under field conditions with client-owned animals, it is possible that natural exposure to infective agents could have occurred without clinical signs of infection. In such cases, the titers measured in the study could be the result of exposure to the disease in addition to vaccinations during the course of the study.

Table 1. Geometric mean titer/number of dogs

<table>
<thead>
<tr>
<th>Time Since Last Vaccination (Months)</th>
<th>Geometric Mean Titer/Number of Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>12–18</td>
<td>149/39</td>
</tr>
<tr>
<td>19–24</td>
<td>462/21</td>
</tr>
<tr>
<td>25–30</td>
<td>465/62</td>
</tr>
<tr>
<td>31–36</td>
<td>385/42</td>
</tr>
<tr>
<td>37–42</td>
<td>417/22</td>
</tr>
<tr>
<td>&gt;48</td>
<td>453/11</td>
</tr>
</tbody>
</table>

REFERENCES:
6. Study 21484-60-01-004, Zoetis Inc.

Vanguard PLUS 5 L4 CV

Asterically hydrate the freeze-dried vaccine (Vanguard Plus 5 L4) with the accompanying vial of liquid vaccine (Vanguard CV), shake well, and administer. It is not advisable to use extra adjuvant for immunization of young dogs. A protective immune response may not be elicited if animals are including an infectious disease, are malnourished or parasitized, are stressed due to shipment or environmental conditions, are otherwise immunocompromised, or are exposed to viruses in combination with the vaccine. For veterinary use only.

U.S. Veterinary License No. 190

Zoetis

Kalamazoo, MI 49007, USA

Canine Distemper

- Adenovirus Type 2
- Coronavirus-Parainfluenza
- Parvovirus Vaccine

Modified Live and Killed Virus

Leptospira Canicola-Grippotyphosa-Icterohaemorrhagiae-Pomona Bacterin

For use in dogs only
SAFETY AND EFFICACY: Laboratory evaluation demonstrated that Vanguard Plus 5 L4 CV aided in preventing disease caused by CD, CAV-1, CAV-2, CPV, CPI, and leptospiruria caused by C. canicola, C. grippotyphosa, C.icterohemorrhagiae, and J. pomona, and that no significant immunologic interference existed among the vaccine fractions. Field safety trials conducted by Zoetis Inc. showed it to be safe in dogs as young as 6 weeks of age under normal usage conditions.

It has been demonstrated that CAV-2 vaccine cross-protects against ICH caused by CAV-1. In addition, the CAV-2 strain used in Vanguard vaccines has been selected specifically for freedom from oncogenic properties characteristic of adenoviruses.

Studies conducted at Zoetis Inc. demonstrated that the CAV-2 strain used in Vanguard vaccines not only protects against ICH, but against CAV-2 respiratory disease as well.1 Although conventional CAV-1 (JH) vaccines cross-protect against CAV-2, they may not prevent subclinical infection and spread of the CAV-2 agent. Canine adenovirus type-2 challenge virus was not increased from CAV-2-vaccinated dogs in tests conducted at Zoetis Inc.

The CPV fraction in Vanguard Plus 5 L4 CV was subjected to comprehensive safety and efficacy testing at Zoetis Inc. It was shown safe and essentially reaction-free in laboratory tests and in clinical trials under field conditions. Product safety was further demonstrated by a backpassage study that included oral administration of multiple doses of the vaccine strain to susceptible dogs, all of which remained normal. The CPV virus in Vanguard Plus 5 L4 CV shows a characteristic with other live CPV vaccine strains in that the vaccine virus may be present in the foci forming following administration. Although this CPV vaccine virus was found occasionally and in low titers in the feces of vaccinated dogs, testing demonstrated that the vaccine strain did not revert to virulence following 6 consecutive backpassages in susceptible dogs.

Research at Zoetis Inc. demonstrated that 3 doses of the vaccine with increased CPV virus titer can overcome serum neutralization (SN) titers associated with maternal antibody. Serum neutralization titers as low as 1:4 have been shown by others to interfere with active immunization using conventional modified live vaccines.2 A clinical trial was conducted with fifty 6-week-old puppies (25 vaccinates [SN titer range = 1:20–1:64] and 25 nonvaccinated controls [SN titer range = 1:64–1:128]). The group of vaccinates received 3 doses, with vaccinations administered 3 weeks apart beginning at 6 weeks of age. After 1 vaccination, 13/25 puppies exhibited a 4-fold or greater increase in CPV SN titer (hemoinhibition). Twelve of these 13 puppies had maternal SN titers ≤ 1:18 at the time of the first vaccination with the remaining puppy having an SN titer of 1:184. Another 9 puppies with initial SN titers between 1:16 and 1:256 seroconverted after the second vaccination. Their maternal antibody SN titers had declined to ≤ 1:16 at the time of the second vaccination. Similarly, the last 3 vaccinates, with initial SN titers of 1:128, seroconverted after the third vaccination, after their maternal antibody CPV titer dropped ≤ 1:16. Therefore, in this study, when 2 doses of vaccine were given beginning at 6 weeks of age, all 25 vaccinates, even those with the highest maternal antibody levels, became actively immunized (GM = 1:1176; range of SN titers = 128–4988). All 50 dogs were challenged 3 weeks after the third vaccination with a heterologous CPV challenge virus. Fourteen of 25 nonvaccinated control dogs died or showed illness severe enough to warrant euthanasia, while all 25 vaccinates remained essentially healthy. The high-titer, low-passage vaccine virus in Vanguard Plus 5 L4 CV is therefore highly immunogenic and capable of stimulating active immunity in the presence of maternal antibodies. The efficacy of the CVV fraction of Vanguard Plus 5 L4 CV was demonstrated in an extensive vaccination challenge study. Seven of 8-week-old puppies were vaccinated with Vanguard SCCV-4, boosted (at 17 weeks) with Vanguard SM (controls). All puppies received three 1-mL doses at 3-week intervals. Three weeks following the third vaccination, puppies were challenged with a virulent strain of CVV CV-6. Clinical observations, temperatures, weights, and blood parameters were monitored for 21 days following infection. CVV vaccines demonstrated a reduction in the occurrence of diarrhea and amount of virulent CVV shed when compared to controls. At 21 days postchallenge, fluorescent antibody staining for virulent CVV of small intestinal sections demonstrated a significant reduction (P < 0.05) in detectable CVV antigen between CVV vaccinates and controls.

DURATION OF SEROLOGIC RESPONSE: In dogs vaccinated and boosted as puppies, and then vaccinated again approximately 1 year later, revaccination with Vanguard Plus 5 L4 CV has been demonstrated (under field conditions) to result in serum antibody titers that persist for 12–48 months against CPV virus (serum neutralization [SN] titer = 1:128). CAV-1 (SN ≥ 1:18), CAV-2 (SN ≥ 1:18), CPI virus (SN ≥ 1:18), and CPV (hemagglutination–inhibition [HAI] titer ≤ 1:80). Protection against infectious agents involves a complex interplay between humoral immunity, cellular immunity, or a combination of both. The purpose of vaccination is to induce effector cells in both these arms of the immune system. During the process, long-term immunity in the form of memory T and B lymphocytes is produced. Memory cells and antibodies interact to provide protection to an animal challenged with the same pathogens at a later date. Depending on the vaccine and the disease, antibodies may be produced that provide complete protection from disease and prevent or reduce shedding. In other cases, antibodies may play a minor or ineffective role and protection from disease relies on systemic, local cellular immunity and/or local antibody production. The role of sustained serological titers in the prevention of disease has not been confirmed.

In companion animals, immunological response to infection or vaccination has generally been evaluated by measuring the level of antibodies in serum and correlating these with protection or susceptibility. For the diseases caused by canine distemper virus, canine parvovirus,4,5 canine adenovirus and leptospiruria,4 evaluation of antibody titers may be a valuable diagnostic indicator to determine when revaccination may be needed. For other diseases, a serological response has not been identified that correlates with protection.

Practical knowledge of the disease, the vaccine, and the patient, along with serological test results when appropriate, is paramount in making the best recommendation for a vaccination protocol for a specific animal.

The duration and character of the immune response to the viral antigens of Vanguard and/or Vanguard Plus were determined in a multi-center serology study involving 47 small animal veterinary clinics located in the United States (44) and Canada (3). Three hundred twenty-two male and female intact and neutered dogs of various ages, breeds, weights, lifestyles and time since last vaccination were enrolled in the study. Dogs were required to be healthy, greater than 2 years old with no history of disease due to CVV, CPI, CAV-1, CAV-2, or CPI and must not have been vaccinated for 12–48 months or longer. Additionally, dogs must have received at least a single vaccination series approximately 2–7 weeks apart as a puppy and a booster vaccination approximately 8–16 months later. All previously administered vaccines were Vanguard products. A blood sample was collected from each dog and serum submitted to Cornell Veterinary Diagnostic Laboratory for determination of CDV (SN), CPI (HAI) titer, CAV-1 (SN), CAV-2 (SN), and CPI (SN). The samples were sent to a single diagnostic laboratory, thus ensuring a standardized test and methodology. As shown in the table below, elevated geometric mean titers were sustained for 12 to 48 months after the last booster. Since the study was conducted...