

# Procedure Development for Repeat Infusions in Juvenile Monkeys

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## ABSTRACT

With the increase of pediatric pharmaceuticals in preclinical studies, the ability to learn and adapt to the use of a younger and smaller test model is necessary to ensure process evolution and stress reduction on the research animals. The cynomolgus macaque is a commonly used nonhuman primate in research. Method development for a repeated-infusion dose in juvenile nonhuman primates required a united effort to create a concise study and equipment design, with animal welfare at the forefront of all considerations. The routine method for infusion restraint included the use of a procedure cage where all limbs were secured, providing limited movement. This method would be highly stressful for the animals needed for the proposed study (juvenile animals 6 to 9 months of age at initiation of dosing). To minimize stress, the snuggle wrap method was developed, to allow young animals to remain immobile while still feeling comforted by a hugging-like sensation. The snuggle wraps were designed for vein accessibility, while the remaining limbs are secure and comfortable. Stress behaviors were noticeably reduced when using the snuggle wrap compared to manual holding as a restraint method.

Given that social pairs needed to remain in proximity, the snuggle board was also developed. Animals were implanted with RFID chips, and the wrapped juveniles were labeled with temporary ID cards to allow for easy identification once snuggled and placed on the board. These boards hold 4 snuggled animals closely together, which keeps social pairs in visual and auditory contact during dose administration. Following catheter placement, dosing limbs were secured with Velcro® straps for the dose duration. Animals were visually monitored, provided treats, juice, light projections, and chewing toys throughout dose duration by trained technicians. The snuggle board restraints were used for ~13 weeks, until the animals were over a year old and large enough for the procedure cage. This method was also successfully implemented in animals as young as 3 months.

## INTRODUCTION

With the increase of pediatric pharmaceuticals in preclinical studies, the ability to learn and adapt to the use of a younger and smaller test model is necessary to ensure process evolution, and stress reduction on the animals. The cynomolgus macaque is a commonly used nonhuman primate in research. Our onsite team has an expansive variety of nonhuman primate experience, cynomolgus macaque, and others, with subjects ranging from newborn to geriatric. Method development for a repeated infusion dose in juvenile nonhuman primates required a united effort to create a concise study and equipment design, with animal welfare at the forefront of all considerations.

## STRATEGIES

- Create a cohesive design that promotes functionality and comfort, provides the necessary equipment/supplies, and allows for long duration of care and support
- Select designated procedure room
- Itemize possible stress factors and reduction plan
- Utilize design with 6 training animals under current SOPs and IACUC approvals
- Train technical staff with training animals

## METHODS

- Startup and development of the juvenile restraint procedure involved oversight by a multi-disciplinary group of professionals.
- The development and refinement of all portions of the procedure was an ongoing process; we started with 6 age-appropriate juvenile cynomolgus macaque with previous history of human interaction as training animals.
- Snuggle acclimation training occurred for 2 weeks every other day, with increased snuggle board time at each training session. Positive reinforcement was provided during and following each session. Body temperatures were taken at intervals to ensure animals were not overheated during procedures.

## DESIGN



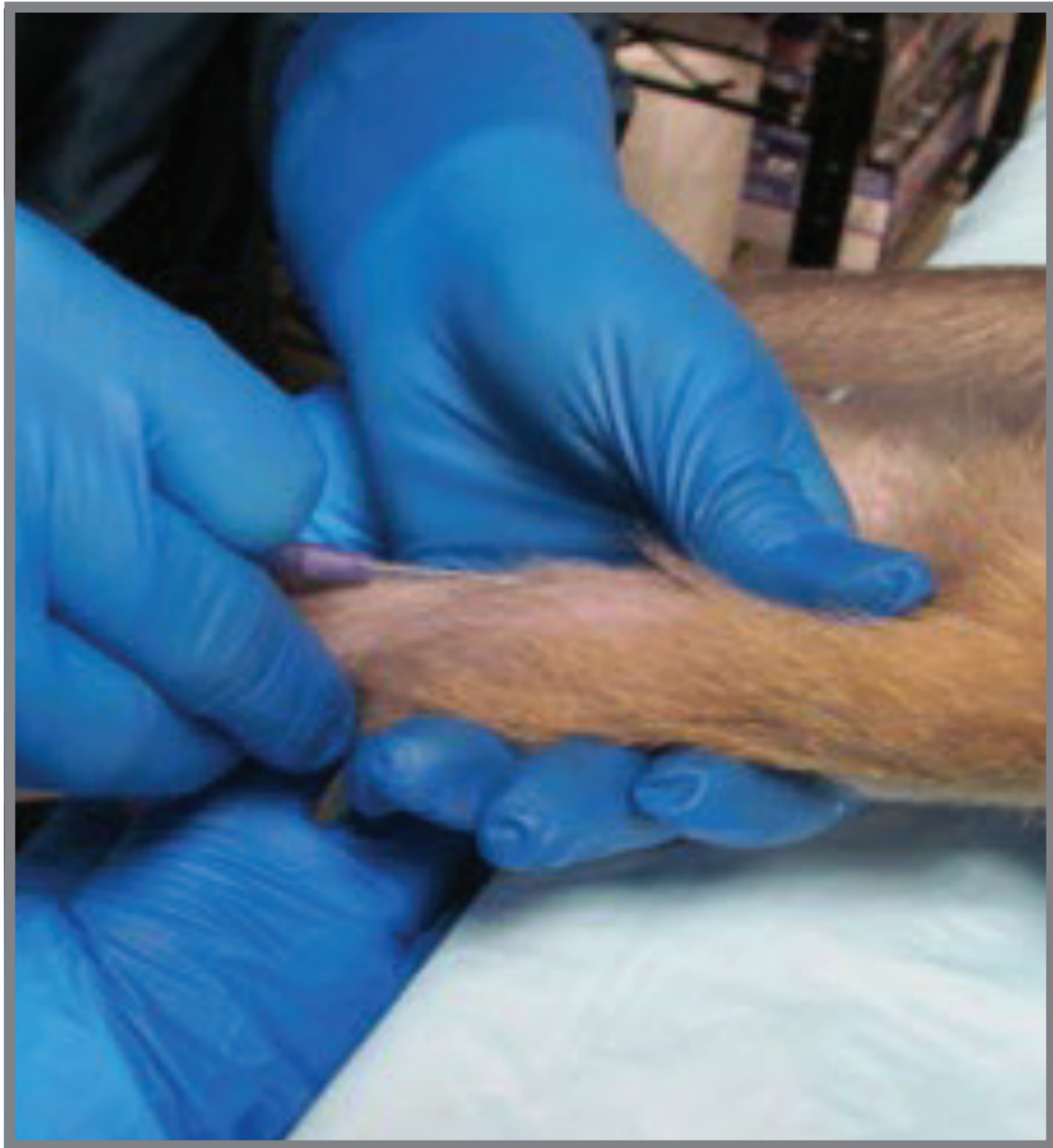
**Figures 1.**  
Small-hole procedure cages were used for transport from study room to designated procedure room.



**Figures 2 and 3.**  
Receiving blankets were used as a base wrap prior to the use of the unique customized snuggle wraps.



**Figures 4 and 5.**  
6 different snuggle wrap sizes were utilized depending on the size of the animal. Wraps were used to expose either 1 arm for cephalic vein or saphenous vein for catheter placement rotation.



**Figures 6.**  
Restraint boards held 4 monkeys per board. Socialized pairs were able to remain close. Infusion pumps were in proximity for vein accessibility.



**Figures 7.**  
Color matching cage cards and Velcro® were used to avoid cross-contamination. Fabric items were washed daily after use.



**Figures 8 and 9.**  
24 animals were monitored, treated, and cared for during weekly dosing by trained staff with assessable equipment.



## BODY TEMPERATURES

Average Juvenile Cynomolgus Macaques	Pre-Snuggle Average	30 Minutes Post-Snuggle Average
37.0 °C - 39.5 °C	38.5 °C	38.8 °C

## EQUIPMENT AND SUPPLIES

Items	
Separate procedure room	Restraint boards
Small hole procedure cage - for transfer	Colored Velcro® straps
Receiving blankets	Color projector
RFID implants	Fruits, veggies, pasta, sweet treats
Transferable ID card	Juice
Velcro® strips	Enrichment toys
Soft cloth ties	Reusable diapers

## CONCLUSION

Drawing on the knowledge and expertise of our team members, we were able to implement a stress-reduced dose infusion administration method for juvenile NHP. The weekly 1-hour infusions for the initial 52-week study were completed under this method in 6-month-old animals, prior to transferring to our standard procedure cage. This method can additionally be used for similar-aged or younger nonhuman primates for standard IV bolus or shorter infusions. This method was successfully utilized in a number of chronic toxicology studies in juvenile nonhuman primates, which could not have been executed using standard restraint methods for animals in this age range.