Dermal Application Calculated Dose Site Size vs. Calculated Body Surface Area in Rats

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INTRODUCTION

Dermal application for test article is a necessary and commonly used dose route in rodents. The standard area for dermal application sites is approximately 10% Body Surface Area (BSA). This BSA represents the approximate surface area of a drug that will be used in humans (e.g., the face for acne medication, the top of the head for hair loss drugs, etc.). Currently in some Contract Research Organizations (CROs), the standard for calculating this dose site area is done by a mathematical equation to find the mean surface area for each sex/group. This area is then measured out on marking templates to mark the "four corners" of the dose site template on the animals. In addition to being time consuming, this method is also inaccurate and requires handling the animals more often than is necessary.

OBJECTIVE

The objective for this project is to determine that the area from the scapulae to the wings of the ilium extending to the lateral midline of the animal, Proposed Dosing Area (PDA), is close to 10% BSA to eliminate the need of marking dose sites. Most study protocols widely use 10% BSA to determine the dose site. The dose site for rodent studies is mostly based off of group/sex mean bodyweights. Using the natural landmarks will provide a less stressful way of acknowledging the dose site without having to restrain the animal for a longer time period than necessary during marking sessions. This will also free up time for technicians who have to repeatedly mark these sites once or twice a week allowing them to focus on other aspects of the study. This time spare will also save the company resources and money. Fewer man hours will be spent in a single room to mark what can be seen clearly once the animals have had their dorsal surfaces shaved free of hair. Each week after body weights are collected, a technician will no longer have to find ranges across a sex group to draw and cut out a new dose site template. Study cost and resources can be reduced by limiting money spent on permanent markers, making of templates, and compiling body weight summaries for the dosing site marking

METHODOLOGY

In order to measure the length and width of each animal's proposed dosing site, a string was taken and held next to a restrained animal. The string was used to help accurately measure the curved area of a live animal. A second person held the animal in order for the dorsal surface to be visible while the first person placed the string along the animal's dorsal midline from the hips to the shoulders. In addition, the width between each shoulder and each hip was collected. The measured lengths of the string were then placed next to a ruler to obtain an accurate measurement. Additional data was gathered on the animals, including:

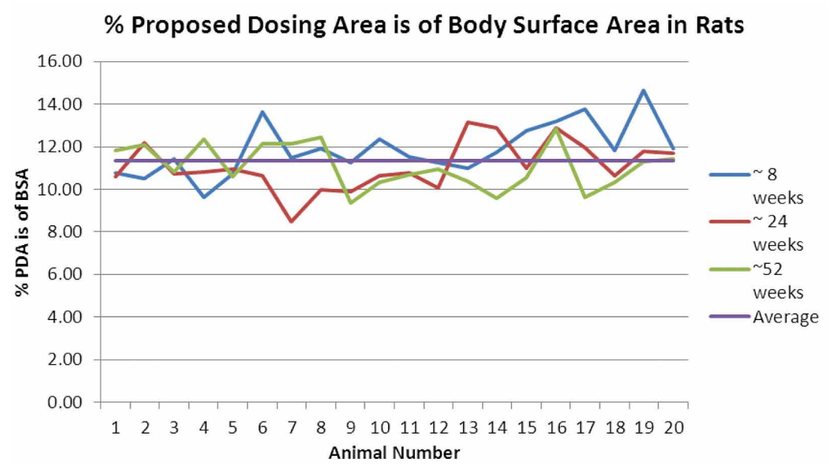
- Current body weight
- Sex
- Current age

Different life stages of animals were examined, at roughly 8 weeks, 24 weeks, and 52 weeks. This helps to show how the dose site would grow with the animal in a natural way; 10 animals per sex were measured in each of the age categories. The following equation was used to calculate the BSA of each animal:

Rat BSA1 = 9.6*W2/3 where A is the estimated area in square centimeters and W is the body weight in grams

RESULTS

Animals at 8 weeks of age had a PDA range of 33.62–53.03 cm^2, and 10% of the BSA ranged from 27.51–40.35. The percentage of PDA of BSA ranged from 9.62–14.65 with an average of 11.87. Animals approximately 24 weeks of age had a PDA range of 48.95–77.95 cm^2, and 10% of the BSA ranged from 38.10–78.99. The percentage of PDA of BSA ranged from 8.49–13.16 with an average of 11.09. Animals approximately 52 weeks of age had a PDA range of 53.11–73.21 cm^2, and 10% of the BSA ranged from 46.29–69.30. The percentage of PDA of BSA ranged from 9.35–12.88 with an average of 11.09.



CONCLUSIONS

In rats it was found that the average range for all age groups did not exceed +/- 1.9% from the 10% BSA used as a marking template in most protocols. These differences from the 10% BSA will not impact the results of toxicology studies, according to our scientific staff. The current templates were not exact in size and could vary between animals due to natural movements and growth patterns. By using each individual animal's physiology, the dose site size will become more accurate to the scale of 10% BSA, which then eliminates the need for an average template. The goal is also to look into a similar conclusion for mice at a later date.

REFERENCES

Dereklanko, Hollinger MJ and MA, editors. CRC handbook of toxicology. 2nd ed. Boca Raton (FL): CRC