# Reproductive management in captive and wild canids: contraception challenges

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## ABSTRACT

Managing reproduction for Canidae species is a challenge for zoological institutions and wildlife sanctuaries. There are four basic options for contraception: separation of sexes, surgical procedures, immunological and hormonal methods. Animal managers face potential challenges for each option, and advantages and disadvantages should be taken into consideration when making a decision. This paper evaluates four common Canidae species with results from hormonal monitoring: Gray wolves Canis lupus/Mexican gray wolves Canis lupus baileyi, Maned wolves Chrysocyon brachyurus, Fennec fox Vulpes zerda and African wild dogs Lycaon pictus. Special focus is given to individuals treated with the Gonadotropin Releasing Hormone (GnRH) agonist, Suprelorin<sup>®</sup>. To date there are considerably more data for African Wild Dogs than other canids, as extensive field observations are available for this species. Therefore they are more extensively covered in this paper. Since GnRH agonists have been designated the safest reversible method for carnivores, continued studies are important. Results outlined below demonstrate individual dosing differences which occur not only across species but also between similar individuals. Though dosing and duration of efficacy still need further investigating, GnRH agonists are still considered to be the safest and most appropriate methods available. As evident in this paper, contraception is a much needed tool for reproductive management.

Key-words: Canidae; contraception; GnRH agonists; Suprelorin<sup>®</sup>.

## INTRODUCTION

The Canidae Family has a wide range of social and physiological mechanisms that are unique to this taxonomic group (Asa *et al.*, 1990). Managing them in captivity can be a challenge and it is important that these mechanisms are taken into consideration for the welfare of the animals and those working with them. One area of focus is reproductive control, which is essential for population management in captivity. Currently it is known that all temperate Canidae species are monoestrous and usually seasonal, which can influence the management styles implemented for controlling reproduction (Asa *et al.*, 1990). These physiological differences between Canidae and other carnivores make it a challenge when developing a consistent plan for contraception practices. Controlling reproduction by reversible contraception is just one tool towards having a healthy and well-managed group in zoological institutions.

There are four potential methods of reproductive control of captive canid species. These are separation of sexes, surgical methods, immunological and hormonal methods. The feasibility for separation of sexes as a method depends on social behaviour of the species and availability of enclosures in a facility. Some pack animals can be separated without impacting social behaviour whereas in many Canidae species, such as the Black-backed jackal *Canis mesomelas* that

occurs in pairs, this would disrupt social behaviour (Harrison-White, personal communication). Separating sexes to prevent breeding is a very effective method of contraception. However, there are strong arguments against this management tool because not only are social groups disrupted but also reintroducing the individuals later can cause aggression in the group as hierarchy is re-established (Bertschinger, unpublished). Another option for some zoological institutions may be to house 'same-sex' groups together in order to manage their collections and prevent unplanned births (van Heerden, 1986, van heerden *et al.*, 1996; Bertschinger, unpublished).

There are two surgical approaches: gonadectomy of both genders and vasectomy of the male or salpingectomy of the female. The former may disrupt social behaviour whereas the latter leaves the gonads and, therefore, sex steroid-related behaviours intact. Both approaches are, for practical purposes, irreversible; however for individuals with little genetic value this may be irrelevant. Housing surgically sterilized individuals together has been successful in many species without behavioural complications. An example of this is the African wild dog where females subjected to salpingectomy were housed with intact males (Bertschinger, unpublished). There is evidence that repeated infertile oestrous cycles, which will occur after both vasectomies and salpingectomies, may lead to the endometrial hyperplasia-pyometra complex (Bertschinger, unpublished). All considerations need to be made before deciding on a permanent method.

Immunocontraception for the control of reproduction in canid species has received little attention to date. Sperm antigens as immunogens has been investigated in the Red fox *Vulpes vulpes* and success rates of up to 75% have been achieved (Boué *et al.*, 2002). This level of contraception, however, is insufficient for use in captive populations. Porcine zona pellucida proteins have been used to induce infertility in female Domestic dogs *Canis lupus familiaris* (Fayrer-Hosken *et al.*, 2000). In the dog, however, the humoral response is accompanied by a cell-mediated response with resulting destruction of ovarian follicles and permanent sterility as the final outcome (Fayrer-Hosken *et al.*, 2000). The method with the most potential, a GnRH vaccine, has not been investigated for wild canids. Besides being reversible it could potentially be used in both genders. Once again, investigations in Domestic dogs have yielded positive results (male dogs, Jung *et al.*, 2005; male and female dogs, Walker *et al.*, 2007) with a possible application to wild canids in the future.

Reversible hormonal contraception products are available in a variety of delivery systems including implants, injections and oral formulations. The two most commonly used hormonal products are synthetic progestins and gonadotropin releasing hormone (GnRH) agonists. Table 1 summarizes the canid species known to have been treated with the more common contraceptive methods: progestins and GnRH agonists (WCC database). Historically progestins have been used on a wide range of species, however, recently they have been found to induce uterine,

mammary gland and hepatic pathology with long-term treatment in felids and most likely other carnivore species (Asa & Porton, 2005; Munson, 2006). According to recommendations available through the Association of Zoos and Aquariums (AZA) Wildlife Contraception Center (www.stlzoo.org/contraception) the current safest method for all carnivores is Suprelorin<sup>®</sup>, which is a slow-release formulation with deslorelin as the active GnRH agonist. GnRH agonists act at the level of the adenohypohysis where they inhibit the release of FSH and LH thus blocking the down-stream effects of these gonadotrophins (Trigg et al., 2006; Wright et al., 2001). Accordingly, they are effective in both sexes of many species (Trigg et al., 2001; Wright et al., 2001). The first deslorelin products (Peptech Animal Health, Sydney, Australia) for use in wildlife became available as 3 and 6mg slow-release implants. These early implants were not formulated by release time but rather doses made for different size dogs (Trigg et al., 2001; Junaidi et al., 2009). Accordingly, in the early wild carnivore work, dose used was based on the sizes of the target animals. For example 12 mg (2 x 6 mg) was used for lionesses while one 6 mg implant was employed to down-regulate cheetahs and African wild dogs (Bertschinger et al., 2001). In 2005 two new formulations became available; known as Suprelorin<sup>®</sup> (4.7 mg) and Suprelorin<sup>®</sup> 12 (9.4 mg), both being produced by Peptech Animal Health (Sydney, Australia) and are registered in Australia, New Zealand and Europe. The 4.7 mg implant was created to have a duration of effect for at least six months and the 9.4 mg implant for at least 12 months. Trigg et al. (2006) describes these new formulations and the application for the domestic dog.

Suprelorin<sup>®</sup> implants have become widely available and the focus of many research projects evaluating efficacy, safety and reversibility. Although Suprelorin<sup>®</sup> is the most commonly utilized GnRH agonist, Lupron<sup>®</sup> depot is another option for those individuals that need to be darted for treatment. However, Lupron<sup>®</sup> is an approved drug for managing a number of human reproductive issues and, therefore, dosing may be cost-prohibitive to zoos and small institutions (Wilson et al. & Plosker & Brogden, 1994). The injectable progestin, Depo-Provera<sup>®</sup>, is administered typically as an interim method and not as often for long-term suppression because of its potential side effects. Depo-Provera<sup>®</sup> is an effective interim method because it is generally short-term and can be administered by dart, therefore anesthetizing the individual is unnecessary. Depending on the individual and the goal of the institution, contraception methods vary.

From Table 1 it is apparent that a wide range of Canidae species can be treated. Though historically the MGA (melengestrol acetate) implants were more commonly used, Suprelorin<sup>®</sup> (either formulation), is now recommended and gaining in popularity (<u>www.stlzoo.org/contraception</u>). Similar to any new method, information is still being gathered and analysed for dosing, efficacy, and reversibility. As more individuals are treated, dosing will become more defined and reversibility information will be available.

## ANIMALS TREATED

The Canidae species for which significant information is available are Gray wolves *Canis lupus*, Mexican gray wolves Canis lupus baileyi, Maned wolves Chrysocyon brachyurus, Fennec fox Vulpes zerda and African wild dogs Lycaon pictus. These Canidae species currently have been treated most commonly with Suprelorin<sup>®</sup>, according to AZA Wildlife Contraception Center (WCC). African wild dogs have not only been treated in North American zoos but also individuals have been monitored consistently at the de Wildt Cheetah and Wildlife Centre in South Africa and the National Zoological Gardens in Pretoria. According to Peptech Animal Health Pty Limited, Suprelorin<sup>®</sup> implants are manufactured for use in Domestic dog contraception management and one implant is sufficient for each dog, irrespective of the size of dog (Product Insert, Peptech Animal Health Pty Limited). In previous years alternative doses (3mg and 6mg) were available. At this time Suprelorin<sup>®</sup> is available in two different sizes, as previously described above, which are formulated for domestic dogs and have a duration of effect for a minimum of either for six or 12 months. However, exotic carnivores may have different physical and physiological demands, therefore, requiring higher doses for suppression (Bertschinger et al., 2001; Bertschinger et al., 2002). Dosing is based on weight of the individual, species being treated and gender. Typically the wolves and African wild dog require multiple implants whereas for the fox species, just one implant is necessary for suppression. Males need higher doses than females to completely suppress spermatogenesis and azoospermia may take up to six weeks after treatment or longer (Boutelle, unpublished).

The main challenges facing animal managers and veterinarians when treating individuals with Suprelorin<sup>®</sup> are dosing and duration of efficacy. Dosing is based on a variety of parameters but there are also individual differences. Records from the WCC Database suggest two implants may sufficiently down-regulate one female but not be a high enough dose for another seemingly identical female. The reasons for these differences need further investigation but a few possibilities are the individual's metabolism, social pressures within the group and/or distinct physiological variations. Duration of efficacy is also variable for each individual and the same parameters for dosing may affect the length of time for suppression as well. More details on dosing for each species is outlined below but additional studies will be necessary to delineate these questions.

# Gray wolf and Mexican gray wolf

Gray wolves originally inhabited most of the Northern hemisphere; however, presently they are only found in the United States, Alaska, Canada and some of Eurasia. Packs generally comprise five to nine individuals with one alpha pair. IUCN (International Union for Conservation of Nature) has delisted the Gray wolf in the United States to Least Concern (IUCN, 2008). Mexican gray wolves are considered to be the rarest subspecies of Gray wolf and their natural range was central to northern Mexico and south-west United States. The United States Fish and Wildlife Service (USFWS) have recently begun reintroduction programs to establish packs back in the wild. Mexican gray wolves are considered threatened, and the United States and Mexico are collaborating to further these reintroduction efforts (www.fws.gov/southwest/es/mexicanwolf).

Gray wolves and Mexican Gray wolves have been treated over several breeding seasons in AZA accredited institutions located in the United States. Because these species are highly seasonal it is only necessary to treat with the six-month formulation just prior to pro-oestrus to ensure downregulation during the breeding season. If treatment occurs during or after pro-oestrus the females will usually ovulate and become receptive to males (Boutelle, unpublished). It is critical to treat prior to this time in order to prevent ovulation resulting in pregnancy or pseudo-pregnancy. By treating prior to pro-oestrus this will also ensure male wolves will likely not have begun spermatogenesis and, therefore, fertilization will be further prevented (Asa et al., 1990). Efficacy and reversibility have been established in both Gray wolves and Mexican gray wolves. Four male Gray wolves treated (each received three 4.7mg implants) prior to the breeding season were azoospermic during treatment but semen production had returned the following season in three out of the four males, demonstrating reversibility (C. Asa, pers. comm.). The fourth male was not able to be captured and therefore semen parameters were not analyzed. Female gray wolves (n=4) were also treated (each received two 4.7mg implants) and monitored for faecal progestin levels. All females showed a return to cycling the following breeding season (C. Asa, pers. comm.). These females were not in a breeding situation, however, so no pups were produced. Though efficacy and reversibility have been demonstrated there have been instances where females were treated with up to three 4.7 mg implants and were not sufficiently down-regulated. This may because they were treated during pro-oestrus, not before, and thus the females presumably ovulated during the stimulation phase. More information is needed as to why these particular individuals did not respond as well as other successful treatments.

# Maned wolves

Maned wolves currently are found in both Brazil and portions of Peru although historically they also were spread across Uruguay and Argentina. In the wild, this species have committed male and female pairs that share a territory; however, they remain fairly independent except during breeding. Observations from captive pairs show an increased amount of interaction and a more active role for the males in paternal care. At this time, the Convention on International Trade of Endangered Species of Wild Fauna and Flora (CITES) considers the data deficient for Maned wolves, and IUCN list the species as Near Threatened (IUCN, 2008), although the exact status is unknown.

Several Maned wolves in AZA accredited institutions have been monitored after Suprelorin<sup>®</sup> treatment and one individual subsequently became pregnant and produced pups, therefore documenting a reversal. No hormone monitoring has been conducted on these individuals but suppression of oestrous behaviour is apparent which is indicative of an effective dose. For each treatment, the female wolves have received two implants each; either two 4.7 mg or two 9.4 mg implants depending on the need for a six or 12 month duration. The female on record had pups after three consecutive years of treatment (two 4.7mg implants for each treatment) and conceived within one year after the last implant expired.

# Fennec fox

Fennec fox are mostly monogamous and both the male and female pairs invest in parental duties. Social groups generally consist of large family groups of approximately ten individuals. This species is found in Central Sahara Desert and currently CITES has not been able to sufficiently evaluate their status thus they are considered 'data deficient', while IUCN lists the species as Least Concern (IUCN, 2008).

Data for Suprelorin<sup>®</sup> treatment are also available in the Fennec fox. Eight females were involved in a research study in which faecal progesterone concentrations hormones were monitored to track suppression of ovarian activity following the insertion of one 3mg Suprelorin<sup>®</sup> implant (Bertschinger *et al.*, 2001). Following treatment as evidenced by low progesterone concentrations, ovarian activity was suppressed in five individuals, however, the duration of suppression varied between individuals. Three of the five individuals had detectable progesterone levels, indicating a return to cycling, within 1.5 years post implant placement. Monitoring did not continue for the last two suppressed individuals and return to cycling is unknown at this time.

## African wild dogs

African wild dogs live in packs of seven to 28 adults and yearlings in a structured hierarchy with the alpha female and male as the dominant pair (Creel and Creel, 2002). Currently the IUCN (2008) designates this species as Endangered and significant efforts are under way to ensure their survival. Wild dog pairs are monoestrous seasonal breeders and in South Africa oestrus and mating are observed during late summer, with pups born February to March. At the de Wildt Cheetah and Wildlife Centre a secondary breeding period may occur during the spring months in packs that have not bred during late summer (Bertschinger, unpublished). The approach of the breeding season is associated with increased aggression within the pack, which is likely related to subordinate animals trying to increase their ranking within the group. Attacks on individuals are often severe and fatalities can occur. This may be worse in captive situations where avoidance by subordinate dogs is less feasible. Two studies on captive dogs in South Africa revealed trauma as

a result of fighting to be the most common cause of fatalities (nine of 15, van Heerden, 1986; 13 of 61, van Heerden *et al.*, 1996). These figures exclude perinatal mortalities. Breeding is confined to the alpha female although sub-ranking females have been known to breed (M. Hofmeyr, personal communication). Multi-sire breeding has been observed with sub-ranking males only mating in the latter stages of oestrus. Parentage analysis has shown up to three sires for a single litter (Mouiex, 2006). Male wild dogs produce sperm throughout the year although there is proof of seasonal variation in semen quality (Nöthling *et al.*, 2002). The reproductive drive of this species appears to be exceptional and this may explain why reproductive control is more difficult than in species with similar social systems. The fact that spermatogenesis is a continuous, year-round process, should be considered if males are to be contracepted. Down-regulation should take place a minimum of eight weeks prior to the breeding season. Treatment of females for contraception should also be carried out prior to the breeding season before pro-oestrus commences.

To the authors' knowledge, the use of same-sex groups to control breeding in African wild dogs has only been practiced with males at the de Wildt Cheetah and Wildlife Centre in South Africa. Group sizes have varied from two to six dogs, some of which have been together for up to five years. Enclosure size appears to have an influence on the incidence of aggression. Where there is sufficient space for avoidance (>2 ha) serious fighting is not observed. In smaller camps, aggression may be common, especially during the main but also during the secondary breeding season Bertschinger, unpublished). According to van Heerden *et al.* (1996) the housing of females in same-sex groups is more likely to lead to mortalities as a result of fighting during the breeding season and should therefore not be practiced.

Once again at de Wildt, salpingectomy of two females as a means of contraception in a group of litter mates [3.2 (3.2)] has worked extremely well. Surgery was carried out in 2003 with no problems having been observed since then. Signs of oestrus have been observed in both females each year.

African wild dogs appear to be extremely sensitive to the side effects of progestins (van Heerden, pers. comm.) as well as repeated pseudo pregnancies (Bertschinger, unpublished). Two females given a single treatment of 400mg proligestone (Delvosteron, Intervet South Africa) to postpone oestrus both developed fatal pyometra within a few months of treatment (J. van Heerden, pers. comm.). As with other carnivore species, both endogenous and synthetic progesterone may increase the risk for uterine pathology (Asa & Porton, 2005 & Munson, 2005). Therefore progestin based contraception is not recommended (<u>www.stlzoo.org/contraception</u>). Salpingectomy of females and vasectomy of males are also not recommended as pseudo-

pregnancies may result when repeated non-fertile cycles occur. As a result, it seems unwise to use any formulation of progestins to control reproduction in female African wild dogs.

African wild dogs have been treated with Suprelorin<sup>®</sup> for both contraception and aggression management in North American zoos. Anecdotal information suggests that these individuals are highly variable in their suppression and duration of efficacy. There are limited data thus far for reversibility. So far, three individuals have reportedly had offspring after one treatment (4.7mg formulation for each) with no associated problems, according to the WCC database. The possible application for Suprelorin<sup>®</sup> in African wild dogs for decreasing aggression among bachelor groups and management practice is especially helpful for institutions housing multiple social groups, which need flexibility for exhibits.

In South Africa at least 19 males (15 treated once; two treated twice; two on three separate occasions) and 18 female dogs overall have been treated with deslorelin (Suprelorin<sup>®</sup>). Eleven of the 18 females, for which there are details available, were initially treated with 6mg deslorelin implants during the period 1999–2000, while in anoestrus and housed with males (Bertschinger *et al.*, 2002). Serum progesterone concentrations revealed that five females ovulated at various intervals following treatment but only two became pregnant: one after four weeks and the other after three months, possibly due to an inadequate dose. Anoestrus was maintained in other six females. Reversal could be demonstrated in five females that were successfully treated with normal-sized litters after 7, 11, 12, 13 and 16 months. The two females that fell pregnant after treatment produced a second litter 14 and 15 months after the implants (Bertschinger *et al.*, 2002). Because the results with the early 6mg deslorelin implants were more reliable in males than females management practices at de Wildt Cheetah and Wildlife Centre changed to targeting largely males for contraception. The treatment remained successful as long as it was applied at least two months prior to the breeding season (Bertschinger, unpublished).

Initial studies with deslorelin implants made available in the late 1990s (6 mg and 5 mg implants) in 6 males yielded promising results (Bertschinger *et al.*, 2002). Males examined at different intervals from one to as long as 14 months after treatment had baseline testosterone levels. Male 141 (Figure 1) was placed with three females at the time of the first treatment. One female that came on heat three weeks later produced a litter, likely because male was not yet azoospermic after treatment. The other two females came on heat 6 weeks after treatment of the male and no pregnancy was observed. Where measured, testicular size (data not shown) was also reduced consistently. Positive proof of reversal of contraception was provided in two of five of dogs. One male mated successfully 16 months after deslorelin treatment and the other had good semen quality and normal plasma testosterone concentrations 12 months after deslorelin administration;







Figure 2: African wild dog treated prior to two consecutive breeding seasons with single deslorelin implants. Twelve months following first implant testosterone was within the normal range. Six months after the second implant testosterone concentrations were baseline and the mean testicular volume small. Reversal of both variables can be seen 6and 9 months later. After 48 months, a single Suprelorin<sup>®</sup> (4.7 mg) implant showed a partial response in both variables 8 months later.

others do not have follow up information. Since the introduction of the new Suprelorin<sup>®</sup> implants in 2005 results have been less consistent. Although testicular size could be reduced in some dogs, most treated males have remained fertile. Figure 2 shows a male that was initially treated successfully with 6 mg implants two consecutive years three to four months before the breeding season. The female that was with him during both seasons following implantation of the male did not fall pregnant. Figure 2 also shows 12 months after the first implant, testosterone

concentrations were within the normal range and were down-regulated six months after the second implant. During the next nine months both testicular volume and serum testosterone concentration increased demonstrating the reversal process. Finally he was treated with a





Suprelorin® 4.7mg implant 48 months after the initial treatment but this only resulted in part downregulation eight months later. Figure 3 shows down-regulation of mean testicular volume in a male treated with a single implant but only partial down-regulation of testosterone production which we would expect to have reached baseline concentrations after four months. Other males treated with the same dose showed no response for either variable. It seemed logical therefore that a double implant of Suprelorin<sup>®</sup> should be sufficient to achieve contraception. As can be seen from the two males in Figure 4(A & B), this was not the case. Four months after treatment Male M325 (Figure 4A) showed no significant reduction in testicular size and testosterone concentration remained within the normal range for African wild dogs (Bertschinger et al., 2002). Male M380 (Figure 4B) showed good down-regulation of testicular size and for testosterone a partial down-regulation was observed. It would seem that the 4.7mg Suprelorin<sup>®</sup> implants result in systemic concentrations that are close to the threshold required to down-regulate male African wild dogs. This would explain why some individuals respond, some partially, remaining fertile and a third group not at all. The precise reason/s for these apparent differences between the original implants and the new formulations are unknown. It is likely these newer implants just need further trials to determine exact dosing in exotic species.

The choice of which sex to target when it comes to the African wild dog may be important from a health and welfare point of view. In females the use of progestins of any kind and duration should





not be considered because of the risk of the cystic endometrial hyperplasia pyometra complex (van Heerden, personal communication). The results achieved with the original 6 mg deslorelin implants were good and no pregnancies occurred in mixed groups when treated prior to prooestrous. Females on the other hand had a failure rate of around 13%. Presuming the protocol for the new Suprelorin<sup>®</sup> 4.7mg or 9.4mg implants can be adapted to achieve the same good results in male dogs once again, these above results may suggest targeting males. Recent evidence, however, may persuade managers to reconsider this decision. During the last two years there has been a sudden increase in the prevalence of cystic endometrial hyperplasia-pyometra complex at de Wildt. Instead of sporadic cases (<1/pear) six cases one of which occurred in a four year-old female were recorded. The other females were older. Concerns are increasing that repeated non-pregnant diestrus (pseudo-pregnancies), as a result of male contraception, may be the cause of the increased prevalence. This is well established in the domestic dog (Dow, 1957). Although the evidence is only anecdotal (Bertschinger, unpublished), it may be better to target the female for contraception by inducing anestrus.

# SUMMARY

In conclusion, reversible contraception is an essential tool for reproductive management. Without responsible management zoological institutions may be faced with hard decisions such as how to control surplus animals. Reversible contraception methods may also be the best option for many individuals within the population, which currently are not essential for breeding but could be called on in the future. For the species mentioned in this paper, all play a critical role in the ecosystem and, thus, ensuring their survival is very important. Many options for controlling reproduction are available, such as separating genders, surgical sterilization, immunological methods or hormonal contraception. However, for these highly social Canidae it is desirable to keep family groups together as a more natural management practice. Hormonal contraception would therefore be a good option to sustain these groups and manage the breeding populations. For animal managers and veterinarians it is essential to keep the welfare of the animal, the overall goals for each species and any institutional constraints in mind when choosing which method is best. Growing evidence suggest treating female Canidae with Suprelorin<sup>®</sup> or Suprelorin12<sup>®</sup> may be the best option in order to avoid uterine pathology after exposure to endogenous progesterone after repeated non-fertile cycles. As outlined above, African Wild Dogs appear to be specifically at risk and therefore it is essential Suprelorin<sup>®</sup> dosing is further studied for this species. For the most up to date recommendations visit the AZA Wildlife Contraception Center webpage (www.stlzoo.org/contraception).

# PRODUCTS MENTIONED IN THE TEXT

**Delvosteron:** synthetic progestational steroid (proligestone) to suppress oestrus, Intervet SA (Pty) Ltd, Isando, South Africa.

**Depo-Provera<sup>®</sup>:** medroxyprogesterone acetate, Pharmacia & Upjohn Company, Kalamazoo, MI 49001, USA.

Lupron<sup>®</sup>: GnRH agonist, TAP Pharmaceuticals Inc., Lake Forest, IL 60045, USA.

**MGA implants:** melengestrol acetate contraceptive implants, ZooPharm, a division of Wildlife Pharmaceuticals, Fort Collins, CO 80522, USA.

**Suprelorin<sup>®</sup> and Suprelorin12<sup>®</sup>:** GnRH agonist, manufactured by Peptech Animal Health Pty Limited, 19–25 Khartoum Road, Macquarie Park, NSW 2113, Australia.

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