Free-ranging African Elephant IMMUNOCONTRACEPTION

A NEW PARADIGM FOR ELEPHANT MANAGEMENT











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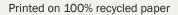
PRINTER

Trident Press, Cape Town

Cover photographs by Audrey Delsink

Published 2012







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Audrey Delsink



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Lynette Fourie



INTRODUCTION

The African elephant (*Loxodonta africana*) is one of the most recognizable, charismatic and iconic wild animals. Well known for their intelligence, strong family bonds and highly socialized groups, they are also engineers of habitat change and their presence or absence has a critical effect on the way in which ecosystems function. The movement of African elephants throughout their historical range has been disrupted by the activities of people over the last two centuries.

In South Africa, elephant populations are confined to reserves and parks, both small and large. It is important to manage such confined elephant populations to slow their growth rates so as to prevent loss of biodiversity, ecosystem function and resilience, harm to human lives or livelihoods, or compromising key management objectives. The National Norms and Standards for the Management of Elephants in South Africa were established in 2008 under the terms of the National Environmental Management Biodiversity Act of 2004. The Norms and Standards recognize that managers may need to control the growth of elephant populations and that one way to do this is through the use of immunocontraception.

Since 1996 The Humane Society of the United States (HSUS) followed by its affiliate Humane Society International (HSI), have funded cutting edge research on the use of non-steroidal, non-invasive contraception of wild elephant populations, called immunocontraception. The PZP vaccine is administered by hand injection or via a dart fired from a dart rifle, CO² pistol or blowgun. Darting is preferred whenever possible, because it avoids the need to capture and handle the animal, and darting from helicopters is often the safest and most efficient way to dart African elephants. Three vaccine injections are given in the initial year, followed by annual boosters. The HSUS is currently funding research into the development of one-shot PZP vaccines that last two or more years for use in elephants (these have been tested successfully on wild horses, deer and other species by The HSUS and other investigators).

One technology used successfully by The HSUS and its collaborators to achieve a one-shot vaccine involves packaging PZP in timed-release pellets, which stimulate annual boosters. The HSUS and HSI continue to support research on developing a one-shot vaccine for elephants, as well as to develop a plant-based substitute for pig PZ.

Research conducted on immunocontraception in elephants over the past fifteen years has resulted in a robust body of scientific work demonstrating that the technique is an effective way to control elephant population growth. It is also fully reversible, allowing managers to fine tune population growth, and has no physical or behavioural side effects.

The South Africa-based elephant immunocontraception research team consists of: Audrey Delsink, Field Director; JJ van Altena, who specialises in immunocontraception implementation; and Prof. Henk Bertschinger, a Veterinarian who specialises in wildlife reproduction and contraception. Jay F. Kirkpatrick, Ph.D., Director, The Science and Conservation Centre, is a U.S-based advisor of the research team. Teresa M. Telecky, Ph.D., Director, Wildlife Department, Humane Society International, is The HSUS headquarter-based coordinator of the research team. Together, they make up the current HSI immunocontraception research team.

The research phase of our work on elephant immuno-contraception has resulted in over two dozen scientific publications. Thirteen South African elephant populations are being actively managed with the immunocontraception technique we developed. In 2007, Tembe Elephant Park, in KwaZulu-Natal Province, became the first public park in the world with elephants under immunocontraceptive management.

South Africa's National Norms and Standards for the Management of Elephants in South Africa prescribe methods that can be used to slow elephant population growth rates; with the exception of fertility control, the methods focus on removing elephants from a population. However, removing elephants from a population merely treats the symptoms of population growth but not the cause - reproduction - which is where many believe potential solutions should focus.

Measures to slow elephant population growth rates must be adaptive and informed by the best available scientific information and must take into account the social structure of elephants and be based on measures to avoid stress and disturbance to elephants.

HSI Immunocontraceptive Research Team

June 2012



THE PZP VACCINE

Q What is an immunocontraceptive?

A Immunocontraception is a non-hormonal form of contraception, based on the same principles of disease prevention through vaccination. The immunocontracep-

tive stimulates the production of anti-bodies against some essential element of the reproductive process, thereby preventing pregnancy.

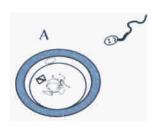
Q What is porcine zona pellucida (PZP), and how does it work to prevent pregnancy?

A non-cellular capsule known as the zona pellucida (ZP) surrounds all mammalian eggs. The ZP consists of several glycoproteins (proteins with some carbohydrate attached), some of which are thought to be the primary component of the sperm receptor (the molecule that permits attachment of the sperm to the egg during the process of fertilization). In nature, a sperm must attach to the ZP protein before it can penetrate the egg. When the porcine zona pellucida (PZP) vaccine (derived from pigs' eggs) is injected into the muscle of the target female

animal, it stimulates her immune system to produce antibodies against the proteins in the vaccine. These antibodies attach to the sperm receptors on the ZP of her eggs and thereby block fertilization (Figure 1).

The specificity of the antibodies for the sperm receptor is absolute, and there is no cross-reactivity with any other organs, tissues or molecules in the mammalian body. Because the cow does not fall pregnant she will continue to show an oestrous cycle that is 15-17 weeks long. This means that she may come on heat up to 2-3 times a year.

See Paterson and Aitkin 1990, Barber and Fayrer-Hosken 2000, Kirkpatrick 2010, Ahlers et al. 2012, Kirkpatrick 2012



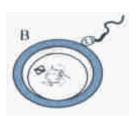






FIGURE 1 Mechanism of PZP action from Bertschinger et al. (2008)

- A When the egg (oocyte) is ovulated into the Fallopian tube it is surrounded by a capsular layer known as the zona pellucida capsule.
- B Before fertilisation can take place the sperm binds to one of thousands of receptor sites on one of the zona proteins. The sperm then undergoes the so-called acrosome reaction.
- C Only once the sperm has undergone the acrosome reaction can it penetrate the ZP-capsule and then a single sperm fertilises the egg.
- D The antibodies formed in response to the PZP vaccine recognise and cover all sperm receptors on the ovulated elephant egg. The binding of sperm is blocked as is fertilisation and thus pregnancy.

Q Are any pigs killed specifically to produce the vaccine?

A Pig ovaries are obtained from the Pork Packers pig abattoir in Olifantsfontein as a by-product of gilts slaugh-

tered for human food. The number of pigs slaughtered is thus not affected by the harvesting of gilt ovaries.

See Bertschinger et al. 2008, Kirkpatrick 2010; 2012

Q What are the advantages of PZP?

A PZP fulfils the requirements of an ideal contraceptive classified as:

- Contraceptive efficacy of at least 90%
- Remote delivery of the vaccine which means that no handling of animals (thereby reducing stress) is required
 and substantially reduces the cost of treatments
- Reversibility of contraceptive effects
- No harmful effects in pregnant animals
- Absence of either short or long-term significant health effects
- No effects on social behaviours in either short or long-term
- Target specificity i.e. the contraceptive agent does not pass through the food chain
- Low cost
- Efficacy across a wide range of species (> 85 in 2012)



Q What is the history of PZP use?

A a) In other species

Immunocontraception first emerged as a possible wildlife contraceptive in the mid-1980's when Dr. Irwin Liu of the University of California, Davis, demonstrated that the PZP vaccine effectively blocked pregnancy in domestic horses. Dr. Liu was joined by long time horse contraception researchers Dr. Jay Kirkpatrick of The Science and Conservation Centre, Billings, Montana, and Dr. John Turner of the University of the Toledo School of Medicine for field tests of PZP on wild horses.

Kirkpatrick and Turner successfully delivered PZP vaccine to wild horses at Assateague Island National Seashore (ASIS) in Maryland using barbless, self-injecting darts fired from tranquilizer guns. Pregnancy was prevented for approximately 8 months and treatments blocked conception with better than 90% effectiveness. Furthermore, when the antibody titres had decreased to lower levels, conception occurred normally.

As a result, the National Park Service has now developed and implemented a management plan to stabilize the horse population at ASIS using immunocontraception. The population has been treated for 22 years, without health problems, and the population has decreased by almost 40%, since management-level application began in 1995. A successful pilot project was also conducted on wild horses in north-eastern Nevada in 1992-1994; and a second collaborative project began in 1996 at Nellis Air Force in south-eastern Nevada. The PZP vaccine is currently being used on at least 25 horse management areas for the National Park Service or the Bureau of Land Management, amongst other agencies.

Turner, Kirkpatrick and Liu began testing PZP on white-tailed deer in the late 1980's, and captive and field tests have indicated that as in horses, the vaccine reduces the individual fertility by 85-95%. Turner and Kirkpatrick stated that based on the feral equine data, it should be possible to raise antibodies to heterologous zona pellucida in many species. Subsequently, it has been demonstrated that PZP prevents pregnancy in a large number of species, including many different kinds of deer, many zoo animals, free-ranging horses, water buffalo etc. At present the PZP vaccine is being used to treat more than 112 mammalian species, with sufficient data to document success in more than 80 of these species.

See Kirkpatrick and Turner 1985, Liu et al. 1989, Kirkpatrick and Turner 1991; 1996, Rutberg 1996, McShea et al. 1997, Deigert et al. 2003, Frank et al. 2005, Kirkpatrick and Frank 2005, Rutberg and Naugle 2008, Kirkpatrick 2010, Kirkpatrick et al. 2011, Kirkpatrick 2012

b) In African elephants

Since 1996, The HSUS followed by its affiliate HSI, have funded cutting edge research on the use of non-steroidal, non-invasive contraception of wild elephant populations, called immunocontraception. The surface structures of the elephant zona pellucida were shown to be very similar to those of the pig zona pellucida and when female zoo elephants were vaccinated with PZP vaccine and an adjuvant, all developed antibodies that persisted for 12-14 months. The antibody titres were similar to those found in horses treated with the immunocontraceptive. Based on these results, field trials were conducted in South Africa's Kruger National Park (KNP) during the period October 1996-2000. The KNP trial in free-ranging African elephants was designed to test and evaluate three components: a) the efficacy of PZP as an immunocontraceptive, b) the dosage and c) administration regimes.

The very first two PZP-immunocontraception field trials at KNP in elephants recorded contraceptive success rates of only 56% and 80%, respectively. In the first trial, 400~ g and 200~ g PZP was used for the primary and booster

vaccinations. In the second trial, 400 g PZP for both the primary and booster vaccinations was used. In both trials, synthetic trehalosedicorynomycolatei (5 mg per vaccinations) (Ribi Immunochem Research, Montana) was used as adjuvant. During the first trial (n=18; efficacy 56%) the booster vaccinations were administered at 6 week and 6 month intervals after the primary vaccination. In the second trial (n=10; efficacy 80%) two boosters were administered at 2-weekly intervals.

The KNP trials also tested the reversibility of the immunocontraceptive and its efficacy following treatment for a second consecutive year. The ultrasound results showed that all the females left untreated for a second year conceived, compared with none of the treated females (even though the treated females were cycling). This demonstrated that PZP treatment is reversible in African elephants after two years of treatment. Furthermore, treatment using PZP vaccine caused no deleterious effect on the ovary and its cyclicity.

See Fayrer-Hosken et al. 1997, Fayrer-Hosken et al. 1999, Fayrer-Hosken et al. 2000;2001, Delsink 2006, Bertschinger et al. 2008







Based on the success demonstrated in the KNP trials, the next phase of the project was initiated consisting of the development of a strategy to use the vaccine to control free-ranging elephant populations. A discrete population of free-roaming elephants at the Greater Makalali Private Game Reserve (GMPGR), Limpopo Province, South Africa, was identified for this experiment (herein after referred to as the Makalali study). Due to its manageable population size, accessibility (due to the elephants' habituation to vehicles as a result of the reserve's gameviewing activities), and the detailed individual elephant identification kits, the Makalali elephant population was ideal for this next phase.

In May 2000, all the adult female elephants aged >12 years (18 animals) were vaccinated with 600 g PZP + 0.5 ml of Freund's Modified Complete Adjuvant (FMA) (Sigma Chemical Co., St Louis). So as to ensure complete vaccine delivery, the target animals were identified and darted

remotely from on foot or from a vehicle using drop-out darts (Dan-Inject International, Denmark) with smooth, barbless needles. As demonstrated in the KNP trials, the vaccination of pregnant elephants with PZP has no effect on gestation, on the foetus or on parturition, so pregnancy status was not a criterion for selection of target animals. After the initial dose, the 18 target animals received two booster vaccinations of PZP (600 g), emulsified with Freund's Incomplete Adjuvant (FIA), two to three weeks apart. In June 2001, the 18 target animals received their first annual booster vaccination.

From 2003 onwards, vaccinations were conducted from a helicopter. In 2012, the twelfth year of the study, 26 animals are being treated and 5 of the originally treated animals were taken off treatment to test for reversibility. The Makalali study has demonstrated close to 100% efficacy.

The Makalali study is the project's longest running elephant immunocontraception study, forming the benchmark for all elephant immunocontraceptive studies. This study has successfully supported the test hypotheses:

- The PZP vaccine can be successfully delivered to free-roaming elephants in a game park.
- PZP treatment does not alter selected social behaviours.
- Treatment of pregnant females with the PZP vaccine does not harm pregnancies in progress or affect the health of the offspring.
- PZP immunocontraception can reduce the rates of population increase and stabilize elephant population numbers in a small game reserve.

See Delsink et al. 2002, Delsink 2006, Delsink et al. 2006, Delsink et al 2007, Bertschinger et al. 2008

A question that arises is why the immunocontraceptive efficacies of the KNP study (56 and 80%) were much lower than was achieved in the Makalali study and other parks where elephants were subsequently treated with PZP. This was despite the fact that the doses of PZP in the KNP were higher than those used later on (see above). Essentially, differences between the KNP and other study protocols may have contributed to the efficacy results obtained. Firstly, both of the KNP trials used trehalosedicorynomycolatei as the adjuvant whilst the later studies made use of Freund's complete modified and incomplete adjuvants. Secondly, in the first KNP trial, the interval between the first and second booster was approximately 4½ months compared to 2-3 and now 5-7 weeks in subsequent studies. The third and final difference was the selection of the target animals. During the

KNP trials, the selection criterion for target cows was pregnancy status which was initially based on whether they had a small calf (< 2 years old) at foot (and were thus unlikely to be pregnant) and later, immobilisation and transrectal ultrasound examination. The only selection criterion in later studies was reproductive age; pregnancy status was not considered. Another factor which may have resulted in different efficacies is that cows selected for treatment in the KNP may have been in anoestrus or already have resumed ovarian cyclicity. Thus, vaccination of cows that were about to resume or had already resumed ovarian cyclicity may have been too late to prevent a pregnancy. PZP antibody titres of these cows were never determined meaning that the precise reasons for differences between efficacies of the first and second trials and later studies cannot be elucidated.

See Fayrer-Hosken et al. 2000, Bertschinger 2010

Q What other methods have been used to contracept elephants and were they successful?

A The PZP field trials in the South African National Parks KNP were run back to back with hormonal trials by another research team using oestradiol implants. During their study, ten elephant cows were treated with subcutaneous silicone rubber implants – each cow receiving 5 implants of Compudose, which slowly released minute amounts of 17B-oestradiol (300ug/animal/day). The effects of these long-lasting oestrogen implants were described as 'an ethological and public relations disaster'. Although the implants did appear to prevent pregnancy, they also induced a prolonged state of sexual attractiveness among the treated cows. This resulted in the continuous harassment of treated cows by bulls, disturbing the affected family groups and endangering the young

calves in those groups. The project was discontinued once the effects of the implants had worn off after 4-6 months. Furthermore, oestradiol treated elephants showed aberrant behaviour by separating from their family group. There was much media coverage regarding this study which has caused tremendous confusion. Even today, some conservation experts continue to confuse immunoand hormonal contraception of wildlife. Those of us working on immunocontraception find that often we still have to deal with the fallout from the steroid project, and must carefully explain that the hormonal trials were responsible for the anomalies, and not our on-going immunocontraception studies.

See Bartlett 1997, Butler 1998, Goritz et al. 1999, Whyte 2001, Whyte et al. 2003, Stout and Colenbrander 2004, Perdock et al. 2007, Bertschinger 2010

Q How is the vaccine made and who manufactures it within South Africa?

A In South Africa, the vaccine is made in the PZP Laboratory, funded by HSI, under Prof. H. Bertschinger of the Section of Reproduction, Department of Production Animal Studies, University of Pretoria, Onderstepoort following the methodology of The Science and Conservation Centre (SCC) in Billings, Montana. The ovaries for manufacture of the vaccine are obtained from Pork Packers pig abattoir in Olifants-

fontein. Each batch is subjected to a qualitative and quantitative quality-control program. In collaboration with other investigators, the SA PZP Laboratory and The SCC continue to conduct research with the contraceptive vaccine, focusing on the ability to produce larger quantities, and increasing the efficacy of long-term contraception through a single inoculation.

See Turner et al. 2002, Turner et al. 2008

Q Is the vaccine registered and how is it classified?

In the USA, after more than two decades of research, the PZP vaccine was officially registered (under the brand name ZonaStat-H) in February 2012 as the first contraceptive vaccine for horses. In addition, the U.S. Food and Drug Administration authorises the use of the vaccine in other species (other than horses) through Investigational New Animal Drug (INAD) exemptions. In South Africa, the vaccine is produced in the PZP Laboratory of the Section of Reproduction at the University of Pretoria. The laboratory is funded by the HSI as well as from the sale (at less than the cost of manufacture) of vaccines for use in game reserves. The use of the vaccine is subject to approval from the Directorate of Animal Health under Section 20 of the Animal Diseases Act, 1984 (Act No. 35 of 1984); ref number 36-5-0251, which was dependent on approval of the Project Protocol Number V049/11: Immunocontraception of Free-Ranging African Elephant (Loxodonta africana) Cows on Game Reserves in South Africa. The project is registered with the University of Pretoria under Prof. Bertschinger's name. Furthermore the use of the vaccine requires approval under Section 21 of Medicine and Related Substances Control Act (Act No. 101 of 1965) or the Fertilizers, Farm and Feeds, Agricultural Remedies and Stock Remedies Act (Act No. 36 of 1947).

All reserves employing PZP vaccine form part of the project V049/11 and require that all reporting is done to Prof. Bertschinger.

How is the PZP vaccine obtained?

Before the vaccine can be used in a new reserve, an elephant management plan detailing numbers of elephants with sex and age classes is required for that reserve. The vaccine is administered by a veterinarian or under a veterinarian's supervision. Supply of the vaccine

requires a veterinary prescription. All reserves are also required to sign a form which indemnifies the University of Pretoria and its staff from any claims that may be attributed to the use of the vaccine.

The vaccine is ordered from:

Prof. HJ. Bertschinger Department of Production Animal Studies Faculty of Veterinary Science University of Pretoria POBox X04, Onderstepoort, 0110

Tel: +27 (0) 12 804 3312 Fax: +27 (0) 12 804 3312 Cell: +27 (0) 82 407 2396

Email: henkbert@tiscali.co.za



In South Africa, the vaccine is not commercially available and is provided at aproximately 25-30 % of the cost of production. The current (2012) price is ZAR500 for each primary dose and ZAR250 per booster (VAT included).

On average, vaccination costs for a single animal in the first year are ZAR1000 - ZAR1200, inclusive of vaccine, adjuvant, darts, helicopter time and professional fees.

Who controls vaccine use in wild elephant populations?

As the vaccine is not commercially available in South Africa, applications for its purchase and use must be forwarded to Prof. Henk Bertschinger of the University of Pretoria. The HSI immunocontraception research team will evaluate the proposal and plan and help implement the use of the vaccine where necessary.



Q Does a reserve have to do an environmental impact assessment (EIA), an environmental impact statement (EIS) or management plan prior to using PZP on elephant in a game reserve or wildlife sanctuary?

A As per the Norms and Standards of Elephant Management in South Africa (NSEM) and the Threatened or Protected Species (TOPS) Regulations, it is an essential requirement that any reserve that accommodates or wishes to accommodate elephants must have a detailed Elephant Management Plan, the format of which is outlined in NSEM. This includes details pertaining to elephant population management,

stocking and carrying capacity rates, the methods of which do involve some EIA's or EIS's. The HSI immunocontraception research team can assist the applicant with tailor-made PZP specific long-term contraceptive management plans. The degree of treatment is interconnected with specific management objectives unique to the target population.

See DEAT 2007; 2008

Q What groups are on the PZP Contraceptive Research Team?

Today, the USA team consists of The Science and Conservation Centre, Billings; Toledo University Medical College, Ohio; University of California-Davis; Tufts Cummings School of Veterinary Medicine, North Grafton, Massachusetts; The HSUS/HSI, Washington, DC; and the University of Iowa, Ames. Many other individuals contribute to the effort in one form or another. Governmental agencies that can be considered team members in the USA include the National Park Service, U.S. Forest Service, U.S. Department of Commerce, and the Bureau of Land Management.

Within SA, team members include the University of Pretoria's PZP Laboratory, the Ezemvelo KwaZulu-Natal Wildlife (EKZNW) agency as well as a number of private game reserve managers and owners.

The entire PZP contraceptive effort involves many people, several institutions, and numerous funding agencies. This team works together, bringing many disparate disciplines and talents together to solve the problems at hand.

Q Who Funds PZP Contraceptive Research?

A In South Africa, funding of the vaccine application to wildlife research has been predominantly funded by the HSI at the Greater Makalali Private Game Reserve (vaccine) and the Tembe Elephant Park (2011 vaccinations). We thank the U.S. Fish and Wildlife Service for funding our initial research on the vaccine in KNP. All other reserves have paid for the vaccine and treatment

fees themselves. Subsequently, implementation into various reserves and parks has been supported by many individual communities, agencies, and organizations, including but not limited to:

- University of Pretoria
- EKZNW

Q What wild elephant populations, within South Africa, are presently being managed with PZP?

A The reserves and year during which each population is currently managed and was initiated are:

- The Greater Makalali Private Game Reserve (2000)
- Mabula Game Lodge (2002)
- ThabaTholo Game Farm (2004)
- Phinda Game Reserve (2004)
- Thornybush Private Game Reserve (2005)
- Welgevonden Private Game Reserve (2005)
- Shambala Private Game Reserve (2004-2007)

- Kaingo Game Reserve (2005)
- Kapama Private Game Reserve (2005-2010)
- Karongwe Game Reserve (2007)
- Tembe Elephant Park (2007)
- Hlambanyathi Game Reserve (2009)
- Amakhala Game Reserve (2010)
- Thanda Private Game Reserve (2011)

See Bertschinger et al. in prep



DELIVERY, APPLICATION and BIOLOGICAL EFFECTS of PZP in AFRICAN ELEPHANTS

Q How is the vaccine delivered?

The PZP vaccine must be injected into the triceps muscles or semimembranous-semitendinous group of muscles of the target animal. PZP may be delivered remotely by dart, making it unnecessary to restrain or sedate an animal, thereby greatly reducing stress. However, it can be delivered by hand if the animal is sedated. There are many commercial dart systems available, but the thick viscosity of the vaccine requires a large needle and a quick injection. Thus far, Dan-Inject (Børkop, Denmark) systems and Pneu-Dart, Inc. (Williamsport, Pennsylvania) systems seem to work the best.

For the Dan-Inject system, the vaccine is delivered with Dan-Inject darts fitted with 60 mm plain 14-guage needles. These so-called 'drop-out darts' can be delivered from a motor vehicle firing into the triceps muscles or semimembranous-semitendinous group of muscles (intramuscular). This is normally used for small populations.

For larger populations, vaccine administration is done from a helicopter as the intervention is much shorter and has been shown to cause much less disturbance with animals settling down within a day. From the helicopter, darts are fired into the rump (intramuscular). Capture or immobilisation of cows is not required for treatment.

See Burke 2005, Delsink et al. 2007, Bertschinger et al. 2008

Generally, Pneu-Dart 'mark and inject' darts are used to facilitate identification of already treated animals in a breeding herd treated from the air. For the Pneu-Dart systems, Pneu-Dart 1.0 cc barbless darts with 50 mm 13guage needles with gelatine collars can be fired from Pneu-Dart projectors or from several other commercially available projectors (PAXARMS, New Zealand or Dan-Inject, for instance) (Figure 2). The darts have a 2-inch long needle to provide a sufficient intramuscular injection of the vaccine.

Additionally, the darts are fitted with a 13-gauge needle thickness and side-ports. The needle thickness is important on thick-skinned animals and the side-ports ensure adequate vaccine administration should a skin plug block the needle opening thus preventing injection. The darts are self-injecting and fitted with barbless needles which will allow the dart to fall out. The darts are disposable, and after hitting the animal intramuscularly (the only acceptable location for darting), they inject by means of a small powder charge, and then drop out. Darts that have not been discharged cannot be discharged by stepping on them or by any other kind of casual contact.



FIGURE 2 Immunocontraception darting equipment -

- a) Pneu-Dart Dart Gun
- b) Pneu-Dart Mark and Inject Dart with gel collar
- c) Pneu-Dart Dart with gel collar
- d) Glass vial with Adjuvant and yellow-topped vial with PZP vaccine
- e) Lochner syringe for mixing vaccine and adjuvant and syringe for drawing up vaccine and adjuvant
- f) Plastic bottle with marking substance
- g) Dan-Inject Dart Gun

The protocol currently used for African elephants

Doses used:

- Primary vaccination: 400 g PZP in 1 ml PBS solution homogenised with 0.5 ml Freund's complete modified adjuvant
- Boosters: 200 g PZP in 1 ml PBS solution homogenised with 0.5 ml Freund's incomplete adjuvant

Year 1 (new reserve or new individual cows):

- Primary vaccination
- 1st booster after 5 7 weeks
- 2nd booster after 5 7 weeks

Year 2 and onwards (unless a cow is allowed to reverse):

- Annual booster to maintain antibody titres

Note: Since the second KNP trials, annual boosters have been adjusted from 400 g PZP to 200 g PZP as elephants are very responsive to the vaccine facilitating lower doses.

Normally, each animal is darted three times during the first year, with the primary vaccination followed by two booster shots (at 5-7 week intervals). Thereafter, a single annual booster should maintain contraception.

With small herds, it is likely that individuals can be identified by age class, sex, and family group as well as individual markings. In the absence of telemetry collars, this detail is used to relocate the treated animals for booster inoculations. With larger herds with or without telemetry collars, one can vaccinate a particular proportion of cows each time – say 90% (or the level determined by the management objectives) – recognizing that coverage for booster inoculations will likely be incomplete but expecting a certain percentage of females not to conceive each year. The models for such an approach have been tested for specific populations and are being further developed.

During administration, special 'marker darts' (Figure 3) are used which leave a dye mark on the animal at the same time it injects the vaccine (Figure 4) thereby enabling the dartsman to distinguish between darted and undarted animals.



FIGURE 3a Pneu-Dart Mark and Inject Dart with stabiliser



FIGURE 3b Close-up of marking fluid being injected into Pneu-Dart

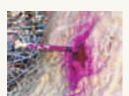


FIGURE 4a Close-up of injected Pneu-Dart showing marking substance at injection site



FIGURE 4b An aerial photo of vaccinated elephants showing marker darts which spray a marking substance at the injection site

An alternative strategy is to administer only a single booster the first year; trial results indicate successful contraception. Retrospective analysis of data have shown that after using three vaccinations during the first year cows may conceive between the first two vaccinations or around the time of the first booster but not after that. Given this information, a protocol, which made use of only two treatments in Year 1, was applied in Tembe Elephant Park. The results so far are encouraging.

See Delsink et al. 2002, Delsink 2006, Delsink et al. 2006, Mackey et al. 2006, Delsink et al. 2007, Bertschinger et al. 2008, Bertschinger 2010, Kirkpatrick 2010, Druce et al. 2011, Kirkpatrick 2012

3 x Photos Audrey Delsink

Why cannot pregnancy be blocked with just one inoculation instead of the two shots you use now?

The current vaccination regime comprises of an initial primer dose, followed by two (a minimum of one booster has been demonstrated to be efficacious) treatments at 5-7 week intervals. The initial 'primer' dose of PZP sensitises the immune system to the antigen and the immune system responds with the production of antibodies by specific cells sensitised. Without a booster a low antibody titre (probably not high enough to prevent fertilisation) is reached which wanes within a period of a few months. The immune system responds more rapidly and with a greater antibody titre after the secondary vaccination, and the duration of high antibody titre will be longer. Each subsequent booster will evoke a similar response. PZP is a relatively small protein that is not especially immunogenic, which is the reason why a strong adjuvant like Freund's is used to evoke a more vigorous response from the immune system.

See Eldridge et al. 1989, Liu et al. 1989, Turner and Kirkpatrick 2002, Turner et al 2002, Frank et al. 2005, Turner et al. 2008







What are the future developments of vaccine delivery – e.g. slow release pellets – and when will they become available?

Because of the need to inoculate animals twice during the first year, and the difficulty of doing this with wild animals, research is proceeding toward a 'one-inoculation' vaccine. Such a vaccine formulation would permit a single treatment to prolong the production of antibodies and thus extend the contraceptive period. The approach under study incorporates the PZP into a nontoxic, biodegradable material, which can be formed into small pellets that result in several years of contraception after a single application. The pellets can be designed to release the vaccine at predetermined times after injection

(at one and three months, currently); much the same way time-release cold pills work. Initial trials in wild horses were encouraging.

In addition to the pellets, there are several other forms being tested. Within the next two years, results for a recombinant booster form of the vaccine and a gel delivery system will be demonstrated. Once mastered, the technology's efficacy will be tested in African elephants. Currently, there are no such pellets available for use in elephants.

See Turner et al. 2002, Turner et al. 2008

Q Isn't darting cows painful and potentially harmful?

As long as the recommended darts are used by experienced administrators, there is almost no risk of injury to the animal. These are very small, light darts. Over a 22-year period during which the recommended darts have been used on wild horses in the U.S, no horse has ever been injured on Assateague Island, the Shackleford

Banks, Carrot Island, the Pryor Mountains, or the Little Book Cliffs (translating to well over 1,000 dartings, over the course of 20 years). Similarly, no elephant has ever been injured within the treated populations in South Africa, spanning a 10+ year period and approximately 1,300 dartings.

See Delsink et al. 2002, Kirkpatrick 2010; 2012, Bertschinger et al, in prep

Q Will PZP harm adult and sub-adult cows physiologically? Have any negative pharmacological side effects been observed?

A The field studies on elephants are conducted by dedicated elephant monitors, managers or the HSI immunocontraception research team. In over 200 PZP-treated female African elephants and over 1,300 dartings, few side effects from vaccine administration were observed. The only minor side effect observed has been the development of swellings in 1-5% of cows after treatment. These swellings, presumed to be the result of

mechanical transfer of skin bacteria to the underlying tissues, resolve spontaneously and have never been accompanied by lameness. Ultimately these nodules are very difficult to discern amongst other natural scars within the skins of elephant cows (with appearance similar to swellings caused by thorn penetration). Furthermore, there is no indication that the presence of these nodules has compromised the quality of life for elephants.

See Bengis 1993, Delsink et al. 2002, Delsink 2006, Delsink et al. 2006, Delsink et al. 2007, Bertschinger 2010

Ovarian activity of free-ranging, PZP-treated African elephant females was monitored non-invasively for 1 year at Thornybush Private Game Reserve, by measuring faecal 5 -pregnan-3 -ol-20-on (5P3) concentrations via enzyme immunoassay. Faecal samples together with simultaneous behavioural observations were made to record the occurrence of oestrous behaviour for comparison. The study demonstrated that within the sampled females, 42.9% exhibited oestrous cycles within the range reported for captive African elephants, 14.3% had irregular cycles, and 42.9% did not appear to be cycling. The average oestrous cycle duration was 14.72 ± 0.85 weeks, in line with ranges documented in the literature.

Oestrous behaviour coincided with the onset of the luteal phase and a subsequent rise in 5P3 concentrations. Average 5P3 levels positively correlated with rainfall. No association between average individual 5P3 concentrations or cyclicity status with age or parity were detected. Thus, the PZP treatment did not affect ovarian activity amongst PZP-treated female African elephants in 2 years after initial immunization.

The study concluded that the absence of an indefinite period of anoestrus within the study population is encouraging as it demonstrates that PZP treatment is not likely to interfere with follicular development and ovulation in the African elephant.

See Ahlers et al. 2012



Q For how many years is a cow generally treated with PZP?

A well-defined contraceptive management plan must be formulated for the specific population and its objectives. It is not the team's practice to treat a female indefinitely.

Q How do you determine which cows within a herd will be treated?

This is once again dependent on the management objectives and level of intervention that is required. A clearly defined elephant management plan with a longterm immunocontraception plan in line with management objectives is essential. As an example, cows at the Greater Makalali Private Game Reserve are treated after the birth of their first calves.





Audrey Delsink

How effective is PZP? Won't some cows still become pregnant after treatment?

PZP treatment in wild horses is about 95% effective. The failure of some horses to respond to the vaccine results from an immune system that either does not 'recognize' the vaccine's antigen or that is compromised. This is true for human vaccines as well (e.g. consider the less than 100% efficacy of influenza vaccines).

To date, the Greater Makalali Private Game Reserve, the longest running program in African elephants, has recorded close to 100% efficacy (with one reversal due to a faulty dart). This is supported by additional results at six other reserves.

This level of efficacy (e.g. 95%) is more than enough to manage wild horse and elephant populations effectively. In other species, efficacy varies in a species-specific manner.

See Turner and Kirkpatrick 2002, Frank et al. 2005, Turner et al. 2008, Bertschinger 2010, Kirkpatrick 2010; 2012, Bertschinger et al. in prep

Q Howlong does it take for PZP to stop or reduce population growth in a herd?

This depends on the percentage of breeding cows treated. If all breeding cows are treated in the first year, population growth is zero by the third year (as cows will be in various gestational stages and the vaccine does not affect pregnancies in progress). Therefore, full reproductive control depends mostly on the percentage of breeding cows treated. However, fertility rates, inter-

calving rates and mortality rates affect the outcome as well. Immunocontraceptive models have demonstrated that contraception of 75% of breeding-age females with an annual mortality rate of 2-3% is sufficient to achieve an annual population growth of 0%. However, it is emphasized that results are site-specific and cannot be generalized.

See Mackey et al. 2006, Druce et al. 2011, Bertschinger et al. in prep

Q How long does it take for PZP to begin reducing a wild elephant population?

A Populations can only be reduced when mortality rates are equal to or exceed growth rates, or growth rates are maintained at 0% for indefinite periods. A 0% growth rate is not encouraged due to the complex social nature of elephant societies. Instead, it is recommended that managers pursue a reduction in growth rates or a lengthening of inter-calving intervals to mimic natural events

such as drought or predation. Within the Makalali population, the contraceptive effect (excluding mortalities, introductions and relocations) by 2010 (Figure 5) was a 60% reduction in overall population growth rate; with vaccinations administered to young cows only after parturition of their first calves.

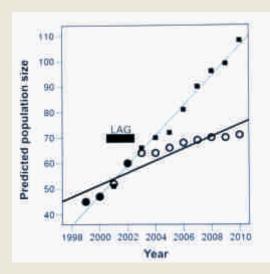


FIGURE 5 The effect of immunocontraception on population size at the Makalali Conservancy from Delsink *et al.* (2006).

Open circles and thick line indicates the projected population size with contraception; the closed squares and thin line represent the projected population without contraception. The black bar above the curves indicates the lag effect before contraception as a result of elephants already pregnant prior to darting.

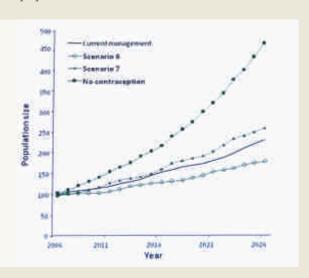
Population models on the elephants at the Munyawana Conservancy (previously Phinda Private Game Reserve) (Figure 6) by Druce *et al.* (2011) predict that with contraceptive treatment alone, the population doubling time was projected to increase to 20 years or longer when the calving interval was lengthened to longer than 6 years and production of the first calf was delayed. Overall, the Munyawana model indicates that changes in calving interval produced relatively large changes in population growth rate, resulting in a 30% reduction in annual growth rate (calculated over 20 years) from 5.06% to 3.48%.

Furthermore, changing the implementation age of contraception from ten to eight years (thereby delaying the first calves), produced an additional reduction of 25% in annual growth rate. Generally, the model projections were not particularly sensitive to age at sexual maturity and the length of conception time after release from contraception.

The most important factor to note is that individual population parameters will play a significant role, particularly in many of South Africa's relocated populations where stable age and sex structures do not occur.

See Delsink et al. 2006, Mackey et al. 2006, Druce et al. 2011, Bertschinger et al. in prep

FIGURE 6 Projected population size for the Munyawana elephant population under different immunocontraception scenarios for a 20-year time period from Druce *et al.* (2011). Results are shown for the current Munyawana immunocontraception plan, no application of immunocontraception on the population, and two contraception scenarios (Scenarios 6 and 7) that resulted in the most extreme projections. Scenario 6 was the prevention of the first calf and allowing the female to calf at 19 years of age, with a baseline contraception-induced calving interval of 8 years thereafter. Scenario 7 examined a shortened calving interval of 6 years.



Q If you treat a pregnant cow, are there any side-effects?

The PZP vaccine is safe to pregnant cows irrespective of the stage of pregnancy during vaccination.

See Fayrer-Hosken et al. 2000, Delsink et al. 2006, Delsink et al. 2007, Bertschinger 2010, Bertschinger et al. in prep

Q Are there PZP drug residues in urine or faeces or in the dead carcasses of treated cows, where PZP could get into the food chain or cause adverse effects to wildlife, or even contaminate water?

Because PZP is primarily protein, it is digested in the gut to form individual amino acids and carbohydrate molecules. No PZP biological activity remains in the

faeces. PZP is target-specific, safe for other wildlife and does not contaminate water or the environment.

See Oser 1965

Q Is the vaccine reversible?

Studies in both wild horses and African elephants demonstrate that the vaccine is reversible. In elephants, studies demonstrated reversibility after two successive years of treatment. On-going reversibility studies are being conducted at the Greater Makalali Private Game Reserve with promising results to date.

See Kirkpatrick and Turner 1991, Fayrer-Hosken et al. 2000, Turner et al. 2002, Kirkpatrick and Frank 2005

What herds do you propose to treat with immunocontraceptives in the near future? Why did you choose these particular herds? Who decides? What are your long-term goals?

To date, the current populations treated with PZP are small to medium-sized (less than 500km², with the largest treated population of approximately 600 elephants) and are privately owned (barring one provincial reserve). The HSI immunocontraceptive research team and key personnel from Ezemvelo KwaZulu-Natal Wildlife are working together to treat a number of additional large provincial populations in South Africa's KwaZulu-Natal Province. The HSI immunocontraceptive research team has demonstrated the success of the PZP vaccine in small to medium-sized populations and reserves (>500 km²) and our objectives include the targeting of larger populations and reserves. With the success demonstrated thus far, the challenge of large populations and reserves is simply a matter of scaling up the efforts and resources. The HSI immunocontraceptive research team will continue to consult with and assist any interested parties in setting up and maintaining a sitespecific immunocontraceptive program.

Q If future reserves opt to treat their populations with PZP, what are the regulatory issues concerning the vaccine protocol and data collection?

In South Africa, the vaccine is still regarded as experimental for research purposes under Prof. Henk Bertschinger of University of Pretoria (Project Protocol Number V049/11: Immunocontraception of Free-Ranging African Elephant [Loxodonta africana] Cows on Game Reserves in South Africa) and is subject to permission from Section 21 of Medicine and Related Substances Control Act (Act No. 101 of 1965) or the Fertilizers, Farm and Feeds, Agricultural Remedies and

Stock Remedies Act (Act No. 36 of 1947). Thus, future reserves must comply with the stipulations of this project protocol, one of which is that certain population data parameters must be submitted to Prof. Bertschinger for on-going data analysis. Upon the reserve's successful application, detailed information regarding the vaccine and data collection protocol will be forwarded to the relevant reserve representative.

(See also Page 7: How is the PZP vaccine obtained?)

BEHAVIOURAL EFFECTS of PZP

Q Is wild elephant behaviour affected by PZP use? Is herd social stability affected negatively? Has any aberrational behaviour been seen in PZP-treated cows, dominant and young adult bulls, or herds where cows have been treated with an immunocontraceptive? What behavioural studies have been conducted on PZP-treated wild elephants?

A The immunocontraceptive trials conducted in the KNP and at Makalali represent a combined 16-year study on the short to medium-term effects on the behaviour and social structure of experimental animals and their herds. To date, these trials have not demonstrated any aberrant or unusual behaviour within the medium-term and during sustained use of PZP on the experimental herds. There is also no evidence to suggest that the PZP vaccine has any adverse effects on the behaviour of matriarchal groups or bulls with important reproductive behaviours such as mate selection and bull dominance. PZP is the only known contraceptive, vaccine-based or otherwise, that does not interfere with the normal cascade of endocrine events associated with reproduction.

Furthermore, the reduced number of calves and lactating females has not significantly altered the herd's ranging behaviour during the course of the Makalali study. Herd fission/fusion has also remained unaltered with herd stability remaining stable. Studies at Munyawana Conservancy (formerly Phinda Private Game Reserve) and Thornybush Private Game Reserve corroborate these findings. In the KNP trials, the behaviour of the PZPtreated cows was similar to untreated animals. The hormonal contraception trials, which made use of oestradiol implants and were conducted by another research group in the KNP, resulted in severe behavioural anomalies within the treated animals. As a result, the trials were immediately suspended and the implants were removed where possible. The cows were rendered permanently infertile. As a result, one of the objectives of the Makalali study is to conduct a detailed behavioural study to ensure the safety of the elephants treated with the PZP vaccine.

The Makalali study is the longest running same population study of elephant immunocontraception globally.

To address long term use of the vaccine and the elephant's longevity, HSI intends to continue to support the program for a further 10 years. The Makalali population will be closely monitored throughout.

Extensive behavioural studies have been conducted on other long-lived species e.g. wild horses, treated with PZP for prolonged periods. What few behavioural changes have been noted in other species (primarily wild horses) are associated with much improved welfare of individual animals following the 'side effects' of successful contraception such as the absence of offspring, better body condition (as the stresses of pregnancy and lactation are removed) and greater longevity.

See Bartlett 1997, Butler 1998, Goritz et al. 1999, Whyte 2001, Whyte et al. 2003, Stout and Colenbrander 2004, Perdock et al. 2007, and Turner and Kirckpatrick 1982, Fayrer-Hosken et al. 2000, Whyte 2001, Delsink et al. 2002, Turner and Kirckpatrick 2002, Turner et al. 2002, Delsink 2006, Delsink et al. 2006, Bertschinger et al. 2008, Druce et al. 2011, Kirkpatrick et al. 2011, Ahlers et al. 2012, Delskink et al. in preparation.



Katie Steve

Q Are any additional behavioural studies planned?

A The HSI immunocontraceptive research team have submitted proposals for additional funding for an innovative and ground-breaking behavioural study that will use technologically advanced proximity collars to gather data

remotely to test reproductive behaviours, and herd/bull associations within the Greater Makalali Private Game Reserve and a sister control herd.

Q Won't cows just keep coming back into oestrus (heat) if they don't get pregnant? Won't prolonged oestrus cycling make elephant bulls 'edgy' and aggressive, creating continuous disturbances?

Under PZP treatment, the frequency of oestrus increases because females are not conceiving. This may cause the cows to receive more attention from musth bulls. However, in the Makalali study, bull dominance and rank remains unchanged and association with cows has actually decreased over time.

See Poole and Moss 1981, Moss and Poole 1983, Whyte 2001, Delskink et al. 2002, Delsink 2006, Bertschinger et al. 2008, Ahlers et al. 2012, Delskink et al. in preparation.

Q Isn't the use of PZP 'against nature'? Why can't you just leave these animals alone?

Elephants have been defined as a keystone species capable of causing major system changes. With natural processes such as migration rarely a possibility due to enclosed (fenced-in) populations, low mortality rates, and many populations displaying high irruptive (density independent) growth rates, elephant populations do need to be managed. Usually, the issue is not whether some management might be necessary, but what form the management should take.

Immunocontraception has been demonstrated as a safe, reliable, effective, target-specific and humane method of elephant population control. Furthermore, immunocontraception mimics natural episodic catastrophic processes such as drought because the treatment lengthens the treated cow's inter-calving intervals i.e. the birth interval between calves. In wild, free-roaming elephant populations, inter-calving intervals as long as thirteen years have been observed as a result of drought.

Alternative management strategies for elephant include translocation and culling. Translocation opportunities are

limited. There are few areas suitable for new elephants and suitable wildlife areas are decreasing in number and size due to burgeoning human population growth.

Culling is widely challenged. Questions remain as to the long-term effects of culling on surviving family members. Furthermore, culling (i.e. a decrease of population density) increases the rate of reproduction which is density dependent. Irrespective, all management methods require human intervention and are thus also 'against nature'.

In summary, any rational debate on the merits or possible effects of immunocontraceptive management of elephants must also consider the impacts of all alternative management approaches and apply the same concern and scrutiny to these alternative approaches – including the 'laissez-faire' or 'no management' approach. With regards to elephant management, there are a limited number of options and the least intrusive and most humane is the logical choice.

See Laws 1970, Owen-Smith 1988, Jones et al. 1994, Kirkpatrick and Frank 2005, Wright and Jones 2006, Kirkpatrick 2007, Grobler et al. 2008, Slotow et al. 2008, Druce et al. 2011



If elephant numbers in Africa have declined to such a degree and poaching is rampant in some African elephant range states, won't using PZP bring wild elephants to extinction?

Traditional elephant population control methods such as culling are permanent. In contrast, immunocontraception is reversible. Therefore, in the event of a crisis (such as drastically reduced populations due to poaching), the administration of the vaccine in treated populations could be stopped or reduced allowing the population to recover.

FEEDBACK from the FIELD



The Greater Makalali Private Game Reserve Immunocontraception initiated in 2000

Ross Kettles, MEnDev : Protected Area Management Warden - The Greater Makalali Private Game Reserve (1994-2012)



The Greater Makalali Private Game Reserve (GMPGR) originally reintroduced 4 breeding herds of elephants between May 1994 and June 1996. By May 2000, our population had grown from 37 to 47, with many pubescent heifers in the herd. It was at this stage that we decided to implement a pro-active rather than re-active intervention strategy to manage our elephant population.

At the time, after researching the various, and more traditional population control intervention options available to wildlife practitioners (culling, relocation and hunting), we decided to initiate PZP immunocontraception to selected elephant cows on the GMPGR, following the recent (at the time) successful field trials conducted in the Kruger National Park.

The program has been a resounding success. Not only has immunocontraception proven to be the least invasive and most humane population control mechanism available to us, it proved to very effective in curbing population growth. By October 2011, our elephant population num-

bered 78, but this included 8 adult bulls which broke into the reserve, as well as calves of numerous 'planned births'. Due to the complex social structure of elephant societies, and the important role calves play in this society, it was never our objective to stop population growth, but rather to slow the recruitment rate down to a manageable targeted 1-3% (from the average 9% prior to the program's inception).

Conservative calculations have indicated that had we not initiated contraception to the GMPGR herds, our population would currently number more than 120 animals, which would have caused a management dilemma, as medium- to long-term damage to the habitat would have been a given, and hard decisions called for relating to elephant removal.

To summarise, we firmly believe that PZP immunocontraception is an effective, affordable and humane elephant population control tool, providing wildlife practitioners understand that it is a pre-emptive measure.



Phinda Private Game Reserve Immunocontraception initiated in 2004

Jaco Mattheus : Asst. Reserve Manager - Phinda Private Game Reserve (2003-2006) Warden - Munyawana Conservancy (2006-2010)

Managing elephant and their impact on Phinda has always been a challenge. There are numerous highly sensitive vegetation types on the reserve that have been affected over the years by the unmanaged and growing elephant population on the reserve. The obvious solution was to reduce the number of elephant on Phinda – easier said than done!

Although we did manage to reduce the population by between 40 - 50 animals over the years through various relocation projects, the fact remains that elephants breed, and that there are fewer and fewer new reserves established that can actually accommodate elephant.

The solution to this was to initiate a PZP immunocontraceptive program, concurrent with the relocation exercises, to curb the growth rate. In the long run this would (and did!) buy the management team some time to look for opportunities to relocate elephant to other suitable reserves. It has also kept the population numbers at a level where we were able to manage and mitigate some of the impacts they had on the more sensitive areas where the effects on vegetation were prominent, such as the rare dry sand forest in the north of the reserve. Several other management options such as exclusion areas and closure of waterholes were also deployed in a holistic manner to tackle this problem. If the numbers had increased with the established growth rate, the pressure on this area would have been hard to deflect, and the damage to this forest would have been irreparable.

Doing the vaccinations from the ground initially was time consuming - we then explored the opportunity to implement aerial vaccinations when the elephant congregated in more accessible areas of the reserve, as it happens at the beginning of the wet season.

Darting from the helicopter significantly reduced the time needed to vaccinate the required animals, as well as the perceived stress on the animals. It literally only takes

an hour or two now!

Utilising immunocontraception as a management tool definitely made my job of managing this species a lot easier, and in the greater context - the integrity of the reserve has been conserved by mitigating elephant impact. I believe the challenge now lies in practical implementation of this method on bigger populations.







Elephants vaccinated from the air



JJ van Altena drawing up PZP vaccine



Welgevonden Private Game Reserve Immunocontraception initiated in 2005

Andrew Parker, MSc: Ecology

CEO - Welgevonden Landowners Association (May 2005 to March 2010)

In 1994, 50 elephants were relocated from the Kruger National Park and introduced into the newly established Welgevonden Private Game Reserve in the Waterberg region of the Limpopo Province. By 2005, this population had grown to 100 individuals.

With a hind-gut digestive system, elephants can compensate for lack of quality by consuming greater quantities of food. However, elephants are also selective feeders and will actively seek out their preferred forage. In the nutrient-limited, broad-leafed savanna environment of the Waterberg, the adaptability of the elephant population's diet enabled the population to grow but their selective feeding behaviour was having negative consequences for certain of their preferred forage species and the less adaptable ruminants that were dependent upon these.

In comparatively small, confined reserves such as Welgevonden, the cumulative impact of an ever-growing elephant population on vegetation composition and structure represents a considerable risk to biodiversity. Consequently, in 2005, Welgevonden adopted an active

elephant management program with the following objectives:

- 1. Control the number and growth rate of the elephant population
- 2. Maintain a demographically viable population
- 3. Prevent negative consequences for biodiversity resulting from cumulative elephant impact
- 4. Maintain a functioning ecosystem
- 5. Contribute to an understanding of biology and management of elephants
- 6. Contribute to the conservation of elephants

Culling as a mechanism to control population growth rate is a highly controversial management practice and is considered acceptable only as a last resort after all other options have been exhausted. Opportunities for translocation were explored but with demand for free-roaming elephants being extremely limited, this was not viewed as a viable mechanism to control population growth on an on-going basis.

Trials at other reserves had shown that PZP immuno-contraception was not only highly effective but also safe and reversible. Therefore, in September 2005, Welgevon-den management teamed up with Audrey Delsink, JJ van Altena and Prof. Henk Bertschinger to initiate an immunocontraception programme on Welgevonden as a mechanism to control the growth rate of the elephant population.

Taking existing pregnancies into account (which are not affected by the vaccine), stabilisation of the population occurs after three years. At the time of implementation in 2005, Welgevonden's population was the largest in the world to be subjected to the PZP immunocontraception programme, with the vaccine being applied to a total of 43 adult cows. By Sep. 2007, the population had stabilised at 121 animals at a total cost of less than R145, 000.00.

The vaccination protocol entails a primary vaccination followed by two boosters at 3 - 4 week intervals during the first year and a single annual booster thereafter. Application is simply applied using drop-out darts delivered from a helicopter and by the second year, all breeding cows on Welgevonden were successfully darted in a single day.

Shortly after implementation of the immunocontraceptive programme, David Powrie was appointed on a full-time basis to monitor and record the elephant population dynamics, especially social interactions between bulls and cows. Spending all day on foot with his beloved pachyderms, David became intimately acquainted with the population and came to understand the traits and characteristics of each individual. Shortly after David's appointment, one cow in each herd was collared to enable the herds to be more readily located in the mountainous Waterberg terrain.

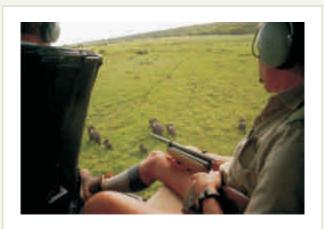
In 2009, a strategic decision was taken to allow one cow in each herd to breed for the purposes of maintaining social cohesion within the herds. To enable this, it simply meant that these cows were not vaccinated that year. In 2011, the

have produced 17 calves in approximately 12 years since

elephant population on Welgevonden welcomed the arrival of several new calves.

The programme has been a resounding success and has provided management with a very effective and efficient means to control the elephant population growth rate. No changes in social behaviour were detected during the monitoring phase and importantly, none of the social problems associated with hormonal contraception were observed. The safety, affordability and efficacy of PZP immunocontraception make it a prudent option, especially for small, confined populations.

Given the ecological requirements for flux within an ecosystem, an elephant population should not be allowed to remain at a constant level over an extended period of time. The challenge is to identify upper and lower limits of acceptable change and manage the population within these limits. The need to reduce numbers from time to time infers that relocation and/or culling of elephants in confined reserves may continue to be necessary, but contraception will enable management to better control the frequency and extent of such interventions.



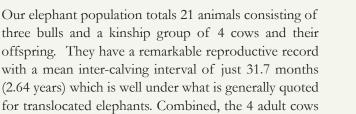
Dr. Dave Cooper during Tembe Elephant Park's aerial vaccinations





Karongwe Game Reserve
Immunocontraception initiated in 2007

Kobus Havemann, BTech: Nature Conservation Warden - Karongwe Game Reserve (2009-2012)



introduction to Karongwe. Prof. Bertschinger suggests that such a reproductive performance probably reflects the low density of elephants and the abundant availability of good nutrition. Since we started our contraception programme, three cows have already passed their previous inter-calving intervals.



Tembe Elephant Park

Immunocontraception initiated in 2007

Nick De Goede, NDip: Nature Conservation & Wayne Matthews, Ph.D: Ecology

Nick De Goede: Conservation Manager Tembe Elephant Park (2007-2009); SANParks Park Manager - /Ai/Ais-Richtersveld Transfrontier Park (2012)

Wayne Matthews: Ezemvelo KwaZulu-Natal Wildlife (EKZNW) Regional Ecologist for Northern Maputaland (1993-2011); Technical Advisor to Space For Elephants (2012)

As management of Tembe Elephant Park, we faced quite a unique environment as well as an overall challenge in direction of reserves based on vision; in this to balance the 3 main biodiversity objectives: sand forest preservation (highest priority); followed by suni and then elephant protection of one of the 4 original elephant populations in SA. This was compounded by a general drive to expand the reserve which was driven by economics and ecotourism.

The current elephant population levels are having an impact on the sand forest directly and indirectly (opening the sand forest up for other species like nyala to enter and having an impact on the vegetation and regrowth) thus first and second priority biodiversity objectives are been negatively affected. But elephant are also a high level biodiversity/conservation objective as well as a key roleplayer in the economics and ecotourism of the reserve and region. Thus a way forward that takes into consideration all these intricacies / currently inharmonious main objectives as per the management plan. Tembe management team had to come up with multi-faceted and innovative, short- and long-term solutions, one of which was immunocontraception of elephants.

We were in the process of establishing the TFCA between SA and Mozambique. We wanted to reinstitute, in some way, old movement and utilisations patterns along the Futi and Rio Maputo nutrient rich areas, which would go a long way in alleviating the pressures on the sensitive and rare sand forest habitats within Tembe. The problem is that this would not happen overnight and we had to do something immediately due to pressure being experienced on the sensitive habitats within Tembe.

Consequently, three actions were initiated:

Firstly, a statistically based contraception model of the reproductive female elephant population at a projected 75% intervention level was initiated. Secondly, to protect biodiversity, enclosure fences around the most pristine sand forest patches were erected. Thirdly, densitydependant culling on the nyala and impala population was implemented, addressing secondary herbivore impacts

on recruitment (in test phase around water points with known past high densities of suni).

Immunocontraception:

The immunocontraception process was funded through donations and special projects after discussions with Prof. Rob Slotow and EKZNW. Through our long-term detailed monitoring of the elephant population, detailed data of the family (breeding) groups in the park existed. As a result of the long-term aerial surveys, we also knew that the breeding groups congregated all along the swamp (Futi) during hot mid-days. All of this was taken into consideration in the planning process. We also knew that vaccinations might need to be conducted over a few days. Thus, the elephants needed to be marked to prevent multiple dartings. During the operation, it was of importance to record the exact numbers, sex and structure of the group so as to ensure future vaccinations and prevent duplicate vaccinations.

Conclusion:

The immunocontraception was a very successful program run on the largest free-roaming wild population. After four years, preliminary results are very positive. During the vaccine administration, we learnt some valuable lessons : pink dye was far more visible than purple dye; a B3/squirrel helicopter was ideal because of its power, size and space given the difficult conditions due to Tembe's dense vegetation. The experience of the darting crew was invaluable as vaccinations were administered quickly with very little disturbance to the elephant and with very good results.

In conclusion, immunocontraception is a very good management tool, especially for the Tembe population as the contraception level can be revised pending dropping of fences in the establishment of the TFCA or any other land expansion opportunities.

We thank Trish Parsons of Parson's Aviation for the support for the helicopter and pilot, and HSI for support for the vaccine, darts and part helicopter for Tembe Elephant Park's immunocontraception programme in 2011.









LITERATURE CITED

Ahlers, M., B. Ganswindt, S. Münschera, and H. Bertschinger. 2012. Faecal 20-oxo-pregnane concentrations in free-ranging African elephants (*Loxodonta africana*) treated with porcine zona pellucida vaccine. Theriogenology 78:77–85.

Barber, M. and R. Fayrer-Hosken. 2000. Possible mechanisms of mammalian immunocontraception. Journal of Reproductive Immunology 46:103-124.

Bartlett, E. 1997. Jumbo birth control drives bull elephants wild. Page 5. In New Scientist.

Bengis, R. 1993. Care of the African elephant *Loxodonta africana* in Captivity. *In* A. McKenzie, editor. The Capture and Care Manual. Wildlife Decision Support Services and The South African Veterinary Association, Pretoria.

Bertschinger, H. 2010. Controlling wildlife reproduction. PhD, Utrecht University, The Netherlands.

Bertschinger, H., A. Delsink, J. Kirkpatrick, M. Bates, T. Dickerson, and D. Powrie. In prep. Immunocontrol of reproductive rate of African elephant cows using porcine zona pellucida vaccine on seven private game reserves in South Africa.

Bertschinger, H., A. Delsink, JJ. van Altena, J. Kirkpatrick, H. Killian, A. Ganswindt, and R. Slotow. 2008. Reproductive control of elephants. Pages 257-328. *In* K. Mennell, and R. Scholes, editors. Elephant Management: A Scientific Assessment of South Africa. Wits University Press, Johannesburg.

Burke, T. 2005. The effect of human disturbance on elephant behaviour, movement dynamics and stress in a small reserve: Pilansberg National Park. MSc, University of KwaZulu-Natal, Durban.

Butler, B. 1998. Elephants: Trimming the herd. BioScience 48:76-81.

DEAT. 2007. National Environmental Management: Biodiversity Act, 2004 (ACT 10 OF 2004): Threatened or Protected Species Regulations. Government Gazette.

DEAT. 2008. National Norms and Standards for the Management of Elephants in South Africa. Government Gazette.

Deigert. F., A. Duncan, R. Lyda, K. Frank, and J. Kirkpatrick. 2003. Immunocontraception of captive exotic species. III. Fallow Deer (*Cervus dama*). Zoo Biology 22:261-268.

Delsink, A. 2006. The costs and consequences of immunocontraception implementation in African elephants at Makalali Conservancy, South Africa. MSc, University of KwaZulu-Natal, Durban.

Delsink, A., JJ. van Altena, J. Kirkpatrick, D. Grobler, and R. Fayrer-Hosken. 2002. Field applications of immuno-contraception in African elephants (*Loxodonta africana*). Reproduction Supplement 60:117-124.

Delsink, A., J. Kirkpatrick, JJ. van Altena, H. Bertschinger, S. Ferreira, and R. Slotow. In prep. Lack of spatial and behavioural responses to immunocontraception application in African elephants (*Loxodonta africana*).

Delsink, A., JJ. van Altena, D. Grobler, H. Bertschinger, J. Kirkpatrick, and R. Slotow. 2006. Regulation of a small, discrete African elephant population through immunocontraception in the Makalali Conservancy, Limpopo, South Africa. South African Journal of Science 102: 403-405.

Delsink, A., JJ. van Altena, D. Grobler, H. Bertschinger, J. Kirkpatrick, and R. Slotow. 2007. Implementing immunocontraception in African elephants at Makalali Conservancy. Journal of South African Veterinary Association 78:25-30.

Druce, H., R. Mackey, and R. Slotow. 2011. How immunocontraception can contribute to elephant management in small, enclosed reserves: Munyawana Population as a case study. PLoS ONE 6. e27952. doi:10.1371/journal.pone.0027952

Eldridge, J., R. Gilly, J. Stass, Z. Moldozeanu, J. Muelbroek, and T. Tice. 1989. Biodegradable microcapsules: Vaccine delivery systems for oral immunization. Current Topics in Microbiology and Immunology 146:59-66.

Fayrer-Hosken, R., H. Bertschinger, J. Kirkpatrick, D. Grobler, N. Lamberski, G. Honneyman, and T. Ulrich. 1999. Contraceptive potential of the porcine zona pellucida vaccine in the African elephant (*Loxodonta africana*). Theriogenology 52:835-846.

Fayrer-Hosken, R., P. Brooks, H. Bertschinger, J. Kirkpatrick, J. Turner, and I. Liu. 1997. Management of African elephant populations by immunocontraception. Wild. Soc. Bull. 25:18-21.

Fayrer-Hosken, R., D. Grobler, JJ. van Altena, H. Bertschinger, and J. Kirkpatrick. 2000. Immunocontraception of African elephants. Nature 407:149.

Fayrer-Hosken, R., D. Grobler, JJ. van Altena, H. Bertschinger, and J. Kirkpatrick. 2001. Population control: African elephants and contraception. Nature 411:766.

Frank, K., R. Lyda, and J. Kirkpatrick. 2005. Immunocontraception of captive exotic species. IV. Species differences in response to the porcine zona pellucida vaccine and the timing of booster inoculations. Zoo Biology 24:349-358.

Goritz, F., T. Hildebrandt, R. Hermes, S. Quandt, D. Grobler, K. Jewgenow, M. Rohleder, H. Meyer, and H. Hof. 1999. Results of hormonal contraception program in free-ranging African elephants. *In* Proceedings: Internationalen symposiums uber die erkrankungen der zoo- und wildtiere. Verhandlungsbericht des 39. Institut für Zoo- und Wildtierforschung, Berlin.

Grobler, D., JJ. van Altena, J. Malan, and R. Mackey. 2008. Elephant Translocation. Pages 241-256. *In* K. Mennell, and R. Scholes, editors. Elephant Management: A Scientific Assessment of South Africa. Wits University Press, Johannesburg.

Jones, C., J. Lawton, and M. Shachak. 1994. Organisms as ecosystem engineers. OIKOS 69:373-386.

Kirkpatrick, J. 2007. Measuring the effects of wildlife contraception: the argument for comparing apples with oranges. Reproduction, Fertility and Development 19:548-552.

Kirkpatrick, J. 2010. Immunocontraceptive reproductive control utilizing Porcine Zona Pellucida (PZP) in federal wild horse populations. Third edition. *In* P. Fazio, editor. Science and Conservation Centre, Billings, Montana.

Kirkpatrick, J. 2012. Immunocontraceptive reproductive control utilizing Porcine Zona Pellucida (PZP) in Federal Wild Horse populations. Fourth edition. *In* P. Fazio, editor. Science and Conservation Centre, Billings, Montana.

Kirkpatrick, J. and K. Frank. 2005. Fertility control in free-ranging wildlife. Pages 17-25. *In C.* Asa, and I. Porton, editors. Wildlife Contraception: Issues, Methods and Applications. John Hopkins University Press, Baltimore.

Kirkpatrick, J., R. Lyda, and K. Frank. 2011. Contraceptive vaccines for wildlife; A review. Amer. J. Reprod. Immunol. 66:40-50.

Kirkpatrick, J., and J. Turner. 1985. Chemical fertility control and wildlife management. BioScience 35:485-491.

Kirkpatrick, J., and J. Turner. 1991. Reversible fertility control in non-domestic animals. J. Zoo Wildlife Medicine 22:392-408.

Kirkpatrick, J., and J. Turner. 1996. Fertility control in wildlife management: a review. *In* P. Cohn, E. Plotka, and U. Seal, editors. Contraception in Wildlife Blackwell Scientific Publications, North America.

Laws, R. 1970. Elephants as agents of habitat and landscape change in East Africa. OIKOS 21:1-15.

Liu, I., M. Bernoco, and M. Feldman. 1989. Contraception in mares heteroimmunized with pig zonae pellucidae. Journal of Reproduction and Fertility 85(1):19-29.

Mackey, R., B. Page, D. Duffy, and R. Slotow. 2006. Modelling elephant population growth in small, fenced, South African reserves. South African Journal of Wildlife Management 36:33-43.

McShea, W., S. Monfort, S. Hakim, J. Kirkpatrick, I. Liu, J. Turner, L. Chassy, and L. Munson. 1997. Immuno-contraceptive efficiency and the impact of contraception on the reproductive behavior of white-tailed deer. Journal of Wildlife Management 61:560-569.

Moss, C., and J. Poole. 1983. Relationships and social structure of African elephants. Pages 315-325. *In* R. Hinde, editor. Primate Social Relations: an Integrated Approach. Sinauer, New York.

Oser, B. 1965. Protein metabolism. McGraw-Hill, New York.

Owen-Smith, R. 1988. Megaherbivores: the influence of very large body size on ecology. Cambridge University Press, Cambridge.

Paterson, M., and R. Aitkin. 1990. Development of vaccines targeting the zona pellucida. Current Opinion in Immunology 2:743-747.

Perdock, A., W. de Boer, and T. Stout. 2007. Prospects for managing African elephant population growth by immunocontraception: A review. Pachyderm 42:92-107.

Poole, J., and C. Moss. 1981. Musth in the African elephant. Nature 292:830-831.

Rutberg, A. 1996. Humane wildlife population control: Immunocontraception. Pages 5-6. In Wildlife Tracks.

Rutberg, A., and R. Naugle. 2008. Population-level effects of immunocontraception in white-tailed deer (*Odocoileus virginianus*). Wildlife Research 35:494-501.

Slotow, R., I. Whyte, M. Hofmeyr, G. Kerley, T. Conway, and R. Scholes. 2008. Lethal management of elephant. Pages 370-405. *In* K. Mennell, and R. Scholes, editors. Elephant Management: A Scientific Assessment of South Africa. Wits University Press, Johannesburg.

Stout, T., and B. Colenbrander. Contraception as a tool for limiting elephant population growth: the possible pitfalls of various approaches. University of Utrecht, 2004.

Turner, J., and J. Kirkpatrick. 1982. Androgens, behaviour and fertility control in feral stallions. Journal of Reproduction and Fertility Supplement 32:79-87.

Turner, J., and J. Kirkpatrick. 2002. Effects of immunocontraception on population, longevity and body condition in wild mares (*Equus caballus*). Reproduction Supplement 60:187-195.

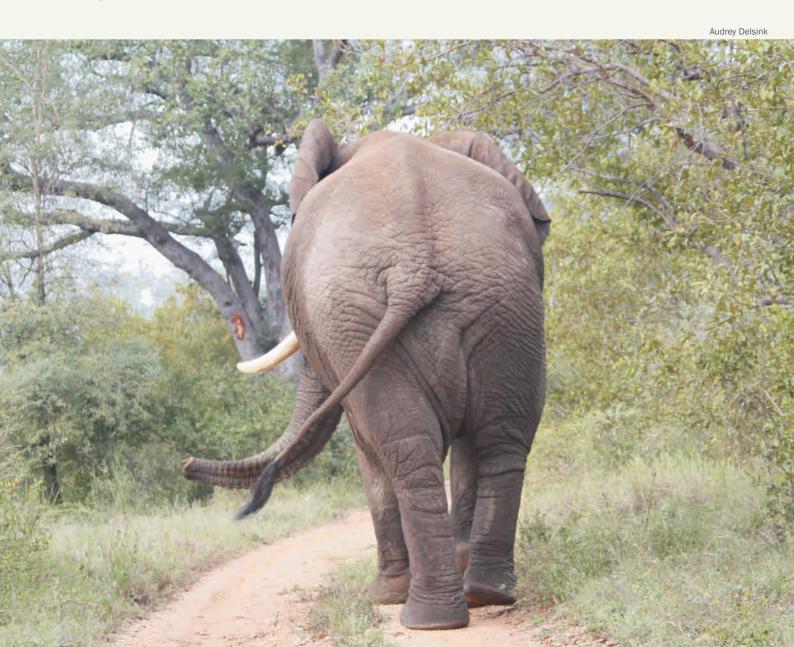
Turner, J., I. Liu, D. Flanagan, K. Bynum, and A. Rutberg. 2002. Porcine zona pellucida (PZP) immunocontraception of wild horses (*Equus caballus*) in Nevada: a 10 year study. Reproduction Supplement 60:177-186.

Turner, J., A. Rutberg, R. Naugle, M. Kaur, D. Flanagan, H. Bertschinger, and I. Liu. 2008. Controlled release components of PZP contraceptive vaccine extend duration of infertility. Wildl. Res. 35:555-562.

Whyte, I. 2001. Conservation Management of the Kruger National Park Elephant Population. PhD, University of Pretoria, Pretoria.

Whyte, I., R. Van Aarde, and S. Pimm. 2003. Kruger's elephant population: Its size and consequences for ecosystem heterogeneity. Pages 332-348. *In* J. du Toit, K. Rogers, and H. Biggs, editors. The Kruger experience: Ecology and management of savanna heterogeneity. Island Press, Washington.

Wright, J., and C. Jones. 2006. The concept of organisms as ecosystem engineers ten years on: progress, limitations, and challenges. BioScience 56:203-209.





Claudia Schnell

APPENDIX 1

ELEPHANT IMMUNOCONTRACEPTION BIBLIOGRAPHY

(in reverse chronological order)

Bertschinger, H., A. Delsink, J. Kirkpatrick, M. Bates, T. Dickerson, and D. Powrie. Immunocontrol of reproductive rate of African elephant cows using porcine zona pellucida vaccine on seven private game reserves in South Africa. In preparation.

Delsink, AK., J. Kirkpatrick, JJ. van Altena, H. Bertschinger, S. Ferreira, and R. Slotow. Lack of social and behavioural responses to immunocontraception application in African elephants. In preparation.

Kirkpatrick, JF., Delsink, AK., van Altena, JJ., and HJ Bertschinger. 2012. Fertility Control and African Elephants: A New Paradigm for Management. *In*: Elephants: Ecology, Behavior and Conservation (Eds: M. Aranovich and O. Dufresne). Nova Publishers, Inc., New York. pp 77-96

Druce, H., R. Mackey, and R. Slotow. 2011. How immunocontraception can contribute to elephant management in small, enclosed reserves: Munyawana Population as a case study. PLoS ONE 6: e27952. doi:10.1371/journal.pone.0027952

Bertschinger, HJ. 2011. Immunocontraception of free-ranging African elephant (*Loxodonta africana*) cows on game reserves in South Africa. University of Pretoria, Research Committee Protocol. Previous No 36.5.251.

Kirkpatrick, JF., RO Lyda, and KM Frank. 2011. Contraceptive vaccines for wildlife; A review. Amer. J. Reprod. Immunol. 66:40-50.

Bertschinger, H. 2010. Controlling wildlife reproduction. The Netherlands, Utrecht University. PhD.

Mackey, RL., BR. Page, D. Grobler and R. Slotow. 2009. Modeling the effectiveness of contraception for controlling introduced populations of elephant in South Africa. African Journal of Ecology 47:747-755. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2028.2009.01075.x/abstract

Fox, D. 2007. Wildlife Contraception. Conservation Magazine October-December 2007 (Vol. 8, No. 4) http://www.conservationmagazine.org/2008/07/wildlife-contraception/

Bertschinger, H., A. Delsink, JJ. van Altena, J. Kirkpatrick, H. Killian, A. Ganswindt, and R. Slotow. 2008. Reproductive control of elephants. pp 257-328. In K. Mennell, and R. Scholes, editors. Elephant Management: A Scientific Assessment of South Africa. Wits University Press, Johannesburg. http://www.elephantassessment.co.za/files/08_ch6_Elephant%20Management.pdf

Kirkpatrick, JF. 2007. Measuring the effects of wildlife contraception: an argument for comparing apples with oranges. Reprod. Fert. Dev. 19:548-552.

Colenbrander, B., HJ. Bertschinger, and T. A. E. Stout. 2007. Immunocontraception of Elephants Using Porcine Zona Pellucida Vaccination. EU-Asia Link Project Symposium "Managing the Health and Reproduction of Elephant Populations in Asia." 8-10 October 2007. Faculty of Veterinary Medicine, Kasetsart University, Bangkok, Thailand. pp 117-119. http://asianelephantresearch.com/file/25%20117-%20119%20Ben.pdf

Delsink, AK., JJ. van Altena, D. Grobler, HJ. Bertschinger, JF. Kirkpatrick, and R. Slotow. 2007. Implementing immunocontraception in free-ranging African elephants at Makalali Conservancy. Journal of the South African Veterinary Association 78(1): 25–30.

https://repository.up.ac.za/upspace/bitstream/2263/5142/1/Delsink_Implementing(2007).pdf

Perdock, A., W. de Boer, and T. Stout. 2007. Prospects for managing African elephant population growth by immunocontraception: a review. Pachyderm 42:92-107.

Delsink, AK., JJ. van Altena, D. Grobler, HJ. Bertschinger, JF. Kirkpatrick, and R. Slotow. 2006. Regulation of a small, discrete African elephant population through immunocontraception in the Makalali Conservancy, Limpopo, South Africa. South African Journal of Science 102:403-405. http://cat.inist.fr/?aModele=afficheN&cpsidt=18681123

Bertschinger, HJ., Delsink, AK., Kirkpatrick, JF., Grobler, D., van Altena, JJ., et al. 2005. The use of PZP and GnRH vaccines for contraception and control of behaviour in African elephants. In: Rutberg AT, ed. The role of immunocontraception, Humane Society Press, Washington. pp 13–18.

Kirkpatrick, JF. 2005. Elephant contraception: looking beyond the pharmacology. In: Rutberg AT, ed. The role of immunocontraception, Humane Society Press, Washington. pp 43–44.

Delsink, A., Bertschinger, HJ., Kirkpatrick, JF., De Nys, H., Grobler, D., et al. 2005. Contraception of African elephant cows in two private conservancies using porcine zona pellucida vaccine, and the control of aggressive behaviour in elephant bulls with a GnRH vaccine. In: Rutberg AT, ed. The role of immunocontraception, Humane Society Press, Washington. pp 69–72.

Stout, TAE., and Colenbrander, B. 2005. Contraception as a tool for limiting elephant population growth; the possible pitfalls of various approaches. In: Rutberg AT, ed. The role of immunocontraception, Humane Society Press, Washington. pp 7–11.

Delsink, AK. et al. 2004. Population regulation of African elephants through immunocontraception. In: EMOA Proceedings of the Elephant Symposium. Pilanesberg National Park.

Delsink, AK., HJ. Bertschinger, JF. Kirkpatrick, D. Grobler, JJ. van Altena, and R. Slotow. 2004. The preliminary behavioural and population dynamic response of African elephants to immunocontraception. In: Proceedings of the 15th Symposium on Tropical Animal Health and Reproduction: Management of Elephant Reproduction. Faculty of Veterinary Medicine, University of Utrecht, the Netherlands.

Stout, T., and B. Colenbrander. 2004. Contraception as a tool for limiting elephant population growth: the possible pitfalls of various approaches. University of Utrecht.

Delsink, AK., HJ. Bertschinger, JF. Kirkpatrick, H. De Nys, D. Grobler, JJ. van Altena, and J. Turkstra. 2003. Contraception of African elephant cows in two private conservancies using porcine zona pellucida vaccine, and the control of aggressive behaviour in elephant bulls with a GnRH vaccine. *In*: Proceedings on the Control of Wild Elephant Populations. Faculty of Veterinary Medicine, University of Utrecht, the Netherlands.

Delsink, AK., JJ. van Altena, JF. Kirkpatrick, D. Grobler, and R. Fayrer-Hosken. 2002. Field applications of immunocontraception in African elephants (*Loxodonta africana*). Reproduction 60: 117-124 http://www.ncbi.nlm.nih.gov/pubmed/12220151

Delsink, AK. 2002. The Makalali Immunocontraception Program. *In*: The proceedings of the EMOA Workshop, Knysna. Vaalwater, Pta.

Fayrer-Hosken, RA., D. Grobler, JJ. van Altena, HJ. Bertschinger, and JF. Kirkpatrick. 2001. Contraception of African elephants. Nature 411:766.

http://www.env.duke.edu/people/faculty/pimm/publications/pimmreprints/165_Pimm_van_Aarde_Nature.pdf

Fayrer-Hosken, RA., D. Grobler, JJ. van Altena, HJ. Bertschinger, and JF. Kirkpatrick. 2000. Immuno-contraception of African elephants. Nature 407: 149.

 $http://www.tiem.utk.edu/{\sim}gavrila/PAPS/conflict_comment.pdf$

Fayrer-Hosken, RA., HJ. Bertschinger, JF. Kirkpatrick, D. Grobler, N. Lamberski, G. Honeymann, and T. Ulrich. 1999. Contraceptive potential of the porcine zona pellucida vaccine in the African elephant (*Loxodonta africana*). Theriogenology 52: 835-846.

http://www.theriojournal.com/article/S0093-691X(99)00176-4/abstract

Whyte, IJ. and Grobler, DG. 1998. Elephant contraception research in the Kruger National Park. Pachyderm 25: 45–52

Fayrer-Hosken, RA., HJ. Bertschinger, JF. Kirkpatrick, JW. Turner Jr., and IK. Liu. 1997. Management of African elephant populations by immunocontraception. Wildlife Society Bulletin 25: 18-21. http://www.jstor.org/stable/3783275

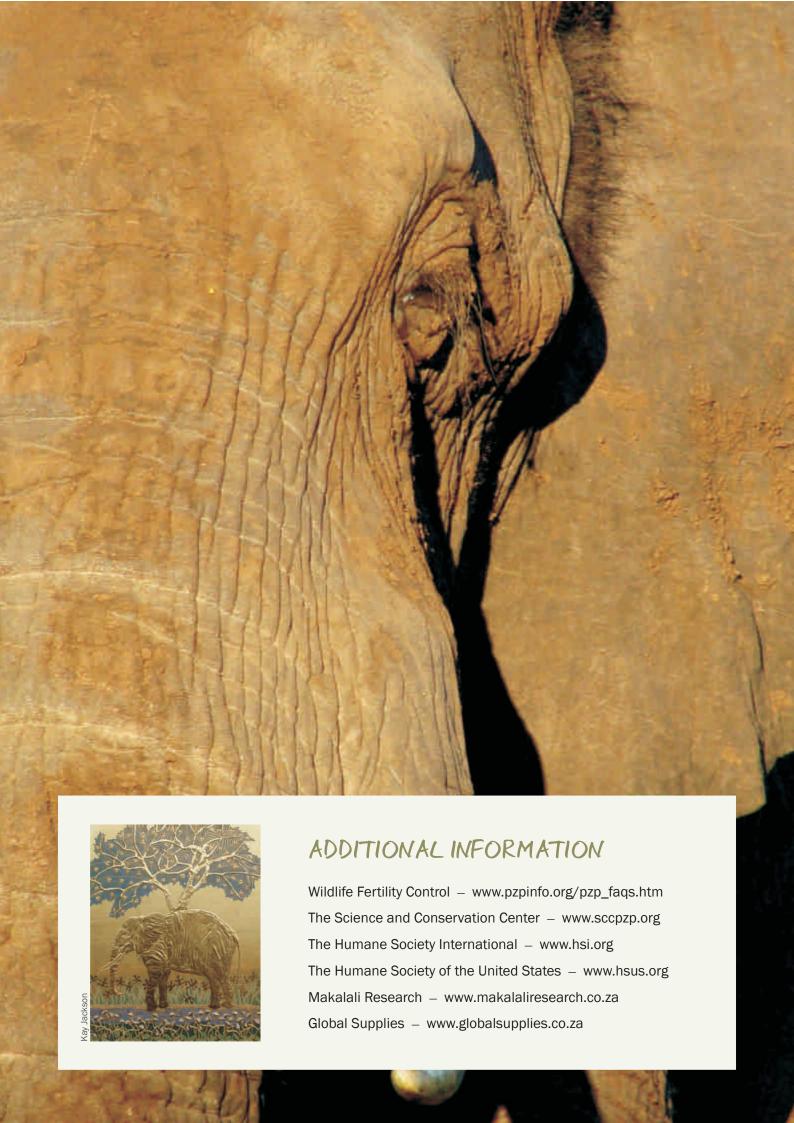
Fayrer-Hosken, R., P. Brooks, J. Kirkpatrick, H. Bertschinger, J. Raath, and J. Soley. 1997. Potential of the porcine zona pellucida (PZP) being an immunocontraceptive agent for elephants. Theriogenology 47:397.

Kirkpatrick, JF., JW. Turner Jr., IK. Liu, and R. Fayrer-Hosken. 1996. Applications of pig zona pellucida immuno-contraception to wildlife fertility control. Journal of Reproduction and Fertility Supplement 50:183-189. http://www.ncbi.nlm.nih.gov/pubmed/8984182

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