Fort Dodge Animal Health
Division of Wyeth
9401 Indian Creek Parkway
Suite 1500
Overland Park, KS 66210

Steve Connell, DVM
Director
Professional Services
(800) 533-8536

July 22, 2002

Dear Doctor:

Thank you for purchasing *ProHeart 6* (moxidectin), Fort Dodge Animal Health's innovative product for six-month protection against heartworm infection in dogs. The purpose of this letter is to provide you with some new information regarding a recently approved label indication for *ProHeart 6,* as well as a review of the adverse events that have been reported for the product during its introduction into the marketplace. This update on the performance of *ProHeart 6* reflects our desire to share information that has been learned about the product after its first year on the market.

ProHeart 6 was launched in June 2001 with an indication to prevent canine heartworm disease caused by *Dirofilaria immitis* for six months, and to treat existing larval and adult stages of the canine hookworm, *Acylostoma caninum.* As a result of ongoing research on the product, the Center for Veterinary Medicine (CVM) recently approved an additional label indication for *ProHeart 6,* treatment of existing larval and adult stages of canine hookworm, *Uncinaria stenocephala.* The addition of *U. stenocephala* to the *ProHeart 6* label broadens the protection provided against canine hookworm infection, and results in a product that more closely meets the needs of practicing veterinarians.

Along with the new indication, a second label change will appear in the "Adverse Reactions" section of the product labeling, and is based on the reporting patterns received from the field. With over six million doses of *ProHeart 6* (moxidectin) sold during the first year, we have seen a number of reported reactions that were not seen in pre-approval clinical studies. This is typical in cases of a new product after introduction to a wide population base. Through our work with CVM, a new label statement has been approved for *ProHeart 6* describing our post-approval experience. The new statement being added is as follows:

Post-Approval Experience: although not all adverse reactions are reported, the following reactions are based on voluntary post-approval drug experience reporting: anaphylaxis/toid reactions, depression/lethargy, urticaria, and head/facial edema. As with anaphylaxis/toid reactions resulting from the use of other injectable products, standard therapeutic intervention should be initiated immediately.

Since introduction, we have received and tracked reports from practicing veterinarians regarding adverse events subsequent to the clinical use of *Proheart 6.* A review of these reports is presented below and includes events observed when *ProHeart 6* was administered alone, as well

as those observed when given with concurrent medications. The numbers presented are unfiltered, as reported to CVM, which include observations subsequently determined to be unrelated to product administration.

During the first twelve months of product use, 105 reports of site reactions post administration (.0016% of doses sold into veterinary clinics) have been received. These events are predominantly swelling, pain, and/or pruritos that are observed post administration. The vast majority are self-limiting in nature, though selected cases have been treated with anti-inflammatories, and in some cases, antibiotics.

A total of 946 reports of allergic responses post administration (.015%) have been received. As with vaccines, this category represents the most frequently reported event. Most of these reactions are mild and have responded to standard medical intervention. Some, however, have been more severe, including a small percentage of anaphylaxis cases. The most frequently reported effects have been vomiting and diarrhea, followed by angioedema and/or facial swelling, urticaria and gastrointestinal symptoms. Other less common events include ataxia, weakness, dyspnea, pale mucous membranes, lethargy and fever.

A total of 685 reports of illness post administration (.011%) have also been received. This category encompasses a wide variety of reports that are received in a broad timeframe (from one day to several months) post administration. There is overlap with the allergic events where both allergy and additional symptoms were recorded. The most frequently reported signs have been vomiting and diarrhea at variable time frames post administration, seizures or other neurological signs and lethargy. Other rare, but more serious reports, include erythema multiforme in 3 cases and autoimmune hemolytic anemia in a low number of patients, most of whom had received vaccines concurrently.

No common predisposing factors have been identified at this time. In rare situations, death has been associated with some of the adverse reactions listed above. While there reactions appear to be idiosyncratic, we want to bring these to your attention so that you may take appropriate measures in the event you encounter one. In the case of allergic reactions, prompt therapy using standard medical intervention (e.g. antihistamine, corticosteroids and fluids as needed; epinephrine as deemed appropriate on an individual case basis) has been found to be curative in most instances.

As is the case when prescribing any medication, careful examination of the dog prior to administration, consideration of appropriate laboratory tests in dogs that may have chronic conditions, and advice to the owner to watch for signs of drug intolerance is good medical practice. If a drug reaction or intolerance is suspected, examine the patient, provide the necessary supportive therapy, and contact Fort Dodge Animal Health Professional Services veterinarians at 1-800-533-8536.

As a manufacturer of novel innovative products, we feel it is important to provide timely information regarding label changes and current information on post-approval experiences. Millions of doses of *ProHeart 6* (moxidectin) have been used safely and effectively during its first year in the market, and we trust that this has been your experience as well. We will continue to provide you with any pertinent information regarding *ProHeart 6.*

Thank you for your attention regarding these important issues. You are encouraged to contact one of our Professional Services veterinarians at the number listed above if you have any additional questions or concerns.

Sincerely,

Stephen A. Connell,
DVM Director,
Professional Services
Fort Dodge Animal Health

ProHeart 6 *is generally well tolerated. Use with caution in sick, debilitated, or underweight animals. A small percentage of dogs showed mild, transient swelling or itching at the injection site. While rare, digestive, neurological or hypersensitivity reactions may occur. Read the attached package insert for more information. To obtain additional information including a copy of the product labeling, visit the website at www.proheart6dvm.com or call 1-800-685-5656.*