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WH&B SEMI-ANNUAL PERFORMANCE/PROGRESS REPORT

Agreement Number: L15AC00145

Study Project Name: Reimmunization of Free-Ranging Horses with GonaCon Immunological Vaccine: Effects on Reproduction, Side-Effects, and Population Performance

Institution: Colorado State University

Reporting Period: April 1, 2017 – October 31, 2017

Principal Investigator(s): Dan L. Baker and Terry M. Nett

Co-Investigators: Jenny G. Powers, Blake E. McCann, Jason E. Ransom, and Jason I. Bruemmer

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Objectives:

1. To determine the most effective reimmunization schedule for GonaCon vaccine for suppressing reproductive rates in free-ranging horses, the duration of effectiveness, and the return to fertility following treatment.

Progress:

During the 2017 field season, we observed all mares (*n* = 92) associated with each of four post-primary revaccination groups and a saline-treated control group for the prescience/absence of a foal. We met our sampling objective of observing more than 95% of all experimental mares at least weekly and 100% of them every two weeks from 1 March to 1 August. It's possible that some foals were born and died without being detected but given the intensity of our sampling observations, we feel that this was an infrequent event. Observations during the remainder of the year (August – December) and following winter were and will be less intense and more opportunistic depending upon available personnel, weather, and road conditions. During this time period, neonatal mortality, if it occurs, will more likely go undetected.

To determine the most effective revaccination schedule for GonaCon vaccine, we randomly assigned females to one of four post-primary revaccination treatments: 4 yr (*n* = 25), 2 yr (*n* = 11), 1 y (*n* = *14), 0.5* yr (*n* = *15*) and compared foaling proportions of each to a control group (*n* = 27). Experimental mares were given a primary vaccination by either hand-injection or remote dart delivery in the fall and subsequently revaccinated according to the above treatment schedule. As of March 2016, all primary and secondary vaccinations had been applied to all mares in the study. We predicted that non-pregnant females revaccinated with GonaCon during the fall would presumably be contracepted the following spring and be infertile in subsequent breeding seasons until anti-GnRH antibodies declined below threshold concentrations and regained fertility. Thus, the first year that contraceptive effectiveness could be determined would be the second foaling season following revaccination.

Foaling proportions for the second post-treatment foaling season were lower ($P \leq 0.09$) than that for control mares for all treatment groups, where it could be determined (4yr, 2yr, and 0.5 yr) (Table 1). This was particularly evident for the 4 yr and 0.5 yr treatments, where none of the reimmunized mares produced a foal (effectiveness = 1.0). Foaling proportions for the 2 yr treatment group were slightly higher 0.27 (3/11) (95% CI = 0.09-0.56) than those for the previous treatments but still lower ($P = 0.09$) than that for control mares. Vaccine effectiveness for this treatment group was 0.68.The proportion of control

mares foaling this season was estimated to be 0.84 (21/25) (95% CI = 0.65-0.94). Foaling proportions and vaccine effectiveness could not be determined for the 1 yr treatment group since data for the second post-treatment foaling season will not be available for these mares until the 2018 foaling season.

Table 1. Comparative foaling proportions (number of mares with foals/total number of mares) and vaccine effectiveness (proportional reduction in foaling between control and treated mares) for four post-primary reimmunization treatments and a saline control group during 2014-2017 foaling seasons at Theodore Roosevelt National Park, North Dakota.

Comparative Parameter Values	Reimmunization Treatment Groups				
	Control	Four Year	Two Year	One Year	0.5 Year
Primary vaccination (yr):	09/2009	09/2009	09/2013	09/2015	09/2015
Revaccination (yr):	09/2013	09/2013	09/2015	09/2016	03/2016
GonaCon delivery:	Hand-injection	Hand-injection	Dart	Dart	Dart
First Post-Treatment Foaling Season:					
Year:	2014	2014	2016	2017	2016
Sample size:	27	25	11	14	15
Foaling proportion %: (y/n)	0.56 (15/27)	0.60 (15/25)	0.36 (4/11)	0.71(10/14)	0.53 (8/15)
95% CI:	0.37-0.72	0.40-0.76	0.15-0.64	0.45-0.88	0.30-0.75
P-value (treatment vs control):		*P* = 1.0	*P* = 0.33	*P* = 0.47	*P* = 0.52
Effectiveness:		-0.07	0.36	-0.21	0.05
[1]**Second Post-Treatment Foaling Season:**					
Year:	2015	2015	2017	2018	2017
Sample size	25	25	11	14	13
Foaling proportion % (y/n):	0.84 (21/25)	0.00 (0/25)	0.27 (3/11)	Data not yet	0.00 (0/25)
95% CI:	0.65-0.94	0.0-0.13	0.09-0.56	collected	0.0-0.23
P-value (treatment vs control):		*P* = 0.0001	*P* = 0.09		*P* = 0.001
Effectiveness:		1.00	0.68		1.00
Third Post-Treatement Foaling Season:					
Year:	2016	2016	2018	2018	2018
Sample size:	25	25			
Foaling proportion % (y/n):	0.84 (21/25)	0.16 (4/25)	Data not yet	Data not yet	Data not yet
95% CI:	0.65-0.94	0.06-0.35	collected	collected	collected
P-value (treatment vs control):		*P* = 0.004			
Effectiveness:		0.81			
Fourth Post-Treatment Foaling Season:					
Year:	2017	2017	2018	2018	2018
Sample size:	25	24			
Foaling proportion % (y/n):	0.76 (19/25)	0.17 (4/24)	Data not yet	Data not yet	Data not yet
95% CI:	0.56-0.88	0.07-0.36	collected	collected	collected
P-value (treatment vs control):		*P* = 0.004			
Effectiveness:		0.78			

[9]

[1]First foaling season that the contraceptive effect of reimmunization could be determined.

2. To determine the safety and physiological side-effects (if any) in feral horses following re-vaccination with GonaCon including visual assessment of general health, body condition, injection site reactions, effects on current pregnancy, and neonatal health and survival.

Progress:

Thirty-two foals were born during the 2017 foaling season (control-19; ConaCon-treated-13). Births occurred from early February to late September with 84% (27/32) observed during the first four months of the foaling season. Average foaling dates for treated and control mares were 27 May (95% CI = 17 April–6 July) and 23 April (95% CI = 29 March-18 May), respectively. These data indicate that average parturition date for treated females was approximately 34 days later than births from control females. While this difference was not statistically different (P = 0.12) and probably due to the small and variable sample size of treated mares, it does portend a biological "red flag" for a potential side effect related to the return to fertility when contraception sufficiently decays. This effect has not been previously reported for GonaCon-vaccinated females but has been observed in porcine zona pellucida (PZP) - treated mares (Ransom et al. 2013). In our study, the consequence of late births in post-treated females did not result in differences in survival rates for foals born to treated and control mares. Post-natal survival rate (birth to 14 da) for foals born to treated mares was 84.7% (11/13) compared to 89.5% (17/19) for foals born to control mares (P = 0.56). Average foal age at first observation across both treatment and control groups was 1.5 da (95% CI = 0.77-2.2). With the exception of two foals in each treatment group, that were in poor condition at birth and subsequently died shortly thereafter, all other foals were classified as vigorous and found to be in good to excellent condition when first observed.

The effects of revaccination on injection site reactions and body condition was previously reported in 2016 for the 4 yr treatment group. Likewise, similar data was collected for all treatment groups in 2017 and is currently being analyzed.

3. To determine the effects of GonaCon re-vaccination on the behavioral side-effects (if any) in free-ranging horses including quantitative assessment of the effects on daily activity patterns and social interactions.

Progress:

Data relevant to the evaluation of the effects of GonaCon revaccination on behavioral side effects in free-ranging horses at THRO has been collected and analyzed and a manuscript describing these effects is currently in preparation with anticipated submission to a peer-reviewed journal in December 2017.

4. To develop and test a safe and effective dart configuration and injection system for remotely administering GonaCon vaccine to free-ranging horses by means of a syringe dart.

Progress:

Results relevant to this objective were reported previously in 2016 and then subsequently submitted and accepted for presentation at the 8th International Conference on Wildlife Fertility Control at Gallaudet University, in Washington, DC during July 18-21, 2017. This abstract was published in the proceedings of this conference and ultimately will be submitted to a peer-reviewed journal.

5. To develop a Bayesian model to forecast the consequences of different GonaCon revaccination treatments on population performance and test the optimum model in a free-ranging horse population.

Progress:

Applying GonaCon to control the growth of feral horse populations will require that resource managers choose specific tactics for treating animals. Choices must be made on the number and age to treat, the frequency of treatment, and the addition of age specific removals to maintain population age structure. Decisions on the best tactics will depend on comparing the effects of alternative management actions on population performance. Once the field experiment at THRO is completed, we will provide support for these decisions by developing an interactive model of feral horse population dynamics. This model will combine knowledge of feral horse ecology with an understanding of the constraints intrinsic in GonaCon contraceptive technology.

Literature Cited

Ransom, J. I., N. Thompson Hobbs, and J. Bruemmer. 2013. Contraception can lead to trophic asynchrony between birth pulse and resources. PloS ONE 8(1): e54972.