

Laying the Foundation: An Overview of Existing Contraceptives and Non-Surgical Sterilants – *Rhodes*

The purpose of this introductory talk is to tell you about the existing contraceptive and sterilant products that are on the market today. Why do we want to start out talking about what is, rather than what might be? To demonstrate that success is possible.

Pet owners and pet population organizations now have products that were unavailable just a few years ago. A key part of the ACC&D mission is to help bring together the people at this symposium — those with a passion for better tools for pet population control, those with knowledge of basic research and science, expertise in drug and vaccine development and manufacture, and pharmaceutical companies interested in investing resources for new products — to generate dialogue and collaboration, spark new ideas and make real progress, not just in demonstrating that a technology works, but in developing technologies and drugs to the point that they can achieve regulatory approval and can be used widely around the world.

For many years, people and organizations working on dog, cat and wildlife population control and basic researchers have been interested in developing an alternative to surgical spay and neuter for sterilization and/or contraception of animals. Hundreds if not thousands of research studies have been published showing progress toward the goal of a non-surgical contraception, but until recently no products were widely available for use in dogs and cats, with the exception of progesterone-related drugs, which provided short-term fertility suppression, but usually at the expense of a risk of undesirable side effects.

When the 1st International Symposium was organized by ACC&D in April of 2002, there were no products available for either contraception or sterilization of dogs and cats. Some information was presented on Neutersol®, an intra-testicular injectable zinc gluconate to sterilize male dogs that would subsequently achieve FDA approval in 2003 and be marketed to veterinarians in the U.S. In 2002, in the U.S., there were no approved alternatives to surgical castration or spay of dogs or cats.

At that same meeting, an Australian company, Peptech Animal Health, presented information on deslorelin, a drug in a class called gonadotropin-releasing hormone (GnRH) agonists. Data showed suppression of fertility in male and female dogs for up to 12 months, but there was as yet no approved product (see the 2002 Proceedings). The deslorelin product obtained its first approval and was launched in 2004 in Australia and New Zealand: Suprelorin®, an implant labeled for use in male dogs for six-month suppression of fertility.

At the 2nd International Symposium in 2004, the landscape didn't change. More information was available on Neutersol® and Suprelorin®, and although several other seemingly promising technologies were presented, they were all in research stage — none were “ready for prime time.”

By the 3rd International Symposium, in 2006, we were ready for some good news, and we got it! Dr. Marc Antoine Driancourt, of Intervet Pharma, presented exciting data on the use of another GnRH agonist implant, containing azagly-nafarelin, called Gonazon®. This product was shown to suppress fertility in female dogs for up to 12 months, and Dr. Driancourt announced that it would achieve regulatory approval in Europe soon after the meeting, which it did. Unfortunately, at that point Neutersol® was no longer being marketed and was unavailable for use; in 2005, production and distribution were discontinued after a “business divorce” between Pet Healthcare and Addison Laboratories.

During 2006, we waited to see the marketing of Gonazon® for bitches in the European Union, but the product didn't appear. To this day, although approved for use in bitches in the European Union, this product is not on the market. In the meantime, in 2007, Peptech achieved approval of a 12-month Suprelorin® in Australia for use in male dogs, followed by an approval in 2008 in Europe for the six-month version for male dogs. (Suprelorin® is being distributed by Virbac in Europe.)

So where does that leave us today? There are currently no products with FDA approval for contraception or sterilization on the market in the U.S. In Europe, one product, Suprelorin®, is on the market, for six-month fertility control in male dogs. It is likely that soon the 12-month product for male dogs will be available, and both the six- and twelve-month Suprelorin® are being sold in Australia.

EsterilSol™, a product basically identical to Neutersol® developed by Ark Sciences, LLC, is an intra-testicular injection for sterilizing male dogs, and is used both in puppies and adults. EsterilSol was introduced in Mexico in 2008. EsterilSol

is now available to private-practice veterinarians, government programs, and non-governmental organizations (NGOs) in Mexico. Ark Sciences has announced plans to extend distribution to other Latin American countries and beyond with plans for two dozen countries in the works. The product is available for limited use outside Mexico. Another zinc gluconate product, Infertile™, was introduced in Brazil in 2009, and currently is only available in Brazil.

ACC&D's EsterilSol Small Grants Program offers financial support to non-U.S. NGOs interested in using this technology to extend the reach of their population control programs. Later in this symposium, you will hear more about this program and ACC&D support of its use, and you can even receive training in its administration.

Finally, I would like to tell you about another development that we think shows progress, albeit in wildlife contraception. Immunocontraception approaches have been stalled by the regulatory hurdles of the FDA, and at the 2006 symposium there was discussion of a unique regulatory approach to helping advance regulatory approval. The group from the USDA National Wildlife Research Center developing a gonadotropin-releasing hormone (GnRH) vaccine for deer announced that the Environmental Protection Agency would be regulating contraceptives for wildlife, instead of the FDA. This approach allowed regulatory review to get past technical and legal hurdles that had stymied FDA approval, and finally, in 2009, the EPA announced approval of a GnRH vaccine contraceptive for deer, developed by researchers at the National Wildlife Research Center. This represents a milestone, and will hopefully encourage additional approvals through the EPA. In fact, it may be possible to consider an approval of a product to be used in feral cats to take this regulatory path.

You may be thinking that this is not much progress since our first gathering in 2002 eight years ago, and we should be impatient for better tools and drugs, but in fact, the drug development process is long and costly. After 30 years of research on the use of GnRH agonists for fertility suppression, two companies have committed the resources to achieve regulatory approval of products, and one is being marketed in major markets. A sterilant that is very effective for male dogs is being used in Latin American communities and is showing great promise in sterilizing male dogs that might never have been able to be castrated surgically.

Animal health companies have said for years that their market research shows veterinarians do not want nor will they use non-surgical alternatives to spay/neuter. These companies are watching their competitors build new markets for this un-met need, challenging old assumptions, and we expect they will be thinking in new ways about the promise of these products, and pay off of investment in research and development needed to bring new approaches to market.

This progress, plus the extremely exciting development of new interest in the area of research in cat and dog contraception and sterilization inspired by the Michelson Prize and Grants, leaves us certain that finally serious progress will be made in providing safe and effective alternatives to surgical spay/neuter for dog and cat population control.