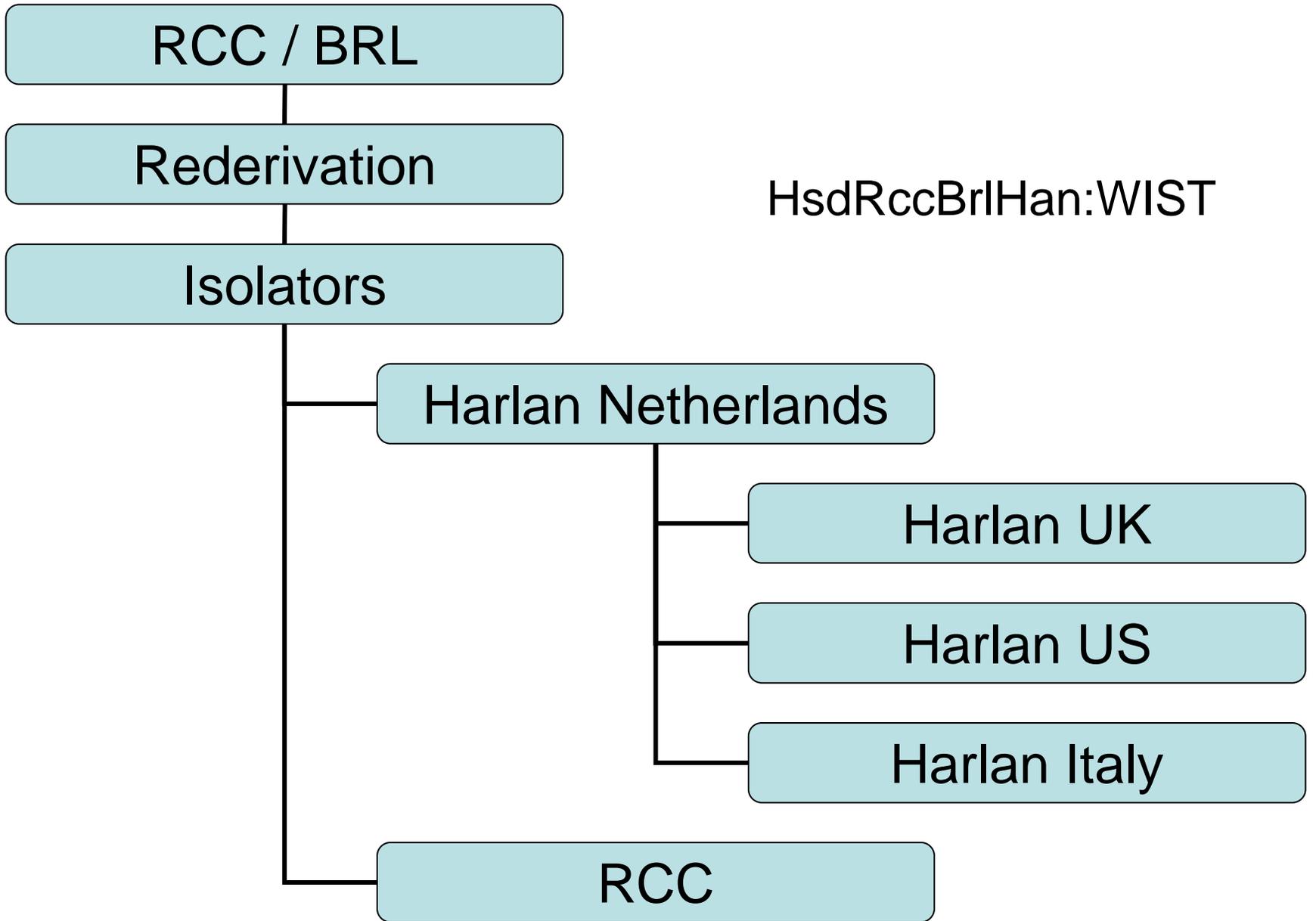
Harlan Netherlands

Harlan UK

Harlan US

Harlan Italy

RCC



• 104 Weeks: HsdBrIHan:WIST-Males - Selected Spontaneous Neoplasms

• 104 Weeks: HsdBrIHan:WIST-Males - Selected Spontaneous Non-Neoplasms

• 104 Weeks: HsdBrIHan:WIST-Females - Selected Spontaneous Neoplasms

• 104 Weeks: HsdBrIHan:WIST-Females - Selected Spontaneous Non-Neoplasms

• Food Consumption: Historical Control Data - Males and Females

• Body Weights: Historical Control Data - Males and Females

• Survival Rate: Historical Control Data - Males

• Survival Rate: Historical Control Data - Females

Other available literature

Huntingdon Life Sciences - A Review of In-Life Parameters and
Tumor Data from Han Wistar Rat Dietary and Oral Gavage
Tumorigenicity Studies

Huntingdon Life Sciences - A Review of the Choice of Rat Strain
in Tumorigenicity Studies

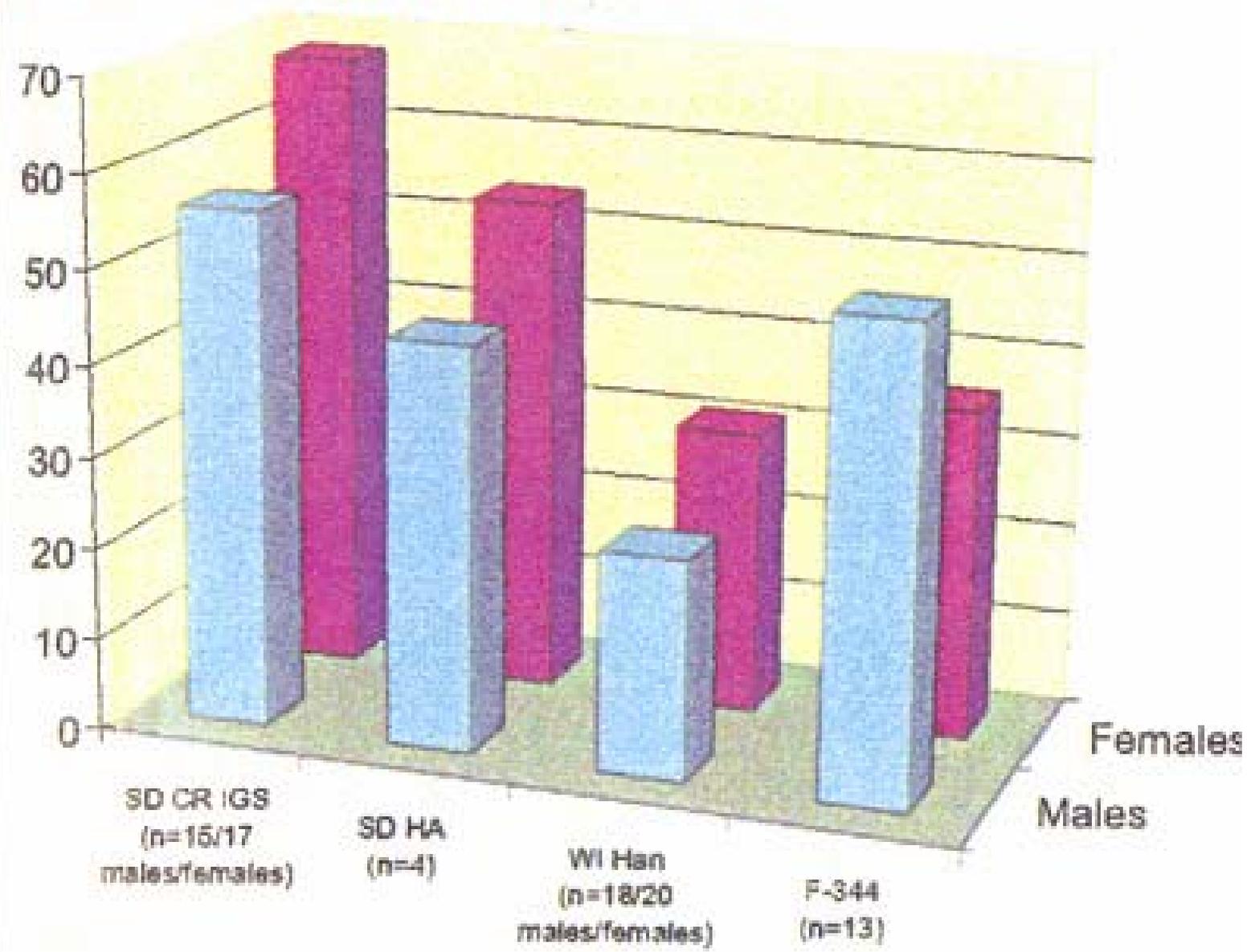


RCC Ltd
Zelgliweg 1
CH-4452 Itingen
Switzerland

Harlan Hannover Wistar Rats

- **Primary Source Colony supplies breeders for all colonies**
- **Multiple equal - sized breeding units**
- **Future Breeders**
Minimal selection pressure
- **Rotational mating program**
- **200 females plus per colony**
- **Mated** **1 X 1 or 1 X 2**
- **Retired** **36-40 weeks breeding**

Figure 1: Mortality at Week 104





HsdRccBrIHan:WIST

Hannover Wistar Rat

Resources Available

- International Commercial Breeders
 - Locations
 - Barriers
 - Health
 - Genetics

Multiple sources of rodents

NTP establish collaboration with all breeders to monitor rodent sources

