Effect of deslorelin implants on follicular development, parturition and post-partum oestrus in the tammar wallaby (*Macropus eugenii*)

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Abstract

The effect of treatment with slow release implants containing the GnRH agonist, deslorelin, was investigated in female tammar wallabies. Pouch young were removed from 16 wallabies presumed to be carrying quiescent blastocysts. Eight received a 5 mg deslorelin implant and eight received a placebo implant. Animals were caught daily from day 25 to day 30 and their pouches inspected for newborn young and their urogenital sinus checked for a copulatory plug. Treatment with deslorelin did not affect reactivation of a dormant blastocyst and subsequent birth in 4/8 animals, but post-partum mating was inhibited in these animals. Five control and five treated animals were killed within 0–48 h post partum and their reproductive tracts analysed. At autopsy, all five control animals had large preovulatory follicles but only one deslorelin-treated animal showed signs of follicular development. These differences were also reflected in the weights of the lateral vaginae, with treated animals showing no evidence of oestrogenic stimulation. The remaining three control and three treated animals were monitored for approximately 2 years. The long-term contraceptive effects of a single 5 mg deslorelin implant lasted for just under one year. These results indicate that slow release deslorelin implants inhibit follicular development in the female tammar wallaby for extended periods of time and may have potential application in reproductive management of captive marsupials in the kangaroo family.

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Introduction

In recent years there has been increasing attention given to the challenges of managing over-abundant marsupial populations in Australia, in particular the large macropodids (kangaroos and wallabies) and the koala. Lethal control techniques, such as shooting and poisoning, are now facing increasing public opposition. Reducing population size over time by artificially reducing the fertility of individuals within the population (fertility control) has been proposed as an alternative method of population control (Bomford 1990). This has resulted in research and development of new technologies to inhibit marsupial reproduction (Nave *et al.* 2000, 2002).

Gonadotrophin releasing hormone (GnRH) agonist treatment has been shown to temporarily suppress ovarian cycles in dogs (Lacoste *et al.* 1989, Trigg *et al.* 2001), ewes (McNeilly & Fraser 1987), marmoset monkeys (Lunn *et al.* 1992), stump-tailed macaques (Fraser & Sandow 1985) and women (Fraser *et al.* 1990). In these species, suppression of ovarian cycles is characterised by an

inhibition of follicular development, with a resultant decline in the concentrations of oestradiol and progesterone and an inhibition of oestrus. In ewes (McNeilly & Fraser 1987), heifers (Mattos *et al.* 2001) and women (Bider *et al.* 1989) ovarian follicular development is arrested at the early antral stages of development, as evidenced by the absence of large follicles in the ovaries. In addition, the luteinising hormone (LH) surge mechanism is inhibited, as is ovulation.

Treatment with long-acting implant formulations containing the GnRH agonist, deslorelin, has resulted in long-term inhibition of reproductive function in cats (Munson *et al.* 2001), dogs (Trigg *et al.* 2001), heifers (D'Occhio *et al.* 1996, 2000) and other wildlife species (Bertschinger *et al.* 2001, 2002). The longevity of these GnRH agonist formulations increases their potential application in the management of over-abundant wild and captive marsupial populations.

The tammar wallaby is well established as a model marsupial species for the study of reproduction and endocrinology (Tyndale-Biscoe & Renfree 1987, Tyndale-Biscoe &

Janssens 1988). It is a monovular, polyoestrous species, with ovulation usually occurring in the alternate ovary in each successive cycle (Tyndale-Biscoe & Renfree 1987). Breeding is highly seasonal, with the majority of births occurring in a synchronised fashion in late January and early February (Renfree & Tyndale-Biscoe 1973, Sadleir & Tyndale-Biscoe 1977, Hinds & den Ottolander 1983). Females mate within 1–2 h of giving birth (Rudd 1994) and the conceptus grows to the stage of a 100-cell blastocyst before entering embryonic diapause. In the wild, these blastocysts usually remain in diapause for 11 months (Berger 1966, Renfree & Tyndale-Biscoe 1973, Flint & Renfree 1982). From the summer solstice until the winter solstice diapause is maintained by the suckling stimulus of the young in the pouch (lactational quiescence) (Tyndale-Biscoe *et al.* 1974). If a young is lost or removed during this period of decreasing day length the quiescent corpus luteum (CL) and blastocyst will reactivate (Renfree 1979), and birth and a new post-partum oestrus will occur approximately 26.5 ± 0.4 days later (Merchant, 1979, Renfree *et al.* 1989). If the young is removed or lost during the period of increasing day length, reactivation of the CL and blastocyst is inhibited by photoperiod (seasonal quiescence). Development will not resume until after the summer solstice (Tyndale-Biscoe *et al.* 1974).

The follicular phase in the tammar begins around mid-pregnancy. Graafian follicles are evident from day 23 after removal of pouch young (RPY) and reach their maximum size at the time of post-partum oestrus (Harder *et al.* 1984). Behavioural oestrus coincides with a post-partum peak of oestradiol in the peripheral circulation (Shaw & Renfree 1984) and in the vein draining the ovary with the Graafian follicle (Harder *et al.* 1984). The oestradiol peak is followed 5–8 h later by a preovulatory LH surge (Tyndale-Biscoe *et al.* 1983, Harder *et al.* 1985, Fletcher & Renfree 1988) with ovulation occurring approximately 24 h after the LH surge (Harder *et al.* 1985) or 40 h after birth (Renfree & Lewis 1996). The period of oestrus and ovulation in the tammar appears to be regulated by both oestradiol and LH, as in eutherians (Hinds *et al.* 1996). The later stages of follicular development appear to be pituitary-dependent. Hypophysectomy results in an absence of the largest (type 8) follicles within three weeks (Hearn 1975, Panyaniti *et al.* 1985) and passive immunisation against GnRH inhibits the late antral stages of follicular development (Short *et al.* 1985). However, the tammar CL is not dependent on gonadotrophins for reactivation or the maintenance of pregnancy, as gestation is unaffected by hypophysectomy (Hearn 1974) or passive immunisation against GnRH (Short *et al.* 1985).

This study investigated the efficacy of using slow release implants containing the GnRH agonist, deslorelin, to inhibit reproduction in the female tammar wallaby. The specific aims were to investigate the effects of deslorelin treatment at the time of RPY on subsequent follicular growth, birth and post-partum oestrus in animals presumed to be carrying a dormant blastocyst. No attempts

were made to measure the hormone concentrations in this study because frequent sampling around the period of parturition, post-partum oestrus and ovulation probably interferes with these processes (Fletcher *et al.* 1990).

Materials and Methods

Animals

The tammar wallabies used in this experiment were captured on Kangaroo Island, South Australia and transferred to the Macquarie University Fauna Park facility in August 1999. For the duration of the experiment they were held in a large outdoor pen, with a ratio of 3 males to 16 females. The animals were fed specially formulated 'kangaroo' cereal pellets (Gordon Specialty Stock Feed, Carlingford, Sydney, Australia) and lucerne hay with water available *ad libitum*. All females selected for this experiment were over two years of age with an average weight of 5.08 ± 0.16 kg. All were nursing pouch young (PY) and were presumed to be carrying a dormant blastocyst from a post-partum mating. Males were used for breeding purposes only and were not subject to any form of treatment. The Macquarie University Animal Ethics Committee approved all experimental work (approval number 99009) and the animal handling and husbandry was conducted in accordance with National Health and Medical Research Council of Australia guidelines (1990).

Experimental design

Sixteen female tammar wallabies were synchronised by RPY on 1 March 2000 (day 0). At the time of RPY the animals were randomly assigned to the treatment ($n = 8$) or the control group ($n = 8$). Treated animals received a 5 mg deslorelin implant and control animals received a placebo implant. Animals were caught once every 7 days to accustom them to catching and handling procedures. From day 25 after RPY the animals were caught daily and their pouches examined for the presence of a copulatory plug, which usually remains in position for at least 24 h *post coitum* (Sutherland *et al.* 1980). Female tammars usually mate 1–2 h post-partum (Rudd 1994), but mating is sometimes delayed until 8 h (Tyndale-Biscoe *et al.* 1983) or even 18 h (Harder *et al.* 1985) after birth when animals are frequently sampled during the birth and post-partum period. The first five animals from each group to give birth and/or mate were killed at the first sign of a copulatory plug. If they had not mated within 24 h of the first observation of a neonate (i.e. within 24–48 h of birth), they were killed at this time.

Sample collection

Five animals from each group were killed by an intravenous injection of pentobarbitone sodium (1 ml/2 kg; Lethabarb, Virbac Pty. Ltd, Peakhurst, NSW, Australia). The reproductive tracts were dissected out and examined.

The ovaries were checked for the presence of follicles or recent ovulations, before weighing (Sartorius electronic analytical balance, Max = 110 g, d = 0.1 mg, 1601MP8) and fixing in 10% neutral buffered formalin. The ovaries were embedded in paraffin wax, serially sectioned at 7 µm and stained with haematoxylin and eosin for subsequent histological examination and confirmation of the gross observations at the time of post-mortem. The uteri were examined for the presence of fetuses or evidence of recent pregnancy and then weighed individually. The lateral vaginae were dissected free of adjacent connective tissue and weighed to give an index of the animal's oestrogenic status (Short *et al.* 1985).

Long-term monitoring

The remaining three control and three treated animals were monitored once every 4–8 weeks from April 2000 until June 2002 to determine the duration of the contraceptive effects and the reversibility of treatment. All PY were removed and their age determined by measuring the head length and calculating the age from tammar wallaby PY growth tables (Poole *et al.* 1991). Following the resumption of reproductive activity in two of the treated animals, all of the three previously treated animals were re-treated on 15 March 2001 with a double dose of deslorelin (10 mg deslorelin).

GnRH agonist implant

The GnRH agonist, deslorelin (D-Trp⁶-Pro⁹-des-gly¹⁰-GnRH ethylamide), was formulated into implants that contained 5 mg deslorelin (Batch DR027A; Peptech Animal Health Pty. Ltd, North Ryde, NSW, Australia) as previously described (Trigg *et al.* 2001). In a real

time dissolution system the release of deslorelin was >1 µg/day for periods of approximately 1 year (Trigg *et al.* 2001). The *in vivo* release rate in tammar wallabies has not been determined. Implants were placed s.c. between the shoulder blades using a single-use commercial implanting device sterilised by e-beam radiation. The injection site was then sealed with a veterinary tissue adhesive (Vetbond, 3M Animal Care Products, St Paul, MN, USA). The dimensions of a 5 mg deslorelin implant were 2.3 mm in width and 12.5 mm in length.

Statistical analyses

Comparisons of the weight of reproductive tract components were analysed using two-sample *t*-tests. Comparisons of the number of pouch young and copulatory plugs for each group were made using the crosstabs chi-square Fisher's Exact test feature of SPSS 1996. Data are presented as arithmetic means ± S.E.M. Results were reported as significant at *P* = 0.05.

Results

Timing of birth

All control and treated females were synchronised by RPY at the time of implant administration, thus demonstrating their fertility at the start of the experiment. Following deslorelin treatment there was no significant difference in the number of animals giving birth from each group ($\chi^2 = 1.067$, degrees of freedom (d.f.) = 1, *P* > 0.05). Six (out of eight) control animals gave birth between days 25 and 27, and four (out of eight) treated animals gave birth, all on day 27 (Table 1). In one treated animal (number 691) the newborn young was found dead in the pouch.

Table 1 Incidence of birth and mating in control and deslorelin-treated female tammar wallabies between days 25 and 30 after removal of pouch young, and structures present in the ovaries at post-mortem.

	Birth	Copulatory plug	Post-mortem	Structures present in ovary	
				Parturient side	Non-parturient side
Control					
692	Day 27	Day 27	Day 27	Old CL	Preovulatory follicle
1BE0558T	Day 27	Day 27	Day 27	Old CL	Preovulatory follicle
1E710E8T	Day 27	Day 27	Day 27	Old CL	Preovulatory follicle
537	Day 27	Day 28	Day 28	Old CL	Preovulatory follicle
548	Day 26	Day 26	Day 26	Old CL	Preovulatory follicle
686	Day 27	No	NA		
1E71BB2T	No	Day 30	NA		
543	No	No	NA		
Treated					
683	Day 27	No	Day 28	Old CL	No large follicles or recent ovulation
1BE05E1T	Day 27	No	Day 28	Old CL	No large follicles or recent ovulation
691	Day 27*	No	Day 28	Old CL	No large follicles or recent ovulation
695	Day 27	No	Day 28	Old CL	No large follicles or recent ovulation
532	No	Day 26	Day 26	Old CL	Preovulatory follicle
689	No	No	NA		
20166E3T	No	No	NA		
542	No	No	NA		

NA, not applicable; *, young found dead in pouch.

Copulatory plugs were observed in a significantly greater number of control than treated females between day 25 and day 30 (control, 6/8; treated, 1/8; $\chi^2 = 6.349$, d.f. = 1, $P < 0.05$). One treated female mated on day 26, but no PY was observed in the pouch. Examination of the reproductive tract of this female suggested that she was recently gravid, as one uterus was significantly larger than the other. Of the six control animals that gave birth, copulatory plugs were observed in all but one animal. This animal was not killed and following RPY a second young was born 27 days later suggesting that a post-partum mating had occurred, but this was not evident from physical examination.

Effects on the reproductive tract

At the time of post-mortem there were marked gross morphological differences between the reproductive tracts of control and deslorelin-treated animals (Fig. 1a and b). This was also reflected in the weights of the various components of the reproductive tract. The vaginal complex (median and lateral vaginae) of control animals was significantly heavier than treated animals (control, 23.10 ± 3.27 g; treated, 7.28 ± 2.70 g; $P < 0.01$). There was a tendency for both uteri to be heavier in control than treated animals, but this difference was not significant (parturient uterus: control, 1.78 ± 0.41 g, treated, 1.04 ± 0.11 g; non-parturient uterus: control 1.04 ± 0.40 g, treated 0.35 ± 0.07 g; $P > 0.05$).

In all five control animals there was a regressing CL in one ovary (Fig. 2a) and a large preovulatory follicle (diameter > 3.5 mm) in the contralateral ovary (Fig. 2b). In contrast, deslorelin-treated

animals showed a normal regressing CL in one ovary (Fig. 2c) and early antral stage follicles (Fig. 2d) in the second ovary. A large pre-ovulatory follicle was only observed in one deslorelin-treated animal (Fig. 2e and f), and this was the same animal that mated within the 24 h preceding post-mortem on day 26. In the remaining four treated animals, there was no evidence of preovulatory follicles or recent ovulations in either ovary.

The ovaries of control animals tended to be heavier than the ovaries of treated animals. For the ovary with the regressing CL, this difference was not significant (control, 201 ± 37 mg; treated, 142 ± 17 mg; $P > 0.05$). For the contralateral ovary (the ovary associated with the non-parturient uterus) there was a significant difference when animal 532 was excluded on the basis that it did not respond to the treatment in the same fashion as the remainder of the population and was therefore an outlier. The ovary with the large preovulatory follicle in control animals was on average double the weight of treated animals without large follicles (control, 229 ± 41 mg; treated, 111 ± 22 mg; $P < 0.05$).

Long-term reproductive success

After the period of daily capture, the remaining six females were monitored at less regular intervals. One treated animal (number 689) gave birth early in May 2000 (Table 2), but did not give birth again before administration of a second deslorelin implant. The remaining two treated females gave birth early the following breeding season, 340 and 359 days after the implant was administered (Table 2). After treatment with a further 10 mg deslorelin, none of the treated animals gave birth for the

Figure 1 Ventral view of the reproductive tracts of (a) control animal no. 537 and (b) deslorelin-treated animal no. 691 within 0–48 h of birth and/or post-partum mating. In both animals the parturient uterus is on the right hand side of the photograph. Scale bar = 10 mm. Ov, ovary; Ut, uterus; LV, lateral vagina; MV, median vagina; BI, bladder; UGS, urogenital sinus.

Figure 2 Ovarian histology of one control and two deslorelin-treated wallabies. (a and b) Control animal 692 showing (a) the regressing CL of the recent pregnancy and (b) a large preovulatory follicle (F); (c and d) treated animal 695 showing (c) the regressing CL of the recent pregnancy and (d) the absence of any large preovulatory follicles; (e and f) treated animal 532 which mated on day 26 showing (e) the regressing CL of the recent pregnancy and (f) a large preovulatory follicle. Scale bar = 1 mm. CA, corpus albicans; IT, interstitial tissue.

remainder of the 2001 breeding season or during the 2002 breeding season, a period of 464 days. Two of the control animals bred within 60 days of administration of a placebo implant (Table 2). The remaining animal died within 3 months of placebo implant administration and did not breed during this time.

Discussion

Treatment with the GnRH agonist, deslorelin, at the time of RPY did not appear to inhibit the reactivation of a quiescent blastocyst and subsequent birth, but successfully inhibited follicular development and post-partum oestrus in 4/5 animals. Moreover, these contraceptive effects can

Table 2 Duration of contraception in long-term deslorelin-treated female tammar wallabies, compared with the reproductive success in control female tammar.

Animal no.	Treatment	Treatment date	Date of birth	Days post-treatment
689	Deslorelin (5 mg)	01-Mar-00	01-Mar-00	61
	Deslorelin (10 mg)	15-Mar-01	—	>464 ^a
20166E3T	Deslorelin (5 mg)	01-Mar-00	04-Feb-01	340
	Deslorelin (10 mg)	15-Mar-01	—	>464 ^a
542	Deslorelin (5 mg)	01-Mar-00	23-Feb-01	359
	Deslorelin (10 mg)	15-Mar-01	—	>464 ^a
1E71BB2T	Placebo	01-Mar-00	28-Apr-00	58
	Placebo	15-Mar-01	02-May-01	48
686	Placebo	01-Mar-00	28-Mar-00	27
	Placebo	15-Mar-01	11-May-01	57
543	Placebo	01-Mar-00	—	— ^b
	Placebo	15-Mar-01	—	— ^c

^a, Duration of contraception to date at the end of the 2002 breeding season; ^b, no births detected following treatment; ^c, animal died on 28 May 2001.

be maintained for periods of approximately 1 year. This demonstrates the potential of deslorelin implants for controlling reproduction in tammar wallabies.

The inhibition of follicular development and oestrus during deslorelin treatment in the present study was consistent with findings from other species. Short-term treatment of heifers with deslorelin resulted in a decline in the numbers of class 2 (6 to 9 mm) and class 3 (>9 mm) follicles, although the number of class 1 (<6 mm) follicles was not affected (Mattos *et al.* 2001). Similarly, ewes treated with the GnRH agonist, buserelin, had no follicles >2.5 mm in diameter (McNeilly & Fraser 1987). In both species, inhibition of follicular development was accompanied by a decline in peripheral plasma follicle-stimulating hormone (FSH) concentrations and an absence of pulsatile release of LH, suggesting that gonadotrophin support is not required for the maintenance of smaller follicles, but is required for the development of larger follicles (McNeilly & Fraser 1987, Gong *et al.* 1996). Although the concentrations of FSH and LH were not measured in the present study, the absence of follicular development suggests that there was inadequate gonadotrophic support for normal follicular development. A similar attenuation in the growth of follicles was reported in female tammar wallabies following passive immunisation against GnRH (Short *et al.* 1985) and hypophysectomy (Hearn 1974, Panyaniti *et al.* 1985).

Studies in heifers have demonstrated that suppression of follicular growth was caused by decreased gonadotrophic support rather than a direct action of GnRH agonist on the ovaries (D'Occhio *et al.* 2000). In addition, no binding sites for GnRH or GnRH agonists have been identified in bovine ovarian tissues (Gong *et al.* 1996). The GnRH receptor transcript has recently been detected in ovarian tissue of tammar wallabies (Cheung & Hearn 2002). Therefore, it is possible that deslorelin is having a direct effect at the level of the ovaries as well as at the level of the pituitary, as occurs during GnRH agonist treatment in the rat (Janssens *et al.* 2000). It has been hypothesised that GnRH agonists may directly affect ovarian steroidogenesis

in the rat via ovarian GnRH receptors which are part of a local autoregulatory system (Roth *et al.* 2001). The role of ovarian GnRH receptors in the tammar wallaby deserves further investigation.

In deslorelin-treated tammar wallabies, oestradiol concentrations would presumably have remained at basal levels, as is the case in heifers (Mattos *et al.* 2001) and mice (Bokser *et al.* 1989), as the preovulatory follicle is known to be the source of the high oestradiol concentrations coincident with behavioural oestrus following the pregnant and oestrous cycle (Harder *et al.* 1985). The inhibition of oestrus and the absence of an oestrogenic response in the vaginae further support this hypothesis.

Deslorelin treatment did not affect normal gestation or parturition in 60% (3/5) of animals. This is in accordance with the results of Short *et al.* (1985) who showed that passive immunisation against GnRH does not inhibit gestation or progesterone secretion after RPY. After hypophysectomy, pregnancies proceed to term but parturition does not occur (Hearn 1974), thereby demonstrating that gonadotrophin secretion is not required for successful luteal reactivation or gestation.

In the control group, parturition successfully occurred and live young were observed in the pouch of all five of the animals in which reproductive tracts were analysed. In the treated group, live young were observed in only three animals. Whether the loss of two out of five young in treated animals compared with none out of five in control animals is a direct result of deslorelin treatment requires further investigation. The three treated animals in which live young were observed successfully suckled these young for periods of between 24 and 48 h suggesting that the early phase of lactation was not affected.

The maintenance of follicular development and subsequent occurrence of oestrus in one treated animal demonstrates that there are individual differences in the response to deslorelin treatment, and highlights the possibility that an unknown proportion of the population may not be responsive to the contraceptive effects of deslorelin treatment. The occurrence of oestrus during deslorelin

treatment has also been noted in individual heifers. Oestrus in these cows indicated that ovarian follicular growth and oestrogen production continued during deslorelin treatment. The higher levels of oestrogen were able to stimulate oestrus but were presumably insufficient to stimulate a preovulatory LH surge and ovulation, because there was no increase in plasma progesterone concentrations after oestrus (D'Occhio *et al.* 1996). It has been demonstrated that treated heifers will not respond to GnRH stimulus with an LH surge, which could explain this presumed lack of ovulation (Bergfeld *et al.* 1996). The current understanding is that cows treated with GnRH agonist can show some growth of ovarian follicles, but ovulation does not occur, either because follicle maturation is not complete or the gonadotroph cells in the pituitary become insensitive to natural GnRH (D'Occhio *et al.* 1996). In the present study, the 'non-responder' was killed before the time of ovulation so we do not know whether ovulation would have occurred normally. It is possible that although there was obviously sufficient gonadotrophic support for follicular development, the pituitary may have been desensitised to the extent that this animal would have failed to generate a preovulatory LH surge, resulting in a failure to ovulate. In a study by Lunn *et al.* (1992), one buserelin-treated marmoset monkey (out of six) appeared to continue to have ovarian cycles based on plasma oestradiol and progesterone concentrations. However, this animal failed to respond to a GnRH challenge 3 weeks after buserelin implant insertion, suggesting that the pituitary was desensitised.

The long-term effects of deslorelin treatment were monitored in the three remaining treated animals. One treated female (689) gave birth within 2 months of deslorelin administration, suggesting that follicular development and ovulation had not been inhibited in this animal. There are two possible explanations for the continued reproductive activity in this animal. The dose administered (5 mg) may have been insufficient to desensitise the pituitary and significantly reduce gonadotrophin secretion within one oestrous/pregnant cycle, or this individual may be resistant to the contraceptive effects of deslorelin treatment. After removal of the pouch young there was no evidence of reproductive activity in this female for 10 months. In addition, after administration of a higher dose the animal did not breed for a period of 16 months (experiment continuing at time of writing). This suggests that this animal is not resistant to the contraceptive effects of deslorelin, but there may have been insufficient time or dose for down-regulation to occur. Ineffective pituitary suppression has been suggested as a potential reason for higher conception rates in heifers treated with low doses of deslorelin (D'Occhio *et al.* 2000). The remaining two treated animals first bred approximately one year after treatment with 5 mg deslorelin. After administration of 10 mg deslorelin, none of the treated animals bred during the following 16 months. The use of higher doses of deslorelin has been associated with longer contraceptive duration in heifers

(D'Occhio *et al.* 2000) and male dogs (Trigg *et al.* 2001). The results from this small tammar trial suggest that a similar dose-response relationship may exist for the tammar. However, these results should be viewed cautiously as the first and second dosages were from different batches of deslorelin implants and the long-term effects of previous treatment on the pituitary in tammar wallabies are unknown.

In summary, deslorelin implants were successful at inhibiting follicular development and mating in the tammar wallaby. The long-term contraceptive effects lasted for approximately one year. This demonstrates the potential of these implants to reversibly inhibit reproduction in macropodid marsupials. The successful reactivation of quiescent blastocysts and the probable maintenance of lactation following their birth may limit the usefulness of this contraceptive in the majority of macropodid species which mate post-partum. However, post-partum mating is not a feature of the eastern grey kangaroo, *M. giganteus*, or the koala, *Phascolarctos cinereus*, which are two of the species presenting widespread management challenges. Therefore, deslorelin may be an efficacious fertility control option for these species and further trials are warranted. The relationship between dose and duration of action should be investigated in an attempt to gain longer contraceptive duration. Trials are also required in a larger group of animals to gain a more accurate estimation of the contraceptive success rate in the tammar wallaby, and the basis for any non-response.

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