

Briefing Prepared for: BLM WH&B National Program Office

Re: contraceptive ideas presented by Drs. Voss and Shiner (2002) relative to the potential for nonsurgical vasectomy or “anti-GnRH” products to sterilize stallions as a means of population control in wild horses

Prepared by: National WH&B Research Advisory Committee

BACKGROUND

In late 2003 the National WH&B Research Advisory Committee was asked to look into ideas presented to the Nevada Wild Horse Commission by Drs. Jim Voss and Kirk Shiner in 2002 relative to the non-surgical vasectomy or treatment of stallions with an anti-GnRH product as a means of population control for wild free-roaming horses. An informal briefing that described the limitations of these approaches was prepared in December 2003 and delivered to John Fend, WH&B Group Manager at that time. A second similar inquiry was received from the NV Wild Horse Commission in late 2007. This briefing is prepared to address that interest.

STEPS TAKEN TO PREPARE BRIEFING

- Review of minutes from December 14, 2002 meeting of NV Wild Horse Commission
- review of available research regarding GnRH agonists, toxin conjugates, and vaccines as fertility control agents in horses
- email and phone conversation (2003) with Dr. Jim Voss (retired)
- email and conversations (2003 and 2007) with Dr. Ed Squires (expert in stallion fertility, Colorado State University, retired)
- consultation with scientists at the US Geological Survey
- review of the 2001 USGS expert panel report, “Development of Contraceptive Agents as a Management Tool to Limit Fertility in Wild Horses”
- review of report “Evaluation of Two Potential Contraceptive Agents in the Domestic Mare,” Dr. Patrick M. McCue, Colorado State University (unpublished)

GENERAL COMMENTS

There appears to be some confusion regarding what was presented by Drs. Voss and Shiner to the Commission in 2002. There seems to be an impression that the ideas and agents discussed by Dr. Voss in 2002 are available on the market for research or management use. However, in a phone conversation with Dr. Voss in 2003, he described that presentation as a “fund raising trip”, to present ideas that they were willing to research for potential future use in the field. We discussed 2 approaches to sterilizing stallions that he had presented in the past: 1) chemical vasectomy achieved by the injection of scarring agents directly into the vas deferens (testicle) and 2) the use of agents (toxins, agonists or vaccines; he wasn't specific) that act against gonadotropin releasing hormone (GnRH) and therefore suppress both sperm production and reproductive behavior. Unfortunately, at this time, Dr. Voss is no longer available for consultation for medical reasons. Attempts to contact Dr. Shiner, who is no longer associated with the University or working in research, received no reply.

Given these limitations, the line of inquiry rekindled now by the Commission can best be addressed as 3 questions (discussed below):

- 1) Is there a surgical or non-surgical vasectomy procedure that could be used to sterilize stallions?
- 2) Is there a product that acts on the GnRH axis that could be used in stallions (or mares) for effective population control?
- 3) Is the stallion approach a promising one for population control in wild horses?

SPECIFIC COMMENTS

1) Vasectomy in stallions is a very rare, essentially unheard of, procedure in veterinary medicine, whether surgical or by the injection of sclerosing agents into the vas deferens (tubule that carries sperm). Both approaches would require general anesthesia and expert technique developed through trial and error specifically for this application. Again, in horses, these are not standard techniques used in veterinary practice or research. Vasectomy can be done in horses, but it is much more difficult compared with vasectomy in rams or bulls. It seems, some time in the past Dr. Voss and perhaps others have done non-surgical vasectomies of stallions by injecting scarring agents into the testicle as an investigational procedure in a University setting. *However, the refinement and testing of a non-surgical vasectomy technique for horses has not been reported in the literature. To our knowledge this work has not been done. There is no product on the market approved for this application, and it is not well established that it would be safe and without significant side effects.* Stallions treated by either technique would be sterile but would retain the physical and behavioral attributes of stallions. The concept is that harem stallions would continue to hold mares and prevent other stallions from impregnating those mares for the duration of the breeding season (see item #3 below).

2) There are 3 agents that act against GnRH and have been used to alter the production of reproductive hormones in horses. All 3 have been investigated for use in mares or stallions to affect reproductive behavior or alter the hormonal cycles associated with reproduction. At least one has been approved for use in another country. Generally, the objective of using these agents in domestic horses is to eliminate unwanted reproductive behavior in mares. *There is currently no “anti-GnRH” product approved for use in stallions in the US, and there are no reports in the literature of “anti-GnRH” products directed toward stallion fertility that have been studied as a means of population control for horses.*

- 2.1) Two GnRH conjugate vaccines have been studied (one approved for use in Australia) for stallions as a means of inhibiting undesirable sexual behavior. These studies have shown that the vaccines (administered as a primary shot followed by one or two booster shots at 4 to 12 week intervals) affect both libido and fertility in some but not all stallions receiving the vaccine and only for a limited period of time (10-12 months) (Burger 2006, Turkstra 2005). Semen production was never entirely suppressed and libido was reduced in about 80% of the stallions. Further, these studies concluded that GnRH antibody titer does not appear to be a useful indicator of immunization effect. Fertility was not measured directly and in the context of these studies, population control was not considered.

- 2.2) In 2003, the USGS and BLM WH&B Program funded a pilot investigation in mares (Patrick McCue, Colorado State University, unpublished data) of 2 promising agents (GnRH-PAP Ablation Conjugate and a GnRH Agonist) available for research use. That study concluded “*administration of a GnRH-PAP ablation conjugate or a potent GnRH agonist in a sustained release implant failed to consistently alter pituitary function, block ovarian follicle development or suppress estrus.*” Treated mares continued to cycle and ovulate with an irregular temporal pattern. It is unclear how these agents would affect stallions. However, because they work on a similar hormonal axis, it is possible but unlikely they would have a better, more reliable and long-lasting effect in stallions. The researcher involved in these studies returned his unspent funds, saw little value in the agents he investigated as a means of fertility control, recommended a different avenue of investigation following this pilot project and expressed no further interest in pursuing contraceptive research.
- 2.3) A single shot GnRH vaccine, Gonacon™, has been developed and approved for experimental use in the females of wildlife species (deer, elk) in the U.S. This vaccine was tested as a means of fertility control in wild horses in Nevada using estray horses. BLM funded a portion of this work using the redirected funds mentioned above. Compared with 25% of control mares that were infertile in the first year, 94%, 60% and 53% of Gonacon treated mares were infertile in years one, two and three, respectively (Killian 2007). The fertility of control mares in years two and three was not described in the literature.
3. The application of fertility control to stallions as a means of population control has been a controversial subject for several years. Anecdotal reports from the field (Coates-Markle, personal communication 2003) suggest that 15-40% of foals in a band may be sired by a stallion other than the dominant harem stallion. This is supported by the literature that reports 15-30% of foals were not sired by a stallion associated with the dam’s band (Bowling 1990, Kaseda 1996). It is important to note that this is under normal conditions with a short individual breeding season limited by pregnancy of a given mare. When mares are bred by an infertile stallion, the mares will continue to cycle 10 to 12 or more times past the normal breeding season and (in addition to extending the foaling season) it is likely the percentage of mares bred by non-harem stallions would increase over time.
- 3.1) The stallion approach, as a means of contraception, has been studied in a small number of stallions in a limited number of herds. Kirkpatrick (1982) studied the effect of a short acting agent (testosterone propionate, lasts 3-6 months) used in bands with only one stallion and reported that foaling was reduced by about 80%. However, Eagle (1993, also reported by Asa 1999) studied the effects of surgical vasectomy in 2 more diverse Great Basin Herds and did not find as promising a result. Foaling rates only seemed lower in one HMA in the first year of the study, with only a marginal effect reported for the second year and no significant affect detected in 6 of 7 observations over two years in a second HMA. The authors concluded that “*although sterilization of dominant males may be an effective treatment to reduce foaling in a small sample of bands selected from a population, this treatment might not limit population growth.*” Further, they

concluded that as the probability of breeding with a sterile male increased, the breeding season (and subsequent foaling seasons) would become extended into the late summer and fall months. Also noteworthy, 5% of the stallions selected for treatment died or were euthanized as a result of complications associated with immobilization for the procedure.

- 3.2) When contraceptive approaches have been reviewed, both the National Research council (1982) and an independent study that used simulation modeling (Garrott 1992) concluded that female-oriented contraceptive techniques would have a higher probability of success when applied on a management scale and only mare-directed approaches were chosen or recommended for further study.

CONCLUSIONS AND RECOMMENDATIONS

The BLM has not ignored or been unaware of contraceptive approaches geared toward the sterilization of stallions or the use of agents that act against GnRH for mares or stallions. In fact the BLM supported research into “anti-GnRH” agents as recently as 2003.

The preponderance of the literature and expert opinion suggest that contraceptive approaches aimed at the sterilization of stallions will have limited usefulness as population control measures. It appears *the idea that a dominant harem stallion controls all the breeding in his band is a myth.* For these reasons the National WH&B Research Advisory Committee has recommended that the field investigation of wild horse contraception as a management tool for controlling population growth focus on trials using the most promising PZP agents available and the only agents approved for investigational use under a research protocol (the one year and 22-month agents developed by Kirkpatrick and Turner). In their present form these agents are currently available for consideration of investigational use in any HMA. Over 1700 mares in about 46 HMAs have been treated as part of ongoing field trials conducted by the BLM using these agents since 2004. BLM funded research to increase the efficacy and extend the period of effectiveness of these agents is ongoing.

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