

## Appendix C. Fertility Control Methods

The following discussion reflects fertility control methods that have been identified for possible use in female wild horses and burros. However, other methods may exist and could be useful in BLM management.

Long-term fertility control methods could be physical, pharmacological, or immunological; several candidate methods are noted below, but the BLM would also consider other humane, surgical and non-surgical, mare sterilization methods. Some, but not all, of the methods below were reviewed in the NAS report (2013), and Kane (2018).

### ***Physical Methods of Long-term Fertility Control or Mare Sterilization***

The BLM continues to view physical methods of contraception and humane sterilization as potential tools for achieving and sustaining AML on specific HMAs. If new physical contraception and sterilization methods are identified as appropriate for use in wild horses and burros, the BLM may need to develop partnerships with veterinary teaching schools to train new professionals to apply the methods. The following physical methods have already been identified for mare fertility control; others are also possible.

#### *Intra Uterine Devices (IUDs)*

IUDs are a non-surgical form of reversible contraception. In 2020, the BLM began using flexible, Y-shaped silicone IUDs in wild mares, following efficacious results from pen trials in which IUD-treated domestic mares lived with fertile stallions but did not become pregnant over two breeding seasons (Holyoak et al. 2021). A flexible magnetic IUD design is also being tested independently (Gradil 2019, Joonè et al. 2021). IUDs can only be inserted in non-pregnant (open) mares because insertion of an IUD will typically cause a pregnancy to end, and / or to cause expulsion of the IUD. Long-term monitoring could reveal how long IUDs are retained in wild mares.

#### *Oviduct Ablation*

Oviduct ablation refers to several possible, minimally invasive procedures that cause long-term blockage of the oviduct, so that fertilized eggs cannot reach the uterus. For example, in one such non-surgical procedure, medical-grade cyanoacrylate glue can be infused into the oviduct (Bigolin et al. 2009). The procedure is transcervical, so treated mares must not be pregnant, and first need to be screened for pregnancy. After successful treatment, a mare would be sterile, although she would retain her ovaries and would continue to have estrous cycles, as can be the case for mares treated with a small number of PZP vaccine doses (e.g., Nuñez 2018; but see Bechert et al. 2013).

#### *Tubal Ligation*

Tubal ligation is an approach in which oviducts are surgically closed to prevent fertilization. The procedure does not require removal of the ovaries and may have less risk of bleeding than ovariectomy. The BLM is aware of only one published study testing tubal ligation in domestic mares (McCue et al. 2000). An unpublished, BLM-funded study exploring a form of tubal ligation via nylon ligature was not successful, (Ball 2017).

## *Ovariectomy*

A number of established veterinary procedures exist for surgical removal of a mare's ovaries. Ovariectomy via colpotomy has been used in feral horse management on US Fish and Wildlife Service lands (Collins and Kasbohm 2016). A proposal review by the National Academies of Sciences indicated that the method is suitable for BLM management applications without further research (NAS 2015), but the BLM has not used ovariectomy in management, up to this time.

## *Research into Male Neutering is not a Priority*

Compared to fertility control for females, additional research into neutering male WHBs is not a priority. The BLM typically uses the word 'neutering' only to refer to the sterilization of a male horse (stallion), either by removal of the testicles (i.e., castration, also known as gelding) or by vasectomy, where the testicles are retained but the vas deferens or epididymis are severed or blocked. Neutering stallions is not expected to reduce female fertility unless a high fraction of stallions are treated (i.e., more than 80%; Garrott and Siniff 1992). Maintaining such a high percentage of treated stallions, and colts as they mature, would require relatively frequent gathers. The BLM funded a study to test whether gelding some stallions led to different wild horse habitat use or behaviors (see Appendix B). Including some neutered males in wild herds may marginally reduce female fertility for a short period of time (USGS, unpublished data), and the neutered males may take the place of fertile females in herds with male-skewed sex ratios.

## ***Pharmacological and Immunological Methods of Mare Fertility Control or Sterilization***

The BLM has not yet identified a pharmacological or immunocontraceptive method, by which one dose humanely and reliably leads to long-lasting contraception (3 or more years effect) or sterilization. However, with advances in pharmaceutical and vaccine technologies there is the possibility that future development and testing could lead to an agent that causes long-term infertility, or sterility from one or two doses. Several promising pharmacological or immunological methods could be refined, further developed, and tested, including but not limited to those noted below.

### *Oocyte Growth Factor (OGF) Vaccines*

A vaccine against oocyte growth factors growth differentiation factor-9 (GDF-9) and bone morphogenic protein-15 (BMP-15) limited follicle development and prevented estrus in a pen trial with domestic mares (Davis et al. 2018). It is possible that this type of vaccine may cause long-term infertility or sterility. The effectiveness of a long-lasting OGF vaccine may depend on adjuvant formulation. Field trials of one OGF vaccine formulation are underway, and additional trials may be warranted when the contraceptive efficacy of the treatment is better understood.

### *Improvements to PZP or GnRH Vaccines*

PZP vaccines and GnRH vaccines are already registered for use in wild horses and burros as ZonaStat-H (EPA 2012) and Gonacon-Equine (EPA 2013), but single doses of these vaccines cause only temporary effects (Rutberg et al. 2017, Baker et al. 2018). Improved formulations of these vaccines could cause longer-lasting effects from single doses. SpayVac is a PZP formulation that

has sometimes led to long-term (3-4 year) fertility control in horses after a single injection (Killian et al. 2008, Roelle et al. 2017), but sometimes has not (Roelle 2015). Also, recombinant PZP vaccines may have comparable contraceptive effects to native PZP vaccines (Joonè et al. 2017a, 2017b), and have the benefit that they do not require the harvest and processing of ovarian tissue from pigs.

### *Other Vaccines*

There are a number of other possible immunocontraceptive vaccine formulations. These include but are not limited to virally-vectored vaccines (Hay et al. 2017), vaccines that target GnRH receptor molecule (Samoylov et al. 2019), RNA inhibition (Horak et al. 2020), RNA vaccines using similar techniques as have been used in human coronavirus vaccines, and other approaches.

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