EAZA RMG
EAZA Reproductive Management Group

Taxon: *Giraffidae*

Fact Sheet Compiled by: Alexandra Corner
Last Updated: January 2022
Fact Sheet Reviewed by: Veronica Cowl, Yedra Feltrer Rambaud DVM, MSc(WAH), DipECZM(ZHM), MRCVS & Tobias Knauf-Witzens
We would recommend assessing any contraceptive bout with behavioural and hormone monitoring. For more information on this, please contact contraception@chesterzoo.org

Contraceptive methods	GnRH vaccine (injection)	GnRH agonist (implant)	GnRH agonist (injection)	Progestagen (oral)	PZP vaccine	Progestagen (implants)	Progestagen (injection)
Contraceptive Product:	GnRH protein conjugate	Deslorelin acetate	Luprolide acetate	Altrenogest	PZP vaccine main components are antigens derived from porcine zona pellucida glycoproteins and an adjuvant to stimulate the immune response (Freund's modified complete adjuvant for primary vaccination and Freund's incomplete adjuvant for boosters).	Etonogestrel 68 mg	medroxyprogesterone acetate;
Commercial Name:	Improvac®, Improvest®	Suprelorin ®	Lupron ®	Regu-mate®	Porcine Zona Pellucida vaccine	Implanon®, Nexplanon®	Depo-Provera®, Depo-Progevera®
Product Availability:	Available through veterinary drug distributors.	4.7mg ('Suprelorin 6') and 9.4 mg ('Suprelorin 12') widely available through veterinary drug distributors in the EU.	Luprolide acetate licenced for human use	Regu-mate® Equine 2.2ml/mg oral solution and Regu-mate® Porcine 0.4% w/v oral solution widely available through veterinary drug distributors.	Not commercially available in Europe. PZP is available to ship to Europe. It is advised that you check with the licensing authority that manages the import of veterinary drugs to obtain a permit to import PZP. Once all necessary authorisations and approvals have been completed, you can order PZP from: Kimberly M. Frank The Science and Conservation Center 2100 S. Shiloh Road Billings, MT 59106 phone 406-652-9718 fax 406-652-9733 e-mail sccpzp@hotmail.com	Manufactured by Bayer Schering Pharma AG. Available through human drug distributors	Manufactured by Pfizer. Widely available throughou through human drug distributors.
Restrictions and/or permit required by Importing Country:	Current knowledge: widely available throughout European countries. The EAZA RMG recommends that you always check with your local licencing authority.	The EAZA RMG recommends that you always check with your local licencing authority.	**Data deficient**	The EAZA RMG recommends that you always check with your local licencing authority.	License required UK and France; all other Countries unknown. The EAZA RMG recommends that you always check with local licencing authority.	The EAZA RMG recommends that you always check with your local licencing authority.	The EAZA RMG recommends that you always check local licencing authority.
Mechanism of action:	Production of anti-GnRH antibodies by the immune system, neutralising endogenous GnRH activity. This results in a reduction of FSH and LH production by the anterior pituitary and, ultimately, in a reduction of ovarian follicular development and /or inhibition of testosterone secretion from the testes and spermatogenesis.	GnRH agonist suppress the reproductive endocrine system, preventing production of pituitary and gonadal hormones. As an agonist of the GnRH initially stimulates the reproductive system -which results in oestrus and ovulation in females or temporary enhancement of testosterone and spermatogenesis in males- therefore additional contraception needed during this time. Please see below and refer to Deslorelin datasheet for detailed information.	GnRH agonist suppress the reproductive endocrine system, preventing production of pituitary and gonadal hormones (similar to Suprelorin)	Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation	The PZP antibodies interfere with fertilisation by binding to the ZP glycoprotein receptors that surround the egg of the vaccinated female, blocking the binding and subsequent penetration of sperm.	Interference with fertilization by thickening cervical mucus, interrupting gamete transport, disruption of implantation, inhibition of LH surge necessary for ovulation	Anti-estrogenic activity. Interference with fertiliz thickening cervical mucus, interrupting gamete tr disruption of implantation, inhibition of LH surge ne ovulation
Insertion/Placement:	Injectable intramuscular or subcutaneously	Sub-cutaneous, in a place where it can be easily detected or seen for removal at a later date (I.e.base of the ear/neck); refer Suprelorin fact sheet for effective method of implant placement (tunnelisation).	Injectable	Administered orally in feed or by syringe. Gloves must be worn when administering Regu-mate® (absorption through the skin can cause disruption to the menstrual cycle and prolongation of pregnancies in humans).	Injectable Intramuscular	Intramuscular or subcutaneous. The EAZA RMG recommends sub-cutaneous, at the base of the ear/neck for visibility (aid for later removal).	Injectable intramuscular
Females			**Data deficient**				
Dose	For full suppression, two injections of 300-600µg are given 35 days apart and boosters are usually administered every 2 months. In some cases, a higher dose (800ug may be necessary). Duration can vary between species therefore we would highly recommend monitoring your females for signs of fertility. If the interval between boosters is extended beyond 2 months, it is encouraged that hormonal monitoring is carried out to ensure efficacy. Effective contraception with 300-400ug Improvac® occurs within the 2-3 weeks after basic immunisation (3 vaccinations in 2 months) in most females.[5] Oestrus behaviour has been observed 5 days after basic immunisation, suggesting that the contraceptive effect is not always achieved immediately after the 3rd injection (onset of efficacy in cow was before 4th injection).[2] In a study of 7 giraffes, females were administered a primer dose (600µg) of Improvest® followed by a booster at 4 weeks (600µg); maintenance boosters (600µg) were continued once every 3 months.[6] Ovarian activity was supressed in all treated females and interest by the males stopped; supplemental contraceptives during the induction of treatment did not impede on the effect of Improvest® treatment.[6]	2 x 9.7mg implants last for at least 1.5-2 years in giraffes[2]. Our records suggest that higher doses of up to 5 implants may need to be administered, as not all females were suppressed at lower doses.	**Data deficient.** Lupron is available in varying dosages from formulations lasting 1-6 months.	The dosage is 0.044 mg/kg administered orally daily.	The first injection would consist of 0.5mL PZP + 0.5mL adjuvant and the second injection should be given no less than 14 days after this. 65-100 ug PZP doses provided effective (97%) in *Giraffa camelopardali* s. 1st booster inoculation was required approx. 3 weeks post initial exposure the PZP vaccine. Annual booster inoculations sustained contraceptive effects thereafter. For giraffidae, recommended booster timing is 7-9 months[7].	3 to 5 implants (0.068g) are recommended for successful contraception in this species.	The recommended dose is 0.8mg/kg every 50 days occurs, increase by increments of 100 mg
Latency to effectiveness:	Latency to effectiveness can be up to 6 weeks so separation of the sexes is recommended if possible. Immunisation against GnRH has variable results linked to individual variation in immuno-competence[a].	Deslorelin will have a latency to effect of 3-4 weeks during which a stimulation of the reproductive system will occur. For this reason separation of both sexes is recommended for approximately 3-4 weeks. If you cannot separate the sexes, in order to suppress the initial stimulation phase, the first contraceptive bout must be supplemented with an oral progestogen such as megestrol acetate pills (Ovarid) or altrenogest (Regumate®) daily, 7 days before and 8 days after the implant is inserted.	3 weeks average as GnRH analogues initially stimulate the reproductive system. Separation of the sexes OR additional contraception needed during this stimulatory phase (~2mg/kg Megestrol acetate pills or altrenogest (Regumate®) daily, 7 days before and 8 days after can be used to suppress the stimulation phase).	It has been demonstrated that 95% of mares will be suppressed within 3 days. However, the sexes should be separated for 7 days after the contraception is administered.	Latency to effectiveness is approximately 2-3 weeks after the final injection in year 1 therefore separation of the sexes from the initial injection until 2 weeks after the final injection is recommended[7]. Procedural failures occurred in 43% of treatments; including individuals who were pregnant ay the initiation of treatment or before complete suppression occurred, as well as inadequate dose or number of initial primers. Care should be taken to ensure the correct protocols are followed, else failures may occur[7]. Of the 13 failures: 6 animals were already pregnant when treatment began; 2 animals did not complete the three-inoculation series; 1 animal had an inadequate injection (dart needle length too short); and 1 animal was bred before completion of the inoculation series[7]. It is presumed that antibody titters hadn't reached contraceptive levels before treated animals were reintroduced to the male.[7] Contraceptive efficacy was calculated at 97% when technical failures were considered[7].	Latency to effectiveness can take up to 1 day when inserted on day 1 to 5 of a cycle when replacing oral progestogen. As the right stage during oestrus cycle is often unknown, it is advised to use other contraceptive methods for at least 7 days after insertion of the implant.	Latency to effectiveness after the initial injection is however, if the exact stage of the giraffes cycle is u extra time (1 week) must be allowed, separation of t advised for at least one week.
Oestrus cycles during contraceptive treatment:	Effective contraception with 300-400ug Improvac® occurs within the 2-3 weeks after basic immunisation (3 vaccinations in 2 months) in most females.5	Initial oestrus and ovulation (during the stimulatory phase) followed by a period of anoestrus. To suppress the initial oestrus and ovulation you can follow the megestrol acetate/altrenogest protocol mentioned above.	Initial oestrus and ovulation (during the stimulatory phase) followed by a period of anoestrus. To suppress the initial oestrus and ovulation you can follow the megestrol acetate protocol mentioned above.	Ovulation and cycling can occur in adequately contracepted individuals (but is unlikely and the degree of suppression is dose dependent).	PZP normally does not interfere with follicular devlopment and ovulation which means that females should cycle normally	Unlikely to occur	Oestrus behaviour may be observed. Ovulation and occur in adequately contracepted individuals (but is the degree of suppression is dose depender
Use during pregnancy:	**Data deficient.** Evidence suggests that there may be no issues when used in females with close to term pregnancies4. Two females treated with Improvac and Improvest, respectively delivered healthy calves after receiving primer and booster vaccinations. Healthy calves were born in both cases, and pregnancies and births were reported to be uncomplicated[5,6]. In the giraffe treated with Improvest, the calf was smaller than average and had issues getting up to nurse originally; however, this could be due to the mother's recurrent medical issues. Note that the mother was lactating well and attentive.[6] In a currently unpublished study, one female treated with Improvac while pregnant aborted at approx. 5 months. Other factors may have been involved.	**Not recommended, can cause abortion**	**Not recommended**	Progestogens are **not recommended** in pregnant animals because of the possibility of prolonged gestation leading to dystocia, stillbirth and abortion in some species.	No known contraindications. Treatment with the PZP vaccine didn't interfere with pregnancy and the health of the offspring.[8] Database records show female reticulated giraffe that continued treatment with PZP 5 years after birth of offspring (65-100ug); treatment effective for 11 years until last updated. Another female continued treatment with PZP 4 months after 1st birth for 1 year. Treatment with PZP continued 7 years after 2nd birth of offspring (65-100ug); treatment effective for 7 years until animal death.	Progestagens are **not recommended** in pregnant animals because of the possibility of prolonged gestation leading to dystocia, stillbirth and abortion in some species[8]	Progestagens are **not recommended** in pregn animals because of the possibility of prolonged gesta to dystocia, stillbirth and abortion in some spe
Use during lactation:	Research suggests that there is no negative effect when used in females that are lactating[12].	No known contraindications once lactation has been established.	No contraindications once lactation established	Considered safe for nursing infant.	No known contraindications	Considered safe for nursing infant.	Considered safe for nursing infant.
Use in prepubertals or juveniles:	**Data deficient** in giraffes, so caution is advised. Based on the experience of EAZA RMG working group members with Improvac use in elephants, prolonged use of Improvac may bear risk to permanent infertility when administered in prepubertal animals.	**Data deficient.**	**Data deficient** in this group but likely to have a similar effect to deslorelin	The use of synthetic progestagens in pre-pubertals or juveniles has not been fully assessed. Possible long-term effects	PZP-treated prepubertal white-tailed deer and feral horses were fertile as adults. Not associated with side effects in elephants. But there is no data for other species	The use of synthetic progestagens in pre-pubertals or juveniles has not been fully assessed. Possible long-term effects on fertility are not known.	The use of synthetic progestagens in pre-pubertals c has not been fully assessed. Possible long-term ef fertility are not known.
Use in seasonal breeders:	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**

Duration	**Unknown for most of species**. Improvac® generates short lived antibodies in the domestic pig (after 7-8 weeks following second injection antibodies start to decline). In mares it lasts one to two seasons after the first booster. Long-term use and duration is **data deficient**. Antibodies may not last longer than 2-3 months as boosters are recommended every 2 months.	As a guide, the **minimum** effective period for 4.7mg implants is 6 months, and a **minimum** of 12 months for 9.4mg implants. There is evidence to suggest that 2x9.4mg implants have a duration of efficacy of between 1.5-2 years[2].	**Data deficient**	Duration of effect is 1-3 days and must be administered daily as long as contraception is required. However latency to cycling and conception can vary between individuals.	Duration is related to the antibody titre the persistence of which varies according to species. Boosters are recommended at 6-month intervals to maintain contraception.	The duration of this product can last 2.5 to 3 years.	Dose dependant: 45-90 days in general. However, ef last 1-2 years in some individuals.
Reversibility	In a study of 20 giraffes reversibility could not be conclusively answered after 7 years. In 50% of females given reversal opportunities, no regular ovarian activity was seen 2 years after cessation of a 3 year treatment with 600ug. In the other 50%, while progesterone concentrations were above baseline 3 years after 45 and 47 week treatment periods with 450ug, no regular oestrus activity was observed.[5] Reversal with a live birth was observed in one female following three primer injections (8 weeks; 450ug).[5] In another study, 3 females were given reversal opportunities after 15 months of treatment with Improvest. Regular ovarian activity was seen <2 years after cessation of treatment (600ug; primer dose at 0 month, booster dose 1 month, followed by maintenance boosters every 3 months).[6] We have three records of reversal in the database for giraffes in which individuals gave birth between 1.5-3 years following their last vaccination. The individuals were treated between 3-11 months. There is record of a female reticulated giraffe administered 2 Improvac injections over 2 years (500ug and 600ug respectively). She was allowed to breed for 18 months before 3rd injection (450ug); no offspring produced. It must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals and that the longer an individual is treated, the longer it will take them to reverse. We encourage that institutions monitor the reproductive hormones of the animals in which a return to fertility is desired.	Deslorelin is designed to be fully reversible and there are 4 records of reversals in giraffes with time to conception varying between 2 months to 2 years after the expected implant expiry date. It is unknown whether implants were removed in these individuals. We would recommend that implants are removed to facilitate reversibility but the risk to the individual of anaesthesia to do so must be carefully considered. As such, implants should be placed in locations with thinner skin e.g. inner thigh, umbilical region, base of the ear.	**Data deficient**	Designed to be fully reversible although this can depend on the individual. There is one record of reversal in the database in which a female giraffe conceived almost immediately after cessation of treatment with regumate for two years; there was immediate male interest one day after treatment end and the female resumed cycling two weeks after treatment end.	Reversibility differs between species; however the longer PZP is given the longer it takes for a female to come back to being fertile. There is potential that individuals are redered infertile following long-term use (>3-4 years). It is therefore suggested that an individual is on PZP for no longer than 3 years if you want the female to breed. (Please visit www.sccpzp.org for more information). Database records show a female reticulated giraffe on treatment for 4 years (65-100ug) that reversed 11 months after cessation of treatment (treatment with PZP continued 5 years after birth of offspring (65-100ug); treatment effective for 11 years until last updated). Another female reticulated giraffe on treatment for 1 years (65-100ug). After her 1st birth, treatment (65-100ug) continued for 1 year before reversal 7 months after cessation of treatment (2nd offspring born 14 months after). Another female treated with PZP (65ug) for 1 year gave birth to offspring 12 years after cessation of treatment Crude PZP vaccines have been confirmed to be reversible in mares treated annually for <5years; time to regain fertility is variable (1-6 years) in wild mares.[9] In another study, white-tailed deer vaccinated with PZP regained fertility and could be rendered infertile again with 1 injection; variability was observed amongst deer for duration of infertility following the initial vaccination.[10]	Implanon is designed to be fully reversible however there are no cases of its use or reversibility in the giraffidae family. There are three recorded cases of its use in artiodactyla, but there is no data available on reversal.	Depo-Provera is designed to be fully reversible and r using this product has been demonstrated numero Individuals have been reported as successfully conce months to over 5 years after their final injection. 92 females in database treated with Depo-Provera all reproduce, reversed. Time to conception ranged bet 88 months (mean = 32.6 months).
Effects on Behaviour	**Data deficient**	Oestrus behaviour should be suppressed. Females display reduced sexual behaviours.[2]	**Data deficient**	Effects on behaviour have not been studied and individuals may react differently. Further research is necessary.	Since usually the vaccine doesn't suppress oestrus cycles it has almost no effects on social behaviour.	Effects on behaviour have not been studied, every individual may react differently. Further research is necessary.	As Depo-Provera binds readily to androgen receptors estrogenic, females may experience male-like qualit increased aggression or the development of secon characteristics.
Effects on sexual physical characteristics		Not reported.	Not reported.	Not reported.	Not reported. No social/behavioural side effects noted in African elephants studied for 12 years	Not reported	
Males	**Recommended**	**Not recommended. GnRH agonists have not been proven to be effective in male ungulates.**	**Not recommended. GnRH agonists have not been proven to be effective in male ungulates.**	**Not recommended**	**Not recommended**	**Not recommended**	**Not recommended**
Dose	Two injections of 400-700µg are given 35 days apart and boosters are usually administered every 2 months, although duration can vary between species. In some cases, a higher dose (800ug may be necessary). From anecdotal experience, we would advise beginning treatment with shorter 2 month intervals, before prolonging the interval period to 5-6 months. We would highly encourage monitoring the animals for any signs of a return to fertility, particularly when extending the booster interval.		**Data deficient.** Lupron is available in varying dosages from formulations lasting 1-6 months.				
Latency to effectiveness:	Latency to effectiveness can be up to 3-4 months for the down regulation of spermatogenesis, so separation of the sexes is recommended if possible. Fertility in males may remain for prolonged periods. Efficacy of Improvac® requires at least three injections at monthly intervals. In 2 young bulls, tetosterone concentrations declined after the 3rd injection (treated with 300µg and 450 µg respectively). In bulls > 3 years, immunisation success was achieved after 4 injections (N=2) and five injections (N=4).[5] In 1 bull, suppression was only achieved after 5 injections as he sired a calf between the 3rd and 4th injection (after the calf was born, immunisation dose was increased from 450µg to 750µg). In another study, a male was administered a primer dose (400µg) of Improvest® followed by a booster at 4 weeks (400µg); maintenance boosters (400µg) were continued once every 3 months for 19 months. Serum testosterone concentrations decreased following the second injection and remained low throughout the 19-month monitoring period.[6] Immunisation against GnRH has variable results linked to individual variation in immunocompetence [12].		**Data deficient**				
Use in prepubertals or juveniles:		-	**Data deficient**				
Use in seasonal breeders:	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**
Duration and Reversibility	We have one record of an individual hormonally reversing 3.5 years after 8x300ug injections. Testosterone concentrations return to pre-treatment levels ~ 1 year after the last Improvest® injection in 1 male (following 9x400ug injections over a 22.4 month time period).6 In another study, testosterone levels and testicular size in one male did not returned to pre-treatment levels 4 years post treatment with Improvac® (8x 450ug doses in 52 weeks). In another male, androgen levels were below threshold 1 year post cessation of treatment (following 25x750ug vaccinations over 3.8 years).5 Behaviourally, we have one record of a male reticulated giraffe treated with Improvest for 2 years (200ug); caused decreased libido and mounting of females. Mounting behaviour of oestrus females resumed a few months later despite supressed testosterone levels. There are a few cases of GnRH vaccines being used in male giraffes for controlling aggression which worked well with no side effects however, effects on fertility were not investigated. If future breeding is desired, it must be taken in to consideration that younger individuals will take longer to reverse in comparison to older individuals, and that the longer an individual is treated, the longer it will take them to reverse. There is evidence from the use of Improvac in stallions and African elephants in which Improvac was reversible following short-term (2-3 years) treatment.	-	**Data deficient**				
Effects on Behaviour	Similar to surgical castration but short-acting (duration of antibody effect). Decrease of androgen-related aggressive behaviour due to down-regulation of testosterone synthesis. Testicular volume will decrease; despite atrophic testicles and decreased androgen concentrations, some bulls show sexual arousal (e.g., mounting, courting) in the presence of females in oestrus.)[5,6]	-	**Data deficient**				
Effects on sexual physical characteristics	Similar to surgical castration but short-acting (duration of antibody effect). Decrease of androgen-related aggressive behaviour due to down-regulation of testosterone synthesis. In many Improvac® treated bulls, scrotum and testicle size is reduced[5]	-	**Data deficient**				
General:							
Side effects	Occasional swelling at the vaccination site - need to inject deep intramuscular in elephants, horses and giraffes.	In general weight gain as would be seen with ovariectomy or castration.	Effects on weight should be similar to those from ovariectomy or castration. Increased appetite will result in weight gain, especially in females. Males may lose muscle and overall weight if not replaced by fat.	Possible weight gain. The EAZA RMG recommends that you always read the manufacturer's data sheet.	Treatment for over 5 years has been associated with ovarian failure in some species (species differences). In some species the failure to conceive can result in longer than usual breeding season (aggression and social disruption). Deleterious side effects are rare and minor in nature; e.g., abscesses have been associated Freunds complete adjuvant (FCA) use – when administered exclusively to the hip or gluteal muscles.[8] However, abscess occur at less than a 1% rate and tend to be < 28mm and can be drained without untoward effects.[8] In most cases, when these adjuvants are used, a small granuloma will form at the site of injection; which will not cause any towards/deleterious health effects long term.[8] In some species, PZP can elicit an immune response that interferes with normal follicular development – it is recommended that animals are not treated for more than 2-3 years if reversibility is not a high priority.[8] PZP-treated animals don't have supressed ovarian activity and are therefore susceptible to the pathological effects of continuous steroid exposure.[8] In the database, 1 record of female treated with PZP (65ug) for 1 year; ended at 12 month expiration date due to reported growth of abscesses at multiple injection sites.	Most ungulates experience few side effects from progestin based contraception; mucometra, pyometra and uterine infections have occurred.[8]	Possible weight gain. The EAZA RMG recommends th the manufacturer's data sheet.One report of uterine on post mortem in a giraffe treated for more than tw Depo-Provera. Most ungulates experience few side e progestin based contraception; mucometra, pyom uterine infections have occurred.[8]

Warnings	It should be handled with extreme care to avoid handler accidents. The EAZA RMG recommends that you read the manufacturer's data sheet. Do not treat females with previous or current history of endometritis/metritis. The use of progestins can exacerbate existing uterine inflammation/infection. sheet	Duration may be reduced if implant is broken. Do not cut the implant. Should not be used in conjunction with Depo-provera or any other long-acting injectable progestagen.	Should not be used in conjuction with Depo-Provera or any other long-acting injectable progestagen.	Do not treat females with previous or current history of endometritis/metritis. The use of progestins can exacerbate existing uterine inflammation/infection.	The only adjuvants used with PZP are Freund's modified complete and incomplete adjuvants. **The complete adjuvant does not cause false positive TB results.** Injection site reactions are less than 0.05%. Following the initial treatments, boosters are required, using only Freund's Incomplete adjuvant.		Please be aware that there is one report of a post-m giraffe where they found uterine pathologies followi of treatment with Depo-Provera. Database report 5.61% of females treated with Depo-Provera; 40% o were institutional failures, 60% were product fa

Reporting Requirements: In order to increase our knowledge of the efficacy of contraception methods in giraffidae it is recommended that all individuals on contraception be reported to the EAZA RMG

References:

1) Asa, C.S. & Porton, I.J. (eds.) (2005) *Wildlife Contraception: Issues, Methods, and Applications* . The Johns Hopkins University press: Baltimore.

2) Patton, M.L., Bashaw, M.J., del Castillo, S.M., Jöchle, W., Lamberski, N,, Nieches, R., Bercovitch, F.B. (2005) Long-term suppression of fertility in female giraffe using the GnRH agonist deslorelin as a long-acting implant. *Theriogenology* , 66(2):431-438.

3) Borkowski, R., Citino, S., Bush, M., Wollenman, P., Irvine, B. (2008) Surgical Castration of Subadult Giraffe (*Giraffa camelopardalis*). *Journal of Zoo and Wildlife Medicine* , 40(4):786-790.

4) Miller, L.A., Rhyan, J.C., Drew, M. (2004) Contraception of bison by gnRH vaccine: a possible means of decreasing transmission ofbrucellosis in bison. *Journal of Wildlife Diseases* , 725-730.

5) Schwarzenberger F, Pia Krawinkel, Jeserschek SM, Schauerte N, Geiger C, Balfanz F, Knauf-Witzens F, Sicks F, Nevado EM, Anfray G, Hein A, Kaandorp-Huber C, Marcordes S, Venshoj B (2020). Immunocontraception of Male and Female Giraffes Using the GnRH Vaccine Improvac®. *Zoo Biology.* 1-15. DOI: 10.1002/zoo.21651

6) Moresco A, Penfold LM, Jankowski G, McCain S, Crook E, Faliano A, Crane J, Wack RF, Goodnight A, Han S (2021). Reproductive Suppression of Giraffe (*Giraffa Camelopardalis*) Under Managed Care Using a GnRH Immunological Product. *Zoo Biology.* 1-9. DOI: 10.1002/zoo.2165

7) Frank KM, Lyda RO, Kirkpatrick JF (2005). Immunocontraception of Captive Exotic Species: IV. Species Differences in Response to the Porcine Zona Pellucida Vaccine, Timing of Booster Inoculations and Procedural Failures. *Zoo Biology* . 24:349–358.

8) Patton ML, Jochle W, Penfold LM (2007). Review of Contraception in Ungulate Species. *Zoo Biology* . 26:311-326

9) Kirkpatrick JF, Turner A (2002). Reversibility of Action and Safety during Pregnancy of Immunization against Porcine Zona Pellucida in Wild mares (*Equus caballus*). *Reproduction Supplement* . 60:197–202.

10) Miller LA, Johns BE, Killian GJ (1999). Long-Term Effects of PZP Immunization on Reproduction in White-Tailed Deer. *Vaccine.* 18(5-6): 568-574

11) Lyda RO, Hall JR, Kirkpatrick JF (2005). A Comparison of Freund's Complete and Freund's Modified Adjuvants Used with a Contraceptive Vaccine in Wild Horses (*Equus caballus*). *Journal of Zoo and Wildlife Medicine* . 36:610–616

12) Balet, L., Janett, F., Hüsler, J., Piechotta, M., Howard, R., Amatayakul-Chantler, S., Steiner, A., Hirsbrunner, G. (2014) Immunization against gonadotropin-releasing hormone in dairy cattle: Antibody titres, ovarian function, hormonal levels, and reversibility. *Journal of Dairy Science,* 97:2193-2203.