BACKGROUND

CANINE INFLUENZA VIRUS (CIV) and
NOBIVAC® CANINE FLU H3N8 VACCINE

I. CANINE INFLUENZA VIRUS (CIV)

The following information on Canine Influenza Virus (CIV) is based primarily on the U.S. Centers for Disease Control and Prevention (CDC), Key Facts About Canine Influenza (Dog Flu) 1.

What is canine influenza (dog flu)?

Dog flu is a contagious respiratory disease in dogs caused by a specific Type A influenza virus. CIV is an influenza A H3N8 virus (not a human flu virus). It spreads among dogs.

How long has canine influenza been around?

The H3N8 equine influenza virus has been known to exist in horses for more than 40 years. In 2004, however, cases of an unknown respiratory illness in dogs (initially greyhounds) were reported. Scientists believe that this virus jumped species (from horses to dogs) and has now adapted to cause illness in dogs and spread efficiently among dogs. This is now considered a new dog-specific lineage of H3N8. In September of 2005, this virus was reported by Dr. Cynda Crawford, University of Florida College of Veterinary Medicine, and Dr. Edward J. Dubovi, Cornell University College of Veterinary Medicine, along with their colleagues, as “a newly emerging pathogen in the dog population” in the United States. 2

What are the symptoms of CIV infection in dogs?

The symptoms of this illness in dogs are cough, runny nose and fever. A small proportion of dogs, however, can develop severe disease.

CIV cannot easily be distinguished from other causes of respiratory infection based on clinical signs alone. It is often mistaken for *Bordetella* (kennel cough) and other respiratory infections caused by pathogens in the canine infectious respiratory disease (CIRD) complex because of shared clinical signs. CIRD complex is a relatively new term used to describe respiratory disease in dogs that may be caused by a number of viral or bacterial pathogens. Some of the better-known pathogens are distemper virus, adenovirus type 2, parainfluenza, canine herpesvirus and *Bordetella*.

How serious is CIV infection in dogs?

CIV is a relatively new cause of disease in dogs and nearly all dogs who are naïve to the virus are susceptible to infection. About 80 percent of dogs will have a mild form of disease. About 20 percent of infected dogs will show no clinical signs, while 10 – 20 percent of infected dogs may progress to a more severe form of the disease. Severe illness is characterized by the onset of pneumonia. The number of dogs infected with this disease that die is up to eight percent.

How does dog flu spread?

Canine influenza virus can be spread by direct contact with respiratory secretions from infected dogs, through the air via a cough or sneeze, and by contact with

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contaminated objects such as dog bowls and clothing, or by people moving between infected and uninfected dogs. Therefore, dog owners whose dogs are coughing or showing other signs of respiratory disease should not participate in activities or bring their dogs to facilities where other dogs can be exposed to the virus. Clothing, equipment, surfaces and hands should be cleaned and disinfected after exposure to dogs showing signs of respiratory disease.

**Is there a test for canine influenza?**

Testing to confirm canine influenza virus infection is available at veterinary diagnostic centers. A nasal swab test can be taken if the dog is seen within a day or two of the onset of signs. The timing of diagnostic testing is critical because there is only a short timeframe in which the virus isolation is successful.

After that, the only practical way to confirm a diagnosis is with a two-sample blood test, the first collected while the animal is sick and the second two to three weeks later.

**How is canine influenza treated?**

Not all dogs with CIV require therapeutic intervention. Therapy relies mainly on supportive care while the viral infection runs its course. There is little evidence to support the use of antitussives for reducing frequency and duration of coughing. Antibiotics are indicated for dogs with secondary bacterial infections evidenced by fever, productive cough, purulent nasal discharge or pneumonia.

**Where has canine influenza occurred?**

Outbreaks have occurred in shelters, kennels, dog day-care centers, veterinary clinics, dog tracks and other facilities in Florida, Pennsylvania, New York, New Jersey, Colorado, Connecticut, Delaware, Virginia and elsewhere. Cases have been identified in 37 states and the District of Columbia.6,7,8

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What is the risk to humans from canine influenza virus?

There is no evidence that this virus infects humans. Not a single human case has been reported. CDC and its partners continue to monitor the H3N8 influenza virus (as well as other animal influenza viruses) along with instances of possible human exposure to these viruses very closely.

Where can I find more information on canine influenza virus?

More information on canine influenza in pet dogs can be found in this article: Influenza A Virus (H3N8) in Dogs with Respiratory Disease, Florida in Emerging Infectious Diseases.\(^9\)

The following websites provide additional information about canine influenza and infection control practices:

- Key Facts About Canine Influenza (Dog Flu)
- Cornell University College of Veterinary Medicine – [www.diaglab.vet.cornell.edu](http://www.diaglab.vet.cornell.edu)
- The Center for Food Security & Public Health, Iowa State University, College of Veterinary Medicine – [http://www.cfsph.iastate.edu/Factsheets/pdfs/canine_influenza.pdf](http://www.cfsph.iastate.edu/Factsheets/pdfs/canine_influenza.pdf)
- [www.doginfluenza.com](http://www.doginfluenza.com) (a Merck Animal Health site)

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II. NOBIVAC® CANINE FLU H3N8 VACCINE

Nobivac® Canine Flu H3N8, the first vaccine for canine influenza virus (CIV), was granted full licensure on June 4, 2010.

Why was the vaccine developed?

The vaccine was developed to provide more comprehensive respiratory protection for dogs, specifically to curb the spread of CIV, which has now been diagnosed in 37 states and the District of Columbia.

In addition, in November 2006, the American Veterinary Medical Association (AVMA) Executive Board issued the following statement: “The AVMA believes there is urgent need for an effective canine influenza virus vaccine to improve the health and welfare of animals and reduce the financial impacts of canine influenza.” (http://www.avma.org/issues/policy/canine_influenza.asp)

What do studies show about the vaccine’s safety and effectiveness?

Nobivac® Canine Flu H3N8, an inactivated virus vaccine, has been shown to significantly decrease the signs, severity and spread of CIV infection. The vaccine reduces the duration and severity of coughing, protects against the formation and severity of lung lesions and significantly reduces the duration and degree of viral shedding, the period when the disease is contagious. The vaccine’s safety was confirmed in a 746-dog field study, with over 30 breeds, age six weeks to 10 years, participating in the testing. Safety and efficacy were further confirmed after a year of clinical use in close to half a million dogs.

The Company has submitted data to the USDA on field experience that shows the vaccine is well-tolerated. Adverse events reported since the 2009 approval are comparable to those seen for other canine vaccines.

Which dogs should be vaccinated against CIV?

Because CIV is a new disease, virtually every dog not previously exposed to the virus will become infected. Many dogs are candidates for the vaccine because of routine contact with other dogs who may be carrying the virus, congregating in

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10 Data on file at Merck Animal Health
such places as dog day-care, veterinary clinics, boarding kennels, breeding kennels, dog shows, training settings, shelters, adoption centers, rescue settings, pet shops and other locations. In addition, dogs that travel with families, particularly to endemic areas, and those belonging to animal healthcare personnel are susceptible.

The vaccine gives veterinarians one more tool in providing their canine patients with more comprehensive respiratory protection. In addition to canine influenza, there are other causes of canine cough, such as *Bordetella*, or kennel cough. The risk factors are the same for both diseases – close contact and closed environments. In addition, *Bordetella* and CIV are difficult to differentiate in early stages because initial symptoms are similar and diagnostic confirmation of CIV can take up to two weeks.\(^{11}\)

**What if a dog has CIV? Should it be vaccinated?**

The vaccine should be given to healthy dogs, six weeks of age or older.

**How is it administered?**

The vaccine is given by subcutaneous (under the skin) injection in two doses, two to four weeks apart.

**What are the possible side effects?**

There were no side effects in the vaccine field safety trial, which included 746 dogs of various ages and breeds. As with any vaccine, allergic reactions may occur in a small percentage of animals. Adverse events reported since the 2009 conditional license approval are comparable to those seen for other canine vaccines.

Can the vaccine cause dogs to get CIV?

No. The vaccine cannot cause the disease because it is made with inactivated virus.

How often should the vaccine be given?

Every year. It is recommended that the vaccine be administered annually along with the *Bordetella*, canine parainfluenza and adenovirus type 2 vaccines to provide more comprehensive protection against canine infectious respiratory diseases.

Is there a particular time of year when it should be given?

The CIV vaccine can be given at any time. Unlike human flu, CIV is not seasonal, and dogs are vulnerable year-round.

Are there new strains of CIV each year, as is the case in human flu?

New strains have not been detected.

Does the CIV vaccine protect against other animal influenzas, such as swine, avian or equine?

The vaccine is specific to dog influenza.

Does the CIV vaccine protect against other infections?

Nobivac® Canine Flu H3N8 has been shown to significantly reduce the risk for pneumonia from the canine influenza virus. Research has also now demonstrated that Nobivac® Canine Flu H3N8 can lessen the severity of another respiratory pathogen, *Strep equi* subsp *zooepidemicus*, a common secondary invader, in cases of dual infections.¹²

In a recent study at the University of Wisconsin, it was demonstrated that clinical disease and lung lesions were more severe in a dual infection compared with

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¹²Larson, LJ, et al., Clinical and Vaccine Immunology, Vol 18, No. 4, April 2011, pp. 559-564.
infection with either CIV alone or *Strep equi* subsp. *zooepidemicus* alone. Of even greater significance, Nobivac® Canine Flu H3N8 reduced the severity of respiratory disease in dogs that were co-challenged with canine influenza virus and *Strep equi* subsp *zooepidemicus*.

**Is Merck Animal Health developing flu vaccines for any other animals?**

Merck Animal Health is the leader in equine flu vaccination with Flu-Alert®, a unique, proprietary intranasal modified live equine influenza vaccine, as well as inactivated equine influenza options in the Prestige® and Encevac® injectable vaccine lines. MaxiVac Excell® 3 killed flu virus vaccine is used as an aid in the prevention of disease associated with swine influenza subtypes H1N1 and H3N2. Nobilis® influenza H7N1 is a licensed European vaccine to protect birds against avian influenza.

**Who developed the vaccine and why?**

The vaccine was developed by research scientists at Merck Animal Health, a leader in respiratory disease prevention and treatment, as a response to the growing incidence of outbreaks and a call for the vaccine from the AVMA.

**Who conducted the studies? Where were they done? Are the results published?**

The studies were conducted by Merck Animal Health. The challenge study was published in Veterinary Therapeutics in Fall 2009. Additional publications are scheduled for 2010.

**Where can veterinarians and animal care professionals go for more information?**

Veterinarians may contact their Merck Animal Health representative or visit www.doginfluenza.com or www.merck-animal-health-usa.com.

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