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5th International Symposium on Non-Surgical Contraceptive Methods of Pet Population Control

Portland, Oregon, U.S., August 1, 2013 – From June 20 to 22, 2013, 156 attendees from 16 countries spanning six continents convened in Portland, Oregon, to discuss the development and use of non-surgical tools for humane management of pet and free-roaming cat and dog populations. Non-surgical methods are attractive because they have the capacity to be faster and less invasive, and thus require a shorter recovery time, than spay or neuter surgery.

The symposium brought together key stakeholders, including veterinarians, shelter organizations, animal welfare and advocacy groups, foundation representatives, and animal drug developers. Participants evaluated the options currently available and defined unmet needs. They also shared the progress toward new non-surgical methodologies in fields that include reproductive biology, molecular biology, immunology, and related scientific disciplines.

Participants found the symposium educational and inspirational. A majority of attendees completed a post-symposium survey and rated the symposium an average of 4.7/5 (with 5 being excellent) for overall quality. Most also reported that they left the symposium more hopeful about future progress and more interested in being involved in efforts to develop non-surgical options than before they arrived.

I had a fantastic experience, and I was highly motivated to stay in this field during my future career.
(Kendall Foley, D.V.M. student, Auburn University College of Veterinary Medicine)

A comprehensive list of speakers and attendees, session summaries, recorded presentations, posters and related Think Tank reports are available at www.acc-d.org/5thsymposium. ACC&D strives to be a catalyst for advancing non-surgical options for humane and effective population control across the globe. We believe that making proceedings available free of charge is key to this goal. This full report that you are now reading provides symposium highlights and brief summaries of sessions and individual presentations. We encourage you to use it as a resource and guide to the online resources that will be of most interest and value to you.

KEY HIGHLIGHTS – OVERALL

The symposium connected leaders from diverse fields. The symposium convened an international audience representing the broad range of partners needed to advance this complex issue. Approximately 25% of attendees identified themselves as scientists, 25% as animal welfare advocates, 25% as practicing veterinarians (either in shelters or private practice), and 25% as representing other sectors. This latter



cohort included animal health representatives, funders, investors, journalists, and more. Attendees included presidents, directors, CEOs, and CSOs of leading animal welfare nonprofits, foundations, and pharmaceutical companies; veterinarians and individuals on the front lines of rabies vaccination and animal population control campaigns; and scientists representing esteemed institutions and schools of veterinary medicine.

[The] ACC&D conferences have become a unique and invaluable interface among the animal welfare, scientific, and bioethics communities. They are the only public events I am aware of at which animal advocates and animal researchers comfortably break bread & drink beer together, building trust & mutual recognition of concerns which I believe is having some very positive effects in either direction. (Merritt Clifton, Editor, Animal People)

Impressive progress has been made since ACC&D's founding. No non-surgical products were available when ACC&D was founded in 2000. Thirteen years later, two products—Suprelorin® and Zeuterin™ (known as EsterilSol™ outside the U.S.)—are on or entering the market in some parts of the world. Additional products are currently under development for cats and dogs. A far greater number of researchers are actively working in this field than even five years ago. In 2008 the Michelson Prize & Grants program made \$50 million available for research into non-surgical sterilant options for both dogs and cats, sparking a new generation of research; other sources are also supporting current research in this field. Numerous new approaches are being explored; this symposium displayed many, but certainly not all, of them.

The field has reached an important juncture. As cutting-edge science is applied to develop new non-surgical approaches, field researchers are evaluating various features of the products currently available: testosterone level impacts, behavioral changes, and long-term effects. With some products on (or close to entering) the market and several promising options at various stages of development, stakeholders are also delving into best practices for ethical and culturally sensitive field trials and implementation of population control programs.

The symposium included general sessions focused on evaluating current technologies, defining what is important to various potential markets, and discussing the ethics of scientific inquiry and animal population control. In addition, two focused symposium tracks were offered: The Sterilant/Contraceptive Discovery Track focused on the science and development of new tools, and the Field Implementation Track explored special considerations to put existing tools to use for free-roaming populations.

KEY HIGHLIGHTS – GENERAL SESSIONS

General sessions provided key background important to both scientific investigation into non-surgical methods and to field implementation of non-surgical interventions.



The plenary sessions were well-targeted and generated robust discussions which lasted into breaktimes. Very interesting and well thought out! (Kate Atema, Program Director, Companion Animals, International Fund for Animal Welfare)

Reproductive Biology

Dr. Amy Fischer (ACC&D Board member and Teaching Associate and Extension Specialist, Animal Sciences, University of Illinois at Urbana-Champaign) presented a primer on canine and feline reproductive biology for non-specialist scientists and laypersons. She covered the basics of fertility and reproduction for each species, described the control of reproduction by the brain via the hypothalamic-pituitary-gonadal (HPG) axis, and reviewed potential targets to interfere in reproduction. Dr. Karin Albers-Wolthers (Resident ECAR, Department of Clinical Sciences of Companion Animals Faculty of Veterinary Medicine, University of Utrecht, Netherlands) subsequently discussed reproductive hormones and whether or not it is desirable to eliminate or reduce them. It has been commonly assumed that keeping hormone levels low reduces undesirable behaviors—a boon in the minds of many pet owners. However, Dr. Albers-Wolthers presented information about possible reasons to maintain levels of some hormones. This is timely as practitioners consider use of Zeuterin, which results in a lesser reduction of testosterone in male dogs than does surgical castration.

Ethical considerations

The field of veterinary ethics, though still in its relative nascence, is gaining traction. Animal population management, as well as the research, development, field-testing, and use of non-surgical options, beg consideration of important ethical questions. ACC&D seeks to be a trusted resource on this topic, and toward this end the 5th International Symposium included several sessions focused on the important ethical questions that must be asked when looking to expand population control options and capabilities, particularly in communities with limited resources.

Betsy Banks Saul (ACC&D Board member and founder of Petfinder.com and Heal House Call Veterinarian) discussed ethical dilemmas, pointing out that when faced with a difficult choice between two equally bad (or good) options, a new third option can create a moral choice and present a clear path. She cited surgical sterilization as one ethical dilemma. The procedure is, to be sure, critical to reducing populations of homeless companion animals. However, research shows some potential long-term health consequences tied to hormone reduction, and surgical sterilization is not universally accepted. Ms. Saul thus called for a new third option to help control animal populations while respecting cultural sensitivities and avoiding risks of surgery. Dr. Monica List, a veterinarian and Philosophy Ph.D. candidate with a background in bioethics, drew from classical ethics to frame and discuss scenarios encountered when working with various animal populations. This theme permeated several other presentations as well, particularly those in the Field Implementation Track. There, Dr. Julie Levy, Director of Maddie's® Shelter Medicine Program at the University of Florida, presented on ethical and welfare considerations around field trials of products destined for underprivileged populations, and several other presenters referenced ethical challenges that arose while working in diverse communities.



Markets and stakeholders

ACC&D's 5th International Symposium highlighted the strides that researchers and scientists are making toward developing safe, effective, affordable options for non-surgical canine and feline sterilant and contraceptive options. Dr. Steve Zawistowski, ACC&D Board Chair and ASPCA Science Advisor, eloquently articulated, however, that these products' benefits will only be realized if stakeholders welcome their arrival and put them to use. Toward this end, the symposium began with two panels whose members spoke to both the need for and potential uses of alternatives to surgery.

ACC&D Board member Dr. Elly Hiby chaired an international panel of leaders in dog and cat population control: Kate Atema, Director of the Companion Animal Program at the International Fund for Animal Welfare (IFAW); Becky Robinson, president and co-founder of Alley Cat Allies (ACA); Charles Rupprecht, Director of Research at the Global Alliance for Rabies Control (GARC); and Ismail Thoya, Veterinarian at the Kenya Society for the Protection and Care of Animals (KSPCA). These experts work with different animal populations and in varied communities, but all see a need for non-surgical alternatives to advance population control, animal welfare, and community and public health. Panelists used their field experience to discuss the attributes and types of products that could best meet the needs of diverse communities.

Whereas the aforementioned panelists spoke to the impetus for non-surgical options, Dr. Zawistowski chaired a panel with leaders from specific stakeholder groups: cat and dog breeding and competition, animal sheltering, and the veterinary profession. Each discussed the desired attributes of non-surgical sterilants/contraceptives for his or her respective constituencies.

Wayne R. Cavanaugh, President of the United Kennel Club (UKC), and Joan Miller, Chair of the Outreach and Education Committee at the Cat Fanciers' Association (CFA), emphasized the value of reversible fertility control to dog and cat breeders, as well as for owners of dogs participating in performance events. Ms. Miller distributed a survey through the CFA website and received 700 responses, largely from breeders. Survey feedback strongly suggests that temporary contraception would be viewed as a valuable tool to support *planned* breeding of pedigreed cats, as long as safety for the cats and removal of secondary behavioral issues (e.g., aggression, urine spraying) are ensured. Mr. Cavanaugh discussed the increasing popularity of performance events, which, unlike their predecessors, permit sterilized animals. Even so, many dog owners have concerns about health issues linked to surgical sterilization, which prompts interest in economical, healthy, and non-invasive methods of sterilization. He also offered a well-articulated suggestion that commercially bred puppies be required (by the USDA, the agency governing commercial breeding facilities) to receive temporary contraception prior to sale.

Dr. Gail Golab, Director of the Animal Welfare Division at the American Veterinary Medical Association (AVMA), discussed the weight that veterinarians give to product safety, efficacy, and cost. She emphasized that veterinarians would benefit from having options to present to clients, and that no one approach would be appropriate for all pet owners. Betsy McFarland, Vice President for Companion Animals at The Humane Society of the United States (HSUS), spoke of "pet resource deserts" in many communities, including urban, in the U.S. Particularly in locations with limited veterinary providers,



animal sheltering and welfare organizations could benefit tremendously from low-cost alternatives able to be deployed in the field. Ms. McFarland additionally pointed out the advantages of a tool that does not require surgery or expensive surgical suites and, as such, could shorten the length of an animal's stay in the shelter.

Available sterilants/contraceptives, and investment in new research

Cathy Moldave, ACC&D Scientific Advisor and co-founder of AlcheraBio, chaired a session devoted to technologies with potential for nearer-term impact, including Zeuterin, GonaCon™, Suprelorin, and calcium chloride injection. Each of these products has either received regulatory approval for some species or is currently undergoing field trials.

Dr. Shirley Johnston, Director of Scientific Research for the Found Animals Foundation, reviewed the first five years of the Foundation's Michelson Prize & Grants in Reproductive Biology (MP&G). This program has helped to raise the profile of the quest for non-surgical sterilants and attracted new scientists to the field from various disciplines. To date, 25 proposals have been funded in areas including neuroscience, oncology, pharmaceutical chemistry, immunology, virology, molecular biology, and reproductive physiology. Preliminary findings from several funded projects were presented in the symposium's Sterilant/Contraceptive Discovery Track.

KEY HIGHLIGHTS – STERILANT/CONTRACEPTIVE DISCOVERY TRACK

This is a field we are hoping to devote a lot of my lab to, and thus the meeting was very timely and provided an excellent overview of the different groups working on, and interested in this problem.
(Bruce Hay, PhD, Professor, California Institute of Technology)

With such high quality scientists working on finding a non surgical solution to sterilization it is simply a matter of time before we have real success in this field. **(Rick DuCharme, Executive Director, First Coast No More Homeless Pets)**

The Sterilant/Contraceptive Discovery Track covered laboratory research, sometimes in cell culture or model animals such as mice or rats, toward development of new non-surgical sterilants or contraceptives for cats and dogs.¹ Approximately half of the presenters in this track received MP&G research funding. The track was organized by type of intervention, and with four major areas addressed: immunological approaches, inactivation of gonadal cells, gonadotropin releasing hormone (GnRH) agonists and antagonists, and novel approaches.

¹ ACC&D's position statement on research using live animals can be obtained at www.acc-d.org/FAQ.



Immunocontraception

For decades, researchers have investigated the potential to control fertility by inducing the immune system to attack cell types or tissues necessary for reproduction. Dr. Linda Rhodes (ACC&D Board member and Chief Scientific Officer of Aratana Therapeutics, Inc.) chaired a session covering current research on immunological approaches to contraception and sterilization of cats and dogs. She began with an overview of the history of the field, starting with the first published work on a GnRH-targeted vaccine in 1975. Though EPA-approved, commercialized vaccines exist for some species, such as GonaCon for deer and wild horses, at the moment there are no vaccines for long-term suppression of fertility in cats or dogs. Dr. Luis Lecuona (Agricultural Specialist in Animal Health, USDA/APHIS/IS México) presented on concomitant administration of rabies vaccine with a new formulation of GonaCon (GonaCon-Canine) specially designed for use in dogs. The study, accepted for publication, found the new formulation to be promising. It yielded fewer and less severe local reactions than the non-canine-specific GonaCon formulation, and researchers did not observe any adverse effect on immune response from simultaneous administration of GonaCon-Canine and rabies vaccine.

Drs. Michael Munks (Instructor of Immunology, National Jewish Health, Integrated Department of Immunology) and Tatiana Samoylova (Associate Research Professor, Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University) presented their work toward developing innovative contraceptive vaccines. Dr. Munks is engineering a novel GnRH-targeted vaccine for cats by modifying an attenuated feline herpesvirus-1 (FHV-1), an FDA-approved vaccine strain. His group has demonstrated the safety and immunogenicity of its FHV-1 vector and is preparing to conduct breeding studies with the engineered vaccine. Dr. Samoylova is generating a GnRH vaccine by engineering filamentous phage. She has found conditions that inactivate the phage while preserving its antigenicity, important for achieving eventual regulatory approval.

The research into development of new vaccine vectors and dog-specific formulations generated optimism that immunocontraceptive approaches may be on the horizon for cats and dogs.

Gonadal ablation

Gonadal ablation, in males also known as chemical castration, consists of inactivating or destroying gonadal stem cells to induce sterility. Dr. Michelle Kutzler (ACC&D Scientific Advisor and Associate Professor of Companion Animal Industries, Department of Animal Sciences, Oregon State University) chaired a session on gonadal ablation in male dogs and cats. This approach has several desirable features, explained Dr. Kutzler. It is inexpensive, not technically challenging, and suitable for large-scale sterilization programs, particularly in remote locations lacking clinical facilities or skilled surgeons. Gonadal ablation is also notable for the fact that, in contrast to surgical castration, it does not completely eliminate gonadal sources of testosterone.

Dr. Kutzler presented an overview of chemical castration and the many agents that have been injected into the testes, epididymis, or vas deferens to cause infertility by means of azoospermia. This approach to producing sterility in male animals extends back as far as 50 years. In recent years zinc gluconate has



received particular attention as Zeuterin (zinc gluconate neutralized by arginine) made its way through regulatory channels, received FDA approval for use in dogs, was launched internationally, and prepares for commercial launch in the U.S. in 2013. However, there are several additional products in the nearer- and longer-term pipelines, some of which were showcased in this session.

Dr. Joseph Tash (Professor of Molecular & Integrative Physiology, Department of Urology, University of Kansas Medical Center) discussed his work with a novel compound that, in a single subcutaneous—*not* intratesticular—injection, results in complete loss of spermatogenic cells in rats. This injection has no significant effect on testosterone levels. His group has conducted dose-response studies to identify the optimal dose in rats and plans to move on to study the compound in dogs. Dr. Kuladip Jana (Senior Scientist, Division of Molecular Medicine, Bose Institute) presented his work evaluating the safety and efficacy of intratesticular calcium chloride injections to induce sterility in male dogs and cats. His studies show a substantial decrease in testosterone levels after treatment. Dr. Raphaël Vanderstichel (Centre for Veterinary Epidemiological Research, Department of Health Management, Atlantic Veterinary College) discussed research on the effect of the intratesticular injection Zeuterin/EsterilSol on canine testosterone levels. In a field study of 118 dogs in Puerto Natales, Chile, a variable response was observed, with approximately 30% of the dogs treated with Zeuterin/EsterilSol having testosterone levels comparable to those of surgically sterilized dogs 6 months after treatment.

Chemical castration offers promise as a means to sterilize male dogs and cats inexpensively and with a single treatment. The various approaches to chemical castration discussed at the symposium present a range of effects on testosterone levels, which may be important as other research investigates effects of testosterone on health and behavior.

Targeting the HPG axis: GnRH agonists and antagonists as contraceptive agents

Targeting the body's master reproductive hormone, GnRH, at the pituitary level could simultaneously induce sterility in both males and females and mimic the suppression of hormones associated with surgical sterilization. GnRH agonists have been used in multiple wildlife species, including wild felids and canids, for more than 15 years, explained session chair Dr. Cheryl Asa. She opened the session by reviewing use of the GnRH agonist Suprelorin (deslorelin acetate) in zoo animals; Suprelorin implants can be used in males and females and are attractive to zoos since fertility resumes once the implant is removed or depleted.

Dr. Asa, ACC&D Scientific Advisor and Director of the AZA Wildlife Contraception Center at the St. Louis Zoo, noted that GnRH agonists were not originally thought to be appropriate or adequate for free-roaming cat and dog sterilization because their effects are temporary and considered to be reversible. However, long-term fertility suppression has been observed in some individuals treated with Suprelorin, inspiring new thoughts about its mechanism of action. This feature, combined with the often-short lifespans of free-roaming animals and some pet owners' desire for contraceptive options that are *not* permanent, potentially makes GnRH agonists a promising option for certain canine and feline populations.



Speakers presented on various applications of deslorelin acetate. Dr. Sandra Goericke-Pesch (Clinic for Obstetrics, Gynecology and Andrology of Large and Small Animals, Justus-Liebig-University, Giessen, Germany) shared work demonstrating that slow-release GnRH agonist implants, such as Suprelorin, are a suitable option for contraception in male dogs and male and female cats. In male dogs, the effects of GnRH agonist implants on testosterone, testicular size, and semen quality are well characterized. She has observed substantial ranges in duration of efficacy among male and female cats. She has also studied different implant sizes, and found efficacy lasting over 18 months in adult females treated with a 9.4-mg implant. A downside was an initial increase in sexual behavior in some toms, and initial estrus induction in some queens. Dr. Goericke-Pesch concluded that implants provide a flexible contraceptive option for owned pets, and that repeated treatments can provide long-term contraception. However, since males are not immediately sterile after treatment, males and females must be separated for a period to prevent pregnancy. Meanwhile, Dr. Iris Reichler (Klinik für Reproduktionsmedizin, Vetsuisse Fakultät Zürich, Universität Zürich, Switzerland) examined the safety of Suprelorin in female dogs. She concluded that the implant may be an alternative to spaying in young dogs and in dogs with a high chance of spay side effects, but that side effects such as persistent heat or uterine disease may preclude use in older dogs.

Three speakers specifically addressed treating prepubertal animals with GnRH agonists to prevent puberty. Dr. Goericke-Pesch observed a statistically significant delay in the onset of puberty when queens were treated at 50% adult body weight with a 4.7-mg implant. Dr. Ana Cristina Carranza-Martin (Faculty of Veterinary Sciences, National University of La Plata, Argentina) presented research administering a GnRH agonist in juvenile domestic cats, demonstrating that a significant proportion of the animals were prevented from reaching puberty or becoming fertile. Marjie MacGregor, a Ph.D. candidate in the University of Wyoming's Department of Zoology and Physiology, presented studies seeking to determine whether a single, high dose (47mg) of deslorelin can induce permanent sterilization in the coyote (with potential applications for domestic canines). Her team has treated adult and prepubertal male coyotes with the high-dose implants. At a two-year follow-up, they observed long-term suppression of sperm production in animals treated as adults. At a one-year follow-up, three of five animals that were treated prepubertally produced no sperm, while two had resumed sperm production.

There is potential for GnRH agonist implants to induce long-term contraception or even sterility in dogs and cats. At the moment, however, this approach seems best suited to pet animals whose owners desire reversible contraception, or who wish to induce long-term contraception while avoiding surgery and are able to monitor the animals for undesirable effects (such as initial increased sexual behavior or persistent estrus) and obtain repeated treatments for the animals once the effect of the initial implant wears off. The health consequences of long-term reduction in levels of reproductive hormones are of great interest to those conducting research in this area.

Novel approaches to attacking the hypothalamic-pituitary-gonadal axis

Dr. Donal Skinner traveled from the University of Wyoming Department of Zoology & Physiology to chair a session on unique approaches to the challenge of non-surgical sterilization and contraception. The speakers in this session, all funded through MP&G, are exploring new approaches with the potential to control fertility in dogs and cats. Although the new approaches to the challenge are in early stages of



development, the audience viewed them to be both refreshing and promising, especially for female animals for whom surgery currently remains the only permanent non-surgical option.

Two presenters discussed targeting the protein, kisspeptin, relatively newly discovered as an important regulator of reproduction in humans. Dr. Karin Albers-Wolthers (Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, University of Utrecht, Netherlands) and Dr. Sergio Ojeda (Division of Neuroscience, Oregon National Primate Research Center) presented sequences of the kisspeptin gene of the dog. Dr. Albers-Wolthers has administered exogenous dog kisspeptin to female dogs, producing a 10-fold increase in plasma luteinizing hormone (LH) levels and indicating that the kisspeptin signaling pathway plays a regulatory role in canine reproduction. Dr. Ojeda is using gene silencing to induce permanent sterility. His group has designed an adeno-associated virus engineered to target the hypothalamus and reduce expression of kisspeptin. When tested in mice, this construct disrupted the estrous cycle. His group is further optimizing this system.

Dr. Scott Struthers, a Crinetics Pharmaceuticals Inc. researcher whose primary focus is human cancer and endocrine disease, discussed the development of targeted toxins, linking GnRH antagonists to cytotoxins with the aim of specifically ablating cells that have GnRH receptors. His group has successfully identified compounds that deliver toxins to the correct cells and is currently working to increase the cytotoxicity of their compounds.

The session revealed the impressive range of approaches being applied to the development of non-surgical sterilization methods. Many of the speakers presented results validating their model systems and setting the stage for exciting future research.

KEY HIGHLIGHTS – FIELD IMPLEMENTATION TRACK

The Field Implementation Track focused on the commercial use of approved products and trials of products with near-term potential. Several sessions in this track also considered the broader issue of optimal design and practice of field research. Experts shared best practices for conducting effective field trials and recovering from challenges that may occur; they also addressed ethical questions and concerns. Several presentations additionally discussed topics that, while not specific to non-surgical options per se, are inextricably linked to such products' success.

Field trials

Having the opportunity to speak with “real” users of these products gave me a true picture of what has been done, what issues need to be addressed, how it is currently being administered but furthermore that the passion to better the lives of many animals is a world-wide effort! (Sonia Hernandez, Companion Animal Spay/Neuter Coordinator, Animal Defense League of AZ/Spay Neuter Hotline)



The ACC&D Symposium brought together a wide array of stakeholders – while seeing that there is still a lot of work to be done to develop non-surgical sterilization technologies, everyone seemed to suddenly realize that there are a number being used in the field and we need to focus on how to best pave the way for their effective use. (Kevin Morris, Consultant, Morris Consulting; Treasurer, ACC&D Board of Directors)

The scope of current field trials with non-surgical sterilants and contraceptives is truly global, with projects currently taking place in Nepal, Northern Canada, Kenya, Oklahoma, Chile, and Mexico.²

What considerations are there for veterinarians, public health professionals, or animal welfare organizations that get involved in such projects? Drs. Linda Rhodes and Julie Levy presented on the details of designing a field trial. Dr. Rhodes advised on study protocol and detailed key features of a well-conducted field study—beginning with the need to record every detail. (Study protocol basics are included in the online proceedings.) Dr. Levy spoke on ethical and welfare considerations in field trials of products destined for underprivileged populations, a presentation that aligned with the earlier talk by veterinarian and Philosophy Ph.D. candidate Dr. Monica List. Dr. Levy prompted the audience to consider, among other issues, the need for and potential pitfalls of trialing products in developing countries, the standards of care with which research ought to be conducted, and the ways in which researchers can and should protect their subjects.

Dr. Judith Samson-French, Founder of the Dogs With No Names™ (DWNN) scientific pilot project and winner of the 2013 Canadian Veterinary Medical Association Humane Award, shared results of a study administering 141 Suprelorin implants to free-roaming female dogs on First Nations reserves in Alberta, Canada. The objective of the three-year study was to evaluate the efficacy of this temporary contraceptive and improve the short lives of free-roaming dogs in harsh conditions. In addition to assessing the reproductive outcomes of the implanted dogs, Dr. Samson-French also spoke to broader considerations of conducting work among animals in underserved communities. A key message: the residents of communities in which DWNN works are not concerned about “overpopulation” per se. Rather, they want to halt the chaos and redirected aggression associated with having large numbers of female dogs in heat. Suprelorin offers bitches—and the communities in which they live—an all-important “pregnant pause” that can improve human-animal relationships and increase community support for permanent sterilization.

Dr. Giovanna Massei (Senior Ecologist, National Wildlife Management Centre, Animal Health and Veterinary Laboratories Agency) presented results of a study in Sauraha, Nepal, to evaluate the efficacy of a single administration of GonaCon-Canine in combination with rabies vaccine. Dr. Massei’s team conducted the study with support from local officials and Nepal’s preeminent veterinary school, and caretaker interviews indicated a desire for controlling reproduction. Soon after the dogs were treated, the team noticed severe injection site reactions in the overwhelming majority of animals; this was traced to the USDA accidentally providing a *non-canine-specific* formulation of GonaCon. Dr. Massei focused

² In this context, “field trials” or “field testing” refers not to the final stage in getting a drug approved by a federal agency, but rather using products on an experimental basis in a field rather than laboratory setting.



much of her presentation on lessons learned from the error, including the need to have community support prior to launching a field study. She also highlighted the need to have sufficient veterinary resources in place to provide affected animals with high-quality veterinary care and ensure best possible welfare during recovery. (The affected dogs in this study received immediate veterinary treatment and close oversight during recovery, including kenneling when necessary.)

Elaine Lissner, Director of the nonprofit Parsemus Foundation, spoke about the potential of calcium chloride to serve as a safe, humane, and affordable injectable chemical sterilant for male dogs and cats. She has facilitated laboratory studies of calcium chloride formulations in both Italy and India, which have shown potential for calcium chloride to cause permanent sterilization with minimal observed discomfort. Parsemus Foundation is supporting this work because of it is not patentable, and therefore not attractive to for-profit groups to develop, and because it might potentially provide a low cost alternative to surgical castration, if it is inexpensively compounded. Ms. Lissner's provocative presentation intrigued some and alarmed other attendees with the suggestion that current research may support use now in a range of international locations, although no regulatory approval yet exists. The foundation has applied to the Center for Veterinary Medicine to open an Investigational New Drug Application, which could pave the way for next steps including conducting field research.

Zeuterin/EsterilSol

A full session was devoted to Zeuterin/EsterilSol. As the first product to receive FDA approval for chemical sterilization of male dogs, and with a late 2013 U.S. launch anticipated, Zeuterin has received significant attention. Four early adopters, three from the United States and one from Kenya, shared their experiences with the product. They represented a variety of operations: an organization providing veterinary care to pets of Portland, Oregon's homeless and low-income citizens; a high-quality, high-volume spay/neuter clinic in Florida that sterilizes 24,000 companion animals annually; a mobile clinic in rural south Texas providing care to animals in pet resource "deserts," where veterinary and animal control services may be as many as 100 miles away; and an organization working to curb rabies and inhumane culling of Nairobi's free-roaming dogs. Presenters expressed the value of Zeuterin/EsterilSol in their specific work environments. They also provided an honest assessment of challenges associated with the product, among them gaining support from veterinarians, veterinary staff, and animal shelters, as well as the potential learning curve associated with the zinc neutering procedure.

Following the panel of veterinary practitioners who use the product, Dr. Raphaël Vanderstichel shared the results of a study conducted by Veterinarians Without Borders on the behavior of free-roaming dogs in Patagonia, Chile, following zinc neutering and traditional surgical castration. The study is notable for being the first known field trial with direct behavioral observation following surgical or chemical sterilization. Dr. Vanderstichel shared preliminary study results, which showed limited behavioral differences in these dogs regardless of neuter status or method. Additional analysis will yield further interpretation, and the audience was hungry for more information on a topic that has to date garnered little objective research.



Complementary topics

Several initiatives discussed show promise to contribute to population management of dogs and cats via traditional surgery, as well as helping make best use of new non-surgical alternatives. Dr. Zawistowski chaired a session on managing populations of free-roaming felines. Dr. Phil Miller, Senior Program Officer at the Conservation Breeding Specialist Group (SSC/IUCN), presented the results of a computer simulation modeling approach tailored to evaluate multiple methods of controlling cat populations (surgical sterilization, non-surgical contraception, and removal) in different geographies and over different timespans. This model accounts for dispersal and abandonment, a pivotal consideration overlooked in most feline population modeling efforts to date. Dr. John Boone (ACC&D Scientific Advisor and Senior Biologist at the Great Basin Bird Observatory), discussed how to use these modeling results and field studies to generate management guidance for free-roaming cats, while Dr. Margaret Slater advised on methods for accurately and effectively counting free-roaming cats—a cornerstone to successfully monitoring and managing feline populations.

In a session on the canine contingent, Dr. Giovanna Massei discussed the use of fertility control inhibitors for dog population management, focusing on the essential questions that must be answered prior to large-scale applications. Among them, what proportion of the population must be targeted to achieve a set reduction in size or growth? What are the long-term effects of fertility control on animal welfare and survival? Do fertility inhibitors affect behavior? John Friar, Founder of the Wise Monkey Foundation, and Kate Atema shared a system for integrated data collection, analysis and modeling, with the outcomes of informing sound monitoring and decision-making for animal welfare, anti-rabies, and community health projects being conducted across the globe. Session Chair Dr. Elly Hiby also advised on how to measure important free-roaming dog population parameters, including population size and density, welfare, zoonotic disease, and public perception—the latter a factor that is commonly missed and yet can provide invaluable evidence of success when lobbying for sustaining effective programs.

Valerie Benka, ACC&D Project Manager, chaired a session on identifying non-surgically sterilized or contracepted dogs and cats. Dr. Raffaella Leoci (Department of Emergency and Organ Transplantation, Section of Veterinary Clinic and Animal Production, University of Bari Aldo Moro, Italy) presented study results comparing the effectiveness and safety of, as well as behavioral response to, ear tagging and freeze branding among sheltered dogs in southern Italy. Ms. Benka presented the results of the ACC&D Think Tank on marking methods, and of an InnoCentive® Challenge posted by ACC&D to identify novel methods for identification, both of which have formed the foundation for a potential project to design an improved method for marking animals. Ms. Benka noted additional potential applications for monitoring wildlife, animals vaccinated against rabies, and even animals that have been surgically sterilized.

Attorney Deborah Press, Manager of Regulatory Affairs at the ASPCA, evaluated some legislative considerations for non-surgical sterilants and/or contraceptives. Many state laws and local ordinances define animal sterilization; some explicitly specify surgery, some explicitly leave open the option for non-surgical alternatives, and some remain ambiguous. Several states have also established sterilization policies for pet adoption and/or municipal licensing. Ms. Press researched the language used in each state



for each of these categories and provided the audience with a state-by-state analysis. She additionally looked at how state and local laws must change to allow for non-surgical options and shared valuable insights and model language to pave the way for laws that accept sterilization options outside surgery. Her presentation and reference documents (available in the online proceedings) offer valuable information for U.S. organizations reviewing the readiness of their communities to utilize Zeuterin and other future technologies.

ADDITIONAL SYMPOSIUM SESSIONS AND EVENTS

ACC&D's 5th International Symposium offered several educational and networking opportunities and highlights beyond the general and track sessions, discussed below.

Keynote Address: “Cats, dogs, and the road to personhood”

ACC&D was honored to have Dr. David Grimm, Ph.D. geneticist, award-winning journalist, and online news editor of *Science*, deliver the Keynote Address at the symposium banquet and awards session. He presented “Cats, Dogs, and the Road to Personhood,” a topic of his upcoming book and one that overlaps at several junctures with work being done by ACC&D and many symposium attendees. As Dr. Grimm noted, “The status of pets in society is changing rapidly...How did we get here? What happens next? And how will the evolving status of cats and dogs impact everything from attempts to control their population to the choices we make about their medical care?” Dr. Grimm has also published an article on non-surgical sterilization in *Science*, the world's largest journal of science news and scientific research.

Achievement Awards

Dr. Min Wang, one of the world's leading reproductive scientists, received ACC&D's Special Achievement Award. This award recognized his scientific expertise, leadership, and commitment to seeing Zeuterin/EsterilSol through the processes of research and development—and eventually to becoming the first FDA-approved non-surgical sterilant for a companion animal species. Dr. Wang received degrees in medicine and biological reproduction from Xian Medical University in Xian, China. Joyce Briggs and Dr. Bob Weedon, ACC&D President and Board Vice Chairman, respectively, commented on the significance of a medical doctor contributing so dramatically to the field of animal health and welfare—a true testament to the meaning of One Health and Dr. Wang's “working from human to humane.”

Ms. Briggs and Dr. Steve Zawistowski surprised ACC&D Board member Dr. Linda Rhodes with the ACC&D Leadership Award. Dr. Zawistowski credited Dr. Rhodes for bringing expertise on the pharmaceutical industry, the veterinary profession, and the regulatory sphere to ACC&D. Ms. Briggs reiterated how essential Dr. Rhodes's insights on the animal health pharmaceutical field have been for ACC&D, as well as her decade-long commitment to advancing the field and her recruitment of colleague Cathy Moldave to the ACC&D Scientific Advisory Board.



Poster Session

ACC&D's Poster Session drew authors from Argentina, Brazil, Italy, Turkey, and the U.S.; the research shared was equally diverse. The majority of posters reported on clinical studies. Research on the efficacy and safety of deslorelin acetate, zinc chloride, and zinc gluconate was presented. Dr. William Ja, an MP&G recipient, displayed a poster on work being done with ligand-toxin conjugates—compounds that link potent cytotoxins to targeting ligands that impart cell-specificity. Other posters took non-surgical options into the field, sharing research on the potential role for immunocontraception in dual animal population management and rabies prevention, contraceptive methods used by pet owners in a community of São Paulo, Brazil; and mathematical modeling of temporary contraception in cats and dogs.

Special Breakfast: “The one-minute contraceptive implant: Where science meets ancient cultures”

Prior to sharing the scientific results of her field study using deslorelin implants, Dr. Judith Samson-French spoke to a packed room about the work of her organization, Dogs With No Names. Her talk—at once poignant, funny, and truly inspiring—relied on photography and video to share the impact of the Dogs with No Names project on both the humans and canines who reside in Canada's First Nations communities. Dr. Samson-French also provided valuable insight on her experience offering a non-surgical technology to people with different cultural heritage, attitudes, and resources toward surgical sterilization.

Zeuterin/EsterilSol Certification Training by Ark Sciences

Following the conclusion of the symposium, Ark Sciences facilitated a certification training for veterinarians and veterinary technicians in administration of Zeuterin/EsterilSol. A limited number of attendees were able to observe the session without seeking certification. Zeuterin is an FDA-approved product to “zinc neuter” male dogs; it offers significant advantages to many nonprofit and government agencies around the world, especially where there is limited access to appropriate surgical facilities and equipment, or where dog owners resist having their dogs castrated. Proper injection technique is important to the safe administration of the treatment.

Now that we have a better picture of Zeuterin (by way of observing a procedure and speaking w/a vet who currently is using the product) this will be a consideration, in the future, to assist the out-lying communities in our state. This will allow for more neuters in a day vs. surgical (if a one day visit is all we can give). (Sonia Hernandez, Companion Animal Spay/Neuter Coordinator, Animal Defense League of AZ/Spay Neuter Hotline)

IN SUMMARY

It was an incredible experience to be surrounded by people who are leaders in their various fields all working toward a common goal. I feel that there will be a solution to this problem in the very near future and I want to be a part of it. (Anonymous)



Inspirational. I met people from all over the world with a common goal; everyone was on the same page. Everyone was willing to share information and experiences, great combination of science with real life practical lessons. (Dr. Sheilah Robertson, Assistant Director, Animal Welfare Division, AVMA)

The symposium offered the opportunity for people interested in non-surgical methods of cat and dog population control to meet, learn about the most recent developments, and discuss the best path forward with regard to research and implementation.

Now that you have read this report, we encourage you to take a deeper dive into the information and resources presented at the symposium. Speakers and poster authors have generously given permission to share their materials on the ACC&D website. The online symposium proceedings include research abstracts, PDFs of PowerPoint slides, and either video or voice-recorded presentations for nearly every speaker, as well as abstracts and PDFs for poster presentations. Several speakers distributed handouts to supplement their talks; these, too, are included in the online proceedings. The results of the post-symposium survey can also be found online. Enjoy!

SPECIAL THANKS

ACC&D's 5th International Symposium was possible thanks to the following sponsors and ongoing supporters: Alley Cat Allies, Aratana Therapeutics, Ark Sciences, Inc., ASPCA, Best Friends Animal Society, Coalition for Pets and Public Safety, Heal House Call Veterinarian, The HSUS, IFAW, IVIS, Kenneth A. Scott Charitable Trust, Michelson Prize & Grants, Morris Animal Foundation, Oregon Humane Society, Parsemus Foundation, PETCO Foundation, PetSmart Charities, Regina B. Frankenberg Foundation, Spay Colorado, Tarshis Foundation, and WSPA.

ADDITIONAL PARTICIPANT QUOTES

The field is clearly attracting new interest on a scientific and 'user' level. The symposium opened up some new possibilities for progressing investigation and experimentation concerning non-surgical sterilization and population control, for example mathematical modeling. (Gregory Castle, Chief Executive Officer, Best Friends Animal Society)

I thoroughly enjoyed this series of presentations and events, and it was clear that a significant amount of effort and organisation was involved in delivering this wonderful symposium. It has more than inspired my desire to make a meaningful contribution to this important field, especially since - as a soon-to-be veterinarian - my skills will hopefully be of relevance. It was also great that the symposium concurrently celebrated the forthcoming release of Zeuterin, not only through acknowledging those involved in the creation of this innovative technology, but also providing the science behind its production and its clinical applications and moreover, the exclusive opportunity to become Zeuterin certified! Thank you all



so much for an enriching and inspiring experience. (Sy Woon, Veterinary Student, University of Sydney, Australia)

This Symposium showed in a high technical level advances and serious research about non-surgical alternatives for dogs and cats and match with a growing need worldwide for more technical info about it. It is a perfect opportunity to be in touch with all people involved/interested in this great topic. (Dr. Luis Lecuona, Agricultural Specialist in Animal Health, USDA/APHIS/IS México)

The group of people was large enough to allow for great varieties in presentations and experiences, but small enough to make networking and meeting new people natural. Excellent conference! (Caitlin Donovan, Ph.D. student, University of California, Davis)

The meeting provided a comprehensive overview of research into ways of bring about non-surgical sterilization; it also provided an introduction to the many people working with their boots on the ground, often using their own funds, to tackle overpopulation using currently available tools. This was very inspiring to see. (Dr. Bruce Hay, Professor, California Institute of Technology)

The diversity of perspectives and representation from different disciplines and backgrounds was especially interesting and informative, something not to be found at other conferences. (Dr. Cheri Asa, Director, AZA Wildlife Contraception Center at the St. Louis Zoo; ACC&D Scientific Advisor)

The symposium was a good place to get an update on the state of the science and the current regulatory status of products under development. It was also inspirational to hear about the work being done to reduce the number of euthanasias in US animal shelters. (Dr. Douglas Oeller, Douglass Oeller Consulting, Inc.)

As someone new to this field, I found the ACC&D conference an amazing learning opportunity. Not only could an attendee learn from the foremost experts in the field, but network with others working on diverse areas. I also found that everyone was genuinely committed, friendly and open to sharing ideas. I had a terrific time! (Anonymous)

I was beyond impressed with the symposium overall. The variety of professionals present led to extremely thought-provoking discussions, and truly allowed the issues at hand to be approached from every angle. It was humbling to be surrounded by so many selfless and open-minded people who all shared the same goals of reducing over-population of cats and dogs, as well as promoting animal welfare. The speakers were excellent; all presentations were very informative and relevant. This symposium highlighted the amazing progress that has been made in the field of non-surgical sterilization, as well as demonstrating projects and ideas that are planned for the future. (Kendall Foley, D.V.M. student, Auburn University College of Veterinary Medicine)

I was incredibly impressed by the openness of debate, the quality of speakers and the range of issues addressed. ACC&D should be commended for the many aspects of work it is doing to promote the best application and coming together of ideas for nonsurgical sterilants and, ultimately, better animal welfare. (Kate Atema, Program Director, Companion Animals, IFAW)



Very eye-opening as to the level of research and clinical studies being conducted worldwide. Great level of compassion amongst attendees, and respect of cultures and ethics. (Dr. Mary Blankevoort, Volunteer and Board Chair, Portland Animal Welfare Team)

The Symposium brought together scientific, veterinary and animal welfare powerhouses from around the globe in a dynamic and inspiring program that detailed accomplishments to date and the challenges of the future. (Anonymous)