

## Canine Distemper-Adenovirus Type 2-Parainfluenza-Parvovirus Vaccine

### **Modified Live Virus**

*For use in dogs only*

### Vanguard® Plus 5

**PRODUCT DESCRIPTION:** Vanguard Plus 5 is for vaccination of healthy dogs 6 weeks of age or older as an aid in preventing canine distemper caused by canine distemper (CD) virus, infectious canine hepatitis (ICH) caused by canine adenovirus type 1 (CAV-1), respiratory disease caused by canine adenovirus type 2 (CAV-2), canine parainfluenza caused by canine parainfluenza (CPI) virus, and canine parvoviral enteritis caused by canine parvovirus (CPV). Vanguard Plus 5 contains attenuated strains of CD virus, CAV-2, CPI virus, and CPV propagated on an established canine cell line. The CPV fraction is high titer ( $>10^{7.0}$  TCID<sub>50</sub>/dose) and was attenuated by low passage (35 passes from the canine isolate with a maximum of 2 additional passes allowed for production) on the canine cell line which gives it the immunogenic properties capable of overriding maternal antibody interference at the levels indicated in Table 2. Some puppies in the field may have higher levels of maternal antibodies than those evaluated in our pivotal efficacy study. Vanguard Plus 5 is packaged in freeze-dried form with inert gas in place of vacuum.

**DISEASE DESCRIPTION:** CD is a universal, high-mortality viral disease with variable manifestations. Approximately 50% of nonvaccinated, nonimmune dogs infected with CD virus develop clinical signs, and approximately 90% of those dogs die.<sup>1</sup> ICH, caused by CAV-1, is a universal, sometimes fatal, viral disease of dogs characterized by hepatic and generalized endothelial lesions. CAV-2 causes respiratory disease which in severe cases may include pneumonia and bronchopneumonia. CPI is a common viral upper respiratory disease. Uncomplicated CPI may be mild or subclinical, with signs becoming more severe if concurrent infection with other respiratory pathogens exists. CPV infection results in enteric disease characterized by sudden onset of vomiting and diarrhea, often hemorrhagic. Leukopenia commonly accompanies clinical signs. Susceptible dogs of any age can be affected, but mortality is greatest in puppies. In puppies 4–12 weeks of age CPV may occasionally cause myocarditis that can result in acute heart failure after a brief and inconspicuous illness. Following infection many dogs are refractory to the disease for a year or more. Similarly, seropositive bitches may transfer to their puppies CPV antibodies which can interfere with active immunization of the puppies through 16 weeks of age.

**SAFETY AND EFFICACY:** Laboratory evaluation demonstrated that Vanguard Plus 5 immunized dogs against CD, ICH, CAV-2 respiratory disease, CPI, and CPV, and that no immunologic interference existed among the vaccine fractions. Extensive field safety trials conducted by Pfizer Animal Health showed it to be safe and reaction-free 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. The CAV-2 fraction in Vanguard vaccines is used as a replacement for CAV-1 because it has significant advantages. Some CAV-1 vaccines may produce undesirable reactions, including persistent kidney infections, uveitis, and corneal opacity (“blue eye”), which have not been reported after vaccination with CAV-2.<sup>2</sup> In addition, the CAV-2 strain used in Vanguard vaccines has been specially selected for freedom from oncogenic properties characteristic of adenoviruses.

Studies conducted at Pfizer demonstrated that CAV-2 not only protects against ICH, but against

CAV-2 respiratory disease as well.<sup>3</sup> Although conventional CAV-1 (ICH) 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 recovered from CAV-2-vaccinated dogs in tests conducted at Pfizer.

The CPV fraction in Vanguard Plus 5 was subjected to comprehensive safety and efficacy testing at Pfizer. It was shown safe and reaction-free in laboratory tests and in clinical trials under field 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 whom remained normal. The CPV virus in Vanguard Plus 5 shares a characteristic with other live CPV vaccine strains in that the vaccine virus may be present in the feces 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 master seed did not revert to virulence following 6 consecutive backpassages in susceptible dogs.

Research at Pfizer 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.<sup>4,5</sup> A clinical trial was conducted with fifty 6-week-old puppies [25 vaccinates (SN titer range <2–256) and 25 nonvaccinated controls (SN titer range 4–1024)] (Table 1). 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 (seroconversion) (Table 2). Twelve of these 13 puppies had maternal SN titers  $\leq$ 1:16 at the time of the first vaccination with the remaining puppy having an SN titer of 1:64. 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  $\leq$ 1:64 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  $\leq$ 1:64. Therefore, in this study, when 3 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 128–4096). 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 vaccinates remained essentially healthy. The high-titer, low-passage vaccine virus in Vanguard Plus 5 is therefore highly immunogenic and capable of stimulating active immunity in the presence of maternal antibodies.

**Table 1.** Initial Serum Neutralization (SN) Titers of Vaccinates and Controls

SN Titers	# Vaccinates Included	# Controls Included
<1:2	3	0
1:4	4	3
1:8	1	3
1:16	4	1
1:32	2	5
1:64	3	1
1:128	6	3
1:256	2	3
1:512	0	5
1:1024	0	1

**Table 2.** Postvaccination Serum Neutralization (SN) Titers Geometric Mean (Range)<sup>a</sup>

Groups	N	Pre-	Postvaccination		
		vaccination	1	2	3 <sup>b</sup>
All Vaccinated Dogs	25	1:24 (<2–256)	1:108 (8–1024)	1:605 (8–4096)	1:1176 (128–>4096)
Responders Post 1st Vaccination	13	1:6 (<2–64)	1:460 (64–1024)	1:1745 (256–4096)	1:1410 (256–4096)
Responders Post 2nd Vaccination	9	1:87 (16–256)	1:20 (8–64)	1:376 (256–1024)	1:1625 (256–4096)
Responders Post 3rd Vaccination	3	1:128 (128)	1:32 (16–64)	1:25 (8–64)	1:203 (128–256)
Nonvaccinated Control Dogs	25	1:64 (4–1024)	1:9 (<2–64)	1:3 (<2–64)	<1:2 (<2–4)

<sup>a</sup> Dogs were vaccinated at 6, 9, and 12 weeks of age.

<sup>b</sup> Pre-challenge SN titers

#### **DIRECTIONS:**

1. *General Directions:* Vaccination of healthy dogs is recommended. Aseptically rehydrate the freeze-dried vaccine with the sterile diluent provided, shake well, and administer 1 mL subcutaneously or intramuscularly.
2. *Primary Vaccination:* Healthy dogs 6 weeks of age or older should receive 3 doses, each administered 3 weeks apart.
3. *Revaccination:* Annual revaccination with a single dose is recommended.

#### **PRECAUTIONS:**

1. Store at 2°–7°C. Prolonged exposure to higher temperatures and/or direct sunlight may adversely affect potency. Do not freeze.
2. Use entire contents when first opened.
3. Sterilized syringes and needles should be used to administer this vaccine. Do not sterilize with chemicals because traces of disinfectant may inactivate the vaccine.
4. Burn containers and all unused contents.
5. Contains penicillin and streptomycin as preservatives.
6. Vaccination of pregnant bitches should be avoided.
7. As with many vaccines, anaphylaxis may occur after use. Initial antidote of epinephrine is recommended and should be followed with appropriate supportive therapy.
8. This product has been shown to be efficacious in healthy animals. A protective immune response may not be elicited if animals are incubating an infectious disease, are malnourished or parasitized, are stressed due to shipment or environmental conditions, are otherwise immunocompromised, or the vaccine is not administered in accordance with label directions.

#### **REFERENCES:**

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4. O'Brien SE, Roth JA, Hill BL: Response of pups to modified-live canine parvovirus component in a combination vaccine. *JAVMA* 188:699–701, 1986.

5. O'Brien SE: Serologic response of pups to the low-passage modified-live canine parvovirus-2 component in a combination vaccine. *JAVMA* 204:1207–1209, 1994.

Technical inquiries should be directed to Pfizer Animal Health Technical Services, (800) 366-5288 (USA), (800) 461-0917 (Canada).

For veterinary use only

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Pfizer Animal Health  
Exton, PA 19341, USA

Div. of Pfizer Inc  
NY, NY 10017

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