



February 15-17, 2017: ACC&D Think Tank on Ethical Decision-Making in Innovation for Animal Welfare

Contraceptive field trial in cats: A Think Tank case study

Background: GonaCon™, a gonadotropin-releasing hormone (GnRH) immunocontraceptive vaccine, was developed by the USDA National Wildlife Research Center and approved by the U.S. EPA for female wild horses, burros, and white-tailed deer. Dr. Julie Levy studied an early formulation (not the version ultimately approved by the EPA) in male and female purpose-bred, specific-pathogen-free cats in a laboratory setting (all were adopted following the study). Results in females were promising: contraception for a median of 39+ months with a single injection. To have “real-world” value, however, the vaccine would need to perform well in cats who were outbred, exposed to pathogens and parasites, and exposed to seasonal variations in temperature and light.

ACC&D recognized that in order to evaluate vaccine efficacy in our target cat population, and to do so according to our standards for research quality, we would need to take the next steps with research. Toward this end, we have sponsored two GonaCon studies in female cats.

The first was conducted in partnership with the Cincinnati Zoo’s Center for Conservation & Research of Endangered Wildlife (CREW) to confirm the safety of the EPA-registered product in cats, and at the same time collect antibody titers as an indicator of vaccine response. (CREW acquires purpose-bred cats from a local hospital for its research on fertility in endangered felids. Cats are ultimately adopted or live out their lives at CREW.) In this study, six CREW cats were vaccinated with GonaCon and monitored for four months. At the end, ACC&D adopted out all cats to persons within our network. The study received IACUC approval from Cornell University.

The case: Based on promising results, we sponsored a study, designed to last up to five years, of the GonaCon vaccine in a simulated free-roaming cat colony. A qualified team and 35-page protocol guided research; an IACUC oversaw research at Clowder Concepts, a facility custom-built for this study by an ACC&D Board member. Morris Animal Foundation was the primary funder.

To create the colony, connections within the animal control and sheltering community identified at-risk cats likely to be euthanized for space. Cats came from four county animal control agencies, one private rescue, and three individuals rehoming a cat on Craigslist.

Intake of forty-five potential feline candidates for the final study yielded the desired 30 queens and 5 toms to be enrolled in the study.

The facility consisted of a 40'x35' two-story space in a climate-controlled pole barn with a cement floor, insulation, electricity, and plumbing. Cats had daytime access to a 1/3-acre outdoor enclosure contained by a 10' wall of aluminum siding, plus ample enrichment opportunities indoors and out.

All cats were provided with core vaccines, parasite treatment/prevention, a regular diet, veterinary care if needed, and extensive socialization from Clowder staff and volunteers (University of Illinois students), who visited daily. Consequently, on many levels, the population represented the desired intermediate step between purpose-bred laboratory cats and an uncontained free-roaming colony.

Cats were subject to the following procedures during the study beyond routine healthcare and ultimate surgical sterilization: an IM injection of either the test vaccine or saline; two ultrasounds at intake to determine if a female was pregnant, followed by monthly ultrasounds starting in Month 4; periodic blood draws to measure contraceptive titers (5 blood draws in Year 1; 2–3 annually in subsequent years). A total of five tomcats were fertility tested. Three were added to the colony starting in Month 4; they were rotated and monitored for acceptably safe behavior and breeding ability and interest. Due to breeding/behavior, two toms were replaced during the course of the study.

Key relevant outcomes: When 70% of test cats became pregnant by the end of Year 1, the study was terminated as not meeting benchmark results, and all cats placed in adoptive homes. In study design, five of ten control cats were eligible for rehoming immediately upon becoming pregnant. Cats not selected for the study were provided with veterinary care as needed and rehomed as quickly as good placement could be found. The majority of rehoming were through private adoptions, but we transferred four cats to shelter partners for adoption, and one cat with health and behavior problems was transferred to Best Friends Animal Sanctuary.

Ethical questions and challenges: The study, both in its design and implementation, posed ethical dilemmas for which ACC&D sought precedent and tools to assist. Several of these ethical complexities could be applicable to other studies and contexts. They include:

- **Sourcing real-world cats:** Moving beyond laboratory cats to outbred cats was a key objective of the study, as was co-housing that allowed them to become pregnant. There was not precedent for how to do this within the restraints of pound seizure policies and laws in the state. Guided by the IACUC and the state veterinarian (who got legal advice), Clowder was ultimately credentialed as both a USDA research facility and an animal shelter under state law, a structure that worked for our

purposes but could be a precedent with repercussions. With this arrangement more sophisticated facilities chose not to participate in providing cats (due to concerns about pound seizure), but others did. A consent form was signed for each cat.

- **Health of cats:** We under budgeted the time and cost to care for some cats that became quite sick after arrival and were excluded from the study. Ailments included ringworm, a virus requiring hospitalization, and a serious infection precluding mobility/behavior issue that required extensive treatment and sanctuary transfer. Given our animal welfare values, it was decided that these cats not be returned to the animal control facilities but be rehabilitated and rehomed. In a few cases a euthanasia decision was considered but avoided, though not by consensus.
- **Possible risk/benefit to individual animals vs. benefit to future cats:** The length of service of these cats to research and their risk participating was judged in this case to be offset by benefits received by the individual. Benefits included exit from probable euthanasia by animal control, plus good care during and responsible rehoming following the study. However, we discussed what level of individual benefit is desirable/required to sanction this type of study?
- **Stress of medical intervention:** Blood analysis for contraceptive titer was a critical measure of vaccine response as was ultrasound to detect pregnancy. Decision-making regarding the frequency of both balanced animal welfare concern with desire for scientific data. Positive reinforcement training helped habituate cats to blood draws.
- **Termination of pregnancy:** We debated the ethics of a study that purposefully positioned cats to become pregnant and ethics of allowing the birth of purposefully conceived kittens vs. pregnant spays. The timing of ultrasounds enabled as early as possible termination following conception. Dr. Levy had previously allowed laboratory cats to give birth in order to address ethical concerns, and we made a different decision driven by concerns about cat overpopulation.
- **Behavioral stress:** Initial months in the colony were surprisingly peaceful prior to male introduction and even afterwards. However when the first females returned to the colony following pregnancy termination and spay, there was an outbreak of fighting that raised stress levels and potentially endangered the safety of the cats. Harmony with the males involved also became challenging. Given the early termination of the study this was resolved within months, but housing decisions had it continued would have had to pit individual welfare against integrity of the study and access to breeding opportunities.