Recombinant Technology: Reducing the Risk of Injection-Site Inflammation with Adjuvant-Free Vaccines
The practice of administering modified-live or whole-killed antigens (adjuvanted and nonadjuvanted) to immunize companion animals is rapidly changing with the introduction of recombinant technology and the genetic encoding of specific antigens. Vaccination recommendations are also changing rapidly and have been revised in recent years. In cats, concerns about feline vaccine-associated sarcomas (VAS) have focused on eliminating vaccination-site inflammation.

Although the etiopathogenesis of feline VAS is not completely understood, there is compelling evidence to support a relationship between postvaccination inflammation and tumor formation. Not all cats share equal susceptibility for tumor formation following vaccination, but induction of tumorigenesis in cats is known to be associated with extrinsic factors such as trauma, suture material, and repository preparations, in addition to adjuvanted vaccines.

**CHANGING VACCINE TECHNOLOGY**

One of the most significant advancements in the biotechnology of vaccines is the ability to isolate and splice (or recombine) gene-sized fragments of DNA from infective bacteria or viruses together with the DNA of non-pathogenic agents, forming a new hybrid agent. When an infective fragment from a pathogen such as rabies or FeLV is combined with a nonpathogenic vector virus such as canarypox, the vector organism integrates the immunogenic DNA fragment into its own genetic code.

**KEY POINTS – Recombinant virus-vectored vaccine**

- Efficacy comparable to live vaccines
- Adjuvant-free
- Cannot cause disease because they contain only nonpathogenic genes
- Cannot revert to virulence
- Provides both cell-mediated and humoral immune response
- Excellent candidate for alternative routes of vaccination (e.g., transdermal)
- Potentially less dangerous to immunosuppressed or malnourished cats
- Minimal to no inflammation at injection site
- Mechanism for immunization in the presence of maternally derived antibodies

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**PUREVAX® steps of manufacture**

1. **STEP 1**
   - The RNA is reverse transcribed into cDNA (a DNA copy of RNA).
   - RNA encoding for rabies glycoprotein G

2. **STEP 2**
   - Using an in vitro procedure, cDNA is inserted into the genome of the canarypox virus, making rRabies virus master seed.

3. **STEP 3**
   - rRabies virus master seed is propagated in chick embryo fibroblast cell culture to produce vaccine virus.

4. **STEP 4**
   - rRabies vaccine virus is used to manufacture PUREVAX® Feline Rabies Vaccine.

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*The 2006 Canine Vaccine Guidelines (AAHA) are expected to be available in March-April ([www.aahanet.org](http://www.aahanet.org)) and the 2006 Feline Vaccine Guidelines (AAFP/AFM) are expected late summer or early fall.*
This hybrid bacterium or virus is used to produce the vaccine. When injected into the host, the immunogenic DNA expresses specific antigenic proteins that induce the desired immune response. Because neither the recombinant DNA nor the vector organism is capable of replicating or inducing disease, recombinant vaccines have an exceptional safety record in humans and animals.†

**SAFETY & EFFICACY**

The most important advantage of using a recombinant virus-vectored vaccine over conventional modified-live and killed vaccine is safety. Recombinant vaccines offer excellent immunogenicity without the use of pathogenic whole, killed, or modified-live organisms. Furthermore, the absence of adjuvant, which is still in use in modified-live and killed vaccines, may be an important issue in reducing the risk of individual cats to vaccine-associated sarcoma formation. Veterinarians are encouraged to follow research reports and recommendations of the AVMA Feline Vaccine-Associated Sarcoma Task Force (FVASTF),† the American Association of Feline Practitioners (AAFP), and the Academy of Feline Medicine (AFM), and become familiar with recombinant vaccine technology for developing vaccination recommendations for their feline patients.

† Today, the only available USDA-approved recombinant virus vectored vaccines for cats are Merial’s PUREVAX® rabies and FeLV.
Rabies

Key Points
- Viral disease transmitted by the bite of an infected animal
- Rabies is an important threat to cats
- In the U.S., cats have been diagnosed with rabies more often than dogs each year since 1982
- Routinely fatal
- A significant public health concern
- The AAFP/AFM Feline Vaccination Guidelines have classified rabies vaccine as CORE for all cats
- Vaccination is usually required by law

**PUREVAX® rabies vaccine highlights**
- Protects against persistent rabies antigenemia equivalent to killed, adjuvanted, vaccine
- Nonadjuvanted, reducing risk of injection-site inflammation
- Contains canarypox virus-vectored, recombinant rabies cDNA (no live or killed rabies virus)
- Initial dose of 1.0 ml as early as 12 weeks of age
- Annual booster
- Can be administered simultaneously with other vaccines

**Recommended vaccination site – Right rear leg (“Rabies Right”)**

FeLV

Key Points
- Contagious disease with no sex or breed predisposition
- Transmission primarily via saliva, contaminated needles, surgical equipment, and blood transfusions
- Virus shed continuously by viremic cats, ill or not
- Kittens most susceptible but adults can also be infected
- Primarily targets lymphocytes, especially in bone marrow
- Potent immunosuppressive virus; increases susceptibility to secondary infections
- Solid tumors, usually lymphoma, develop in about 20% of persistently infected cats
- Interval between infection and clinical disease varies from weeks to years
- Vaccination, not treatment, is key to protecting cats from the consequences of FeLV infection

**PUREVAX® FeLV vaccine highlights**
- Protects against persistent FeLV antigenemia
- Nonadjuvanted, reducing risk of injection-site inflammation
- Canarypox virus-vectored, recombinant vaccination agent (contains no live FeLV virus)
- Initial dose of 0.25 ml at 9 weeks of age; second dose of 0.25 ml 3 weeks later
- Annual booster vaccination recommended in cats at risk
- Appropriate for revaccinating cats vaccinated with other types of FeLV vaccine
- Exclusive, needle-free, VETJET™ transdermal (TD) vaccination system
- VETJET™ transdermal vaccination system is the only approved delivery route
- No false positives on testing
- Produces a cell-mediated (T-cell) immune response
- Can be administered simultaneously with other vaccines

**Recommended vaccination site – Left rear leg (“Leukemia Left”)**
- In contrast to parenterally administered FeLV vaccine, the transdermal recombinant FeLV vaccine should be administered over the lateral left leg at the level of the mid-femur and caudal to the femur.

**REFERENCES**


**PUREVAX® injection-site inflammation in rats**

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S = saline; V = vaccine; M/F = sex; LN = normal lymph node; I = inflammation

**Cats positive for FeLV p27 antigen after challenge**

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<th>Cats</th>
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<td>Placebo (n=10)</td>
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* PUREVAX® FeLV

**Transdermal technology**

Developed by Merial® for vaccine administration through the skin without the use of a needle. VETJET™ transdermal vaccination technology disperses the antigen into the dermis, subcutis, and muscle, optimizing exposure to antigen-processing cells and avoiding inflammation.

Targets delivery of a reduced-volume dose (0.25 ml) for vaccination in less than 1 second without needles.

**PUREVAX® is a registered trademark of Merial, Duluth, GA.**

Content for this summary was compiled from materials provided by Dr. Richard B. Ford and research findings as reported in the cited references as well as data on file at Merial.