Juvenile toxicology cross-fostering – a better way forward?

“ A cross-fostering approach to juvenile rat studies not only simplifies the time and cost involved but refines the quality of data too! ”

Why focus on juvenile animal allocation?

By improving study design and the removal of unnecessary endpoints we have focused our efforts on reducing animal usage and wastage in addition to refining juvenile rat toxicology study data.

+ Following technical instruction animals are littered and cross-fostered at supplier
+ Litter standardised on day of birth and delivered from at least 3 days of age
+ The selection criteria used ensures a consistent age of offspring at fostering
+ Utilises natural breeding stock with proven foster dams (defined by successfully littered offspring to rearing on up to 5 previous occasions)
+ Signed documentation received confirms technical instruction adherence (Acceptable to UK GLP).

Advantages

+ Practically feasible for animal suppliers
+ Utilising supplier colony enables:
  - Wider genetic diversity, refining data
  - Allows allocation of all cross-fostered offspring to study, decreasing numbers of litters required
  - Removes natural wastage
  - At animal suppliers, unused natural offspring and dams returned to breeding stock
  - No culling required
+ Simplifies study logistics, e.g. no in-house littering allows better planning
+ Using dams of proven maternal quality reduces maternal bias and virtually eliminates litter losses
+ Can reduce lead time to study initiation.
+ No supplier time-mating needed for smaller studies

Summary

The benefits of using a cross-fostering process

+ Vast reduction in number of animals used on juvenile rat studies at Sequani as a direct consequence of changes in allocation
+ Superior method of allocation, ultimately increasing genetic diversity thereby refining quality of data obtained
+ Simplifies logistics, time and cost
+ Currently Sequani are the only UK CRO routinely using supplier cross-fostered litters for juvenile studies. We have run over 60 studies since 2009.
Cross-fostered

+ The natural offspring from each dam are fostered to multiple foster dams
+ Each cross-fostered litter has no siblings

Advantages:
- Simplifies operational procedures
- Reduces risk of cross-contamination
- Less impact from litter loss

Disadvantages:
- Highest wastage - 50% to 83% of the litter wasted, plus dams
- Typically dams are primagravid, increasing risk of poor maternal behaviour
- Higher risk of maternal genetic bias.

Between litter

Selects up to three per sex of the dams offspring to allocate to a single study dose level/group in the same litter.

Advantages:
- Less wastage than between litter allocation
- Less impact from litter loss
- Any bias spread across dose levels/groups

Disadvantages:
- Higher potential for sibling cross-contamination
- Compound-related clinical signs could bias pup survival
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- More difficult operationally e.g. clinical observations and dosing.

Within litter

Within the same litter, the dam’s offspring are allocated to different dose levels/groups.

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Most common method of allocation in industry

Cross-fostered

+ Enables allocation of all offspring to study, and commonly one group / dose level.

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Most uncommonly used

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For more information visit: www.sequani.com/cross-fostering