**Parvovirus Vaccine**

**Modified Live Virus**

For use in dogs only

**PRODUCT DESCRIPTION:** Vanguard Plus CPV is for vaccination of healthy dogs 6 weeks of age or older for the prevention of canine parvovirus enteritis caused by canine parvovirus (CPV). Vanguard Plus CPV contains a strain of CPV attenuated by low passage on an established canine cell line. The vaccine is high titer (≥ 10^12.1 TCID50/dose) and was attenuated by low passage (≤ 150) from the canine isolate with a maximum of 2 additional passages allowed for production on the canine cell line which gives it the immunogenic properties capable of overriding maternal antibody interference at the levels indicated below. Some puppies in the field may have higher levels of maternal antibodies than those evaluated in our pivotal efficacy study. Vanguard Plus CPV is packaged in liquid form.

**SAFETY AND EFFICACY:** Vanguard Plus CPV was subjected to comprehensive safety and efficacy testing at Zoetis Inc. Extensive field safety trials conducted by Zoetis Inc. showed it to be safe and reaction-free in dogs as young as 6 weeks of age under normal usage conditions.

Product safety was further demonstrated by a backpassage study which included oral administration of multiple doses of the vaccine strain to susceptible dogs, each of which were monitored for reaction-free status.

**PRODUCT SAFETY:** Safety was further demonstrated by a backpassage study which included oral administration of multiple doses of the vaccine strain to susceptible dogs. Product safety was further demonstrated by a backpassage study which included oral administration of multiple doses of the vaccine strain to susceptible dogs and three weeks of age to ensure that the CPV vaccine strain in the vaccine virus may be present in the feces following administration. Although this CPV vaccine virus was found occasionally and in low titer in the feces of vaccinated dogs, testing demonstrated that the vaccine strain did not revert to virulence following 6 backpassages or become acceptable to 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 anti body. Serum neutralization titers as low as 1:4 have been shown to be effective in interference with active immunization using conventional modified live vaccines. A clinical trial was conducted with 60-week-old puppies [35 vaccines (SN titer range ≤ 2–298) and 25 nonvaccinated controls (SN titer range 4–1204)]. The group of vaccinated puppies received 3 doses, with vaccinations administered 3 weeks apart beginning at 6 weeks of age. After 1 vaccination, 13/35 puppies exhibited a 4-fold or greater increase in CPV SN titer (seroconversion). Twelve of these 13 puppies had maternal SN titers ≤ 1:4 at the time of the first vaccination with the remaining puppy having an SN titer of 1:84. 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 ≤ 1:4 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 ≤ 400. Therefore, in this study, when 3 doses of vaccine were given beginning at 6 weeks of age, all 25 vaccinated puppies, even those with the highest maternal antibody levels, became actively immunized (BM: ≥ 1:1176), range of SN titers 128–4096. 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 vaccinated remained essentially healthy. The high titer, low passage CPV vaccine strain in Vanguard Plus CPV is therefore highly immunogenic and capable of stimulating active immunity in the presence of maternal antibodies.

**DURATION OF SEROLOGIC RESPONSE:** In dogs vaccinated and boosted as puppies, and then vaccinated again approximately 1 year later, revaccination with Vanguard Plus CPV has been demonstrated (under field conditions) to result in serum antibody titers that persist for 12–48 months against CPV (hemagglutination inhibition [HAI] titer range 1:100–1:1,800). Protection against infectious agents involves a complex interplay between humoral immunity, cellular immunity, or a combination of both. The purpose of vaccination is to stimulate specific antibodies 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 pathogen 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, canine adenovirus and leptospirosis, evaluation of antibody tilters 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 antibody titer range appropriate to a species, 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 Vanguard Plus have been determined in a multi-center serology study involving 47 small animal veterinary clinics located in the United States (44) and Canada (3). Twenty-six to 24-month-old 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 CDV, CPV, CAV-1, CAV-2, or CMV and must not have been vaccinated for 12–48 months or longer. Additionally, dogs must have received at least a priming vaccination series approximately 3–7 weeks apart as a puppy and a booster vaccination approximately 8–10 months prior to vaccination. This product has been shown to be efficacious in progeny of vaccinated animals. A protective immune response cannot be elicited if animals are incubating an infectious disease, are malnourished or parasitized, are stressed due to shipment or anxiety, or are otherwise compromised or the vaccine is not administered in accordance with label instructions.

**REFERENCES:**


9. Biologic Testing Laboratory.”

10. The role of sustained serological titers in the prevention of disease has not been confirmed.

11. The duration and character of the immune response to the viral antigens of Vanguard and Vanguard Plus have been determined in a multi-center serology study involving 47 small animal veterinary clinics located in the United States (44) and Canada (3).

12. Twenty-six to 24-month-old 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 CDV, CPV, CAV-1, CAV-2, or CMV and must not have been vaccinated for 12–48 months or longer. Additionally, dogs must have received at least a priming vaccination series approximately 3–7 weeks apart as a puppy and a booster vaccination approximately 8–10 months prior to vaccination.

13. Depression of the growth rate may occur with a severe case of CDV. The affected dogs may require replacement fluids and electrolytes, and in some cases, may require corticosteroids.

14. The duration and character of the immune response to the viral antigens of Vanguard and Vanguard Plus have been determined in a multi-center serology study involving 47 small animal veterinary clinics located in the United States (44) and Canada (3).
PRODUCT DESCRIPTION: Vanguard Plus CPV is for vaccination of healthy dogs 6 weeks of age or older for the prevention of canine parvovirus (CPV). Vanguard Plus CPV contains a strain of CPV obtained by attenuation of dog cell line from the canine isolate with a maximum of 2 additional passages allowed for production on the canine cell line which gives it the immunogenic properties capable of overriding maternal antibody interferences at the levels indicated below. Some puppies in the field may have higher levels of maternal antibodies than those evaluated in our pivotal efficacy study. A high-titer, reduced-passage CPV is packaged in liquid form.

SAFETY AND EFFICACY: Vanguard Plus CPV was subjected to comprehensive safety and efficacy testing at Zoetis Inc. Extensive field safety trials conducted by Zoetis Inc. showed it to be safe and reaction-free in dogs as young as 8 weeks of age under normal usage conditions. Product safety was further demonstrated by a backpassage study which included oral administration of multiple doses of the vaccine strain to susceptible dogs, all of which remained normal. Vanguard Plus CPV vaccine virus shares a characteristic with VCP vaccine strains in that the vaccine virus may be present in the feces following vaccination. Although this CPV vaccine virus was found occasionally and in low titers in the feces of vaccinated dogs, testing demonstrated that the vaccine master seed 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 anti body. Serum neutralization titer as low as 1:4 have been shown by others to interfere with active immunization using conventional modified live vaccines. A clinical trial was conducted with fifty 6-week-old puppies [25 vaccines (SN titer range 1:2–528) and 25 nonvaccinated controls (SN titer range 1:6–1024)]. The group of vaccines 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 (seroconversion). Twelve of these 13 puppies had maternal SN titers ≤ 1:16 at the time of the first vaccination with the remaining puppy having an SN titer of 1:84. Another 9 puppies with initial SN titers between 1:16 and 1:256 seroconverted after the second vaccination. Their maternal antibody SN titer had declined to ≤ 1:4 at the time of the second vaccination. Similarly, the last 3 vaccinates, with initial SN titer of 1:128, seroconverted after the third vaccination, after their maternal antibody CPV titer dropped ≤ 1:64. Therefore, in this study, when 3 doses of vaccine were given beginning at 6 weeks of age, all 25 vaccines, even those with the highest maternal antibody levels, became actively immunized (IM = 1:1776), range of SN titers 128–4096. All 36 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 vaccinated remained essentially healthy. The high-titer, low-passage vaccine virus in Vanguard Plus CPV is therefore highly immunogenic and capable of stimulating active immunity in the presence of maternal antibodies.

DURATION OF SEROLOGIC RESPONSE: In dogs vaccinated and boosted as puppies, and then vaccinated again approximately 1 year later, revaccination with Vanguard Plus CPV has been demonstrated (under field conditions) to result in serum antibody titers that persist for 12–18 months against CPV (hemagglutination inhibition [HAI] titer range 1:80–1:1,800).

Protection against infections 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 is developed in the form of memory T and B lymphocytes is produced. Memory cells and antibodies interlock to provide protection to an animal challenged with the same pathogen 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, canine adenovirus and leptospirosis, evaluation of antibody titer 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 serologic 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 Vanguard Plus® vaccines have been determined in a multi-center serology study involving 47 small animal veterinary clinics located in the United States (46) and Canada (1). Three hundred twenty-two male and female (intact and neutered) dogs of various ages, breeds, weights, lifespans and time since last vaccine administration were entered in the study. Dogs were required to be healthy, greater than 2 years old with no history of disease due to CPV, CAV-1, CAV-2, or CPV and must not have been vaccinated for 12–48 months or longer. Additionally, dogs must have received at least a priming vaccination series approximately 3–7 weeks apart as a puppy and a booster vaccination approximately 8–18 months later. These products are not intended to be used in pregnant bitches. If used in pregnant bitches, the vaccine is not considered a teratogen. All vaccine products are non-pathogenic, non-virulent, modified live Vanguard products. A blood sample was collected from each dog and serum submitted to Cornell Veterinary Diagnostic Laboratory for determination of CPV (SN), 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.

<table>
<thead>
<tr>
<th>Vaccine Product</th>
<th>Description</th>
<th>Code</th>
<th>Use incombination with</th>
<th>USES</th>
<th>Number of vaccinates</th>
<th>Geometric Mean Titer</th>
<th>Level of Protection</th>
<th>Protection Failure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanguard Plus CPV</td>
<td>Vaccine for Dogs only</td>
<td>Vanguard Plus CPV</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Since the study was conducted under field conditions, it is possible that natural exposure to infectious agents could have occurred without complete control. In such cases, the results measured in the study could be the result of exposure to the disease in addition to vaccinations during the course of the study.

REFERENCES:
5. W. W D: 21564-00-01-004, Zoetis Inc.
7. Technical inquiries should be directed to Zoetis Inc. Veterinary Services, (888) 963-8471 (USA), (800) 461-0917 (Canada).
8. For veterinary use only.
9. U.S. Veterinary License No. 190

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