An Update on Canine Influenza Virus Vaccine Options

***John A. Ellis**, DVM, PhD, DACVP, DACVM (Immunology, Virology)*
University of Saskatchewan Western College of Veterinary Medicine, Saskatoon, Saskatchewan, Canada

Abstract

Group A influenza viruses exist as many serotypes and many strains within serotypes. There are 2 serotypes of canine influenza virus (CIV): H3N2 and H3N8. Currently in North America, only variants of CIV H3N2 are circulating. In 2025, two new CIV vaccines were introduced: TruCan Ultra (Elanco) and Nobivac NXT (Merck). Experimental CIV infections have shown that both new vaccines confer similar efficacy. Use of CIV vaccines should be based primarily on assessment of anticipated risk for exposure to circulating CIVs. Other risk considerations are based on breed predilection or comorbidities.

Take-Home Points

- There are 2 serotypes of CIVs, H3N2 and H3N8, of which only variants of H3N2 are currently circulating in North America.
- Clinical immunity to influenza viruses is serotype-specific, best predicted by neutralizing antibodies, commonly measured in surrogate hemagglutination inhibition tests.
- TruCan Ultra is a new purified, reduced-dose, bivalent (H3N2/H3N8) whole inactivated virus vaccine, which skews immune response toward antibody production.
- Nobivac NXT is a new self-amplifying RNA vaccine that stimulates antibody and cytotoxic lymphocyte responses.
- Both new vaccines confer significant disease-sparing responses in experimentally infected dogs, as measured by reduction in CIV-induced pulmonary lesions.
- Use of CIV vaccines should be based on a risk assessment of anticipated exposure to circulating CIVs.

ORION PRODUCTION/shutterstock

Canine influenza viruses (CIVs) are relatively recent additions to the family of influenza A viruses, which comprise many serotypes and many strains within each serotype. In 2005, the first CIV was recognized, an H3N8 serotype that emerged among racing greyhounds in Florida as a spillover infection with equine influenza virus, likely around 1999. CIV H3N8 has not been reported globally since 2016 and seems to be extinct and not currently circulating.[1] In 2015, a second serotype, CIV H3N2, was identified during a respiratory disease outbreak in Chicago.[2] This strain of CIV H3N2 originated from a spillover infection from birds in approximately 2004 and adapted to and then circulated among dogs in Asia. CIV H3N2 was likely first introduced to North America via imported dogs from South Korea. As of this writing, a more recently introduced CIV H3N2 variant is circulating in the United States.[2]

Both serotypes of CIV are highly contagious and capable of sustained dog-to-dog transmission, usually in outbreak situations among commingled dogs. They can cause a range of clinical signs (e.g., coughing, fever, nasal discharge) and can lead to severe illness in immunologically naïve populations and when complicated by secondary bacterial infections.[1,2]

Dogs (and cats) are also susceptible to various strains of avian influenza viruses, such as H5N1 variants, for which there are currently no vaccines.[3]

This article focuses on new additions to the prophylactic armamentarium for CIV, their mechanisms of action, efficacy data, and recommendations for use.

History of CIV Vaccines

CIV vaccines were developed shortly after CIV H3N8 emerged. The first CIV H3N8 vaccine, Nobivac, developed by Merck Animal Health, was approved in 2009. The emergence of CIV H3N2 prompted development of a second vaccine specifically targeting this serotype, by both Merck Animal Health (approved in 2015) and Zoetis (fully approved in 2016).

Shortly thereafter, given the cocirculation of serotypes H3N8 and H3N2 of CIV, Merck and Zoetis introduced bivalent vaccines against both serotypes. All of these vaccines are/were conventional whole inactivated virus formulations containing unspecified adjuvants. Of these, only the Zoetis bivalent vaccine, Vanguard CIV H3N2/H3N8, is still widely available.

Current Status of CIV Vaccines

In response to continuing CIV threats, vaccine development and improvement have continued, and in 2025, the USDA approved 2 new CIV vaccines (**TABLE 1**).

TruCan Ultra CIV H3N2/H3N8

TruCan Ultra, a whole inactivated virus bivalent vaccine, is produced by using Elanco's PureFil technology, a proprietary purification process.[4] According to the manufacturer, this process removes excess proteins and impurities that can contribute to adverse reactions and allows the reduction of an immunizing dose to 0.5 mL.[4] Information as to how, or if, this vaccine is adjuvanted is vague.

TABLE 1 Comparison of TruCan Ultra CIV H3N2/H3N8 and Nobivac NXT Canine Flu H3N2

FEATURE	TRUCAN ULTRA	NOBIVAC NXT
Manufacturer	Elanco Animal Health	Merck Animal Health
Technology	Inactivated virus vaccine	RNA particle vaccine
Target viruses	H3N2 and H3N8 (bivalent)	H3N2 only (monovalent)
Dose volume	0.5 mL	0.5 mL
Patient age of use	7 weeks and older	8 weeks and older
Administration	Subcutaneous; 2 doses 2–3 weeks apart	Subcutaneous; 2 doses 3–4 weeks apart
Types of immune responses stimulated	Primarily humoral (antibody-mediated) immunity	Innate, humoral, and cellular immunity
Storage	2–8 °C (35–46 °F); do not freeze	2–8 °C (35–46 °F); do not freeze

CIV = canine influenza virus

Nobivac NXT Canine Flu H3N2

Nobivac NXT, a nonadjuvanted monovalent vaccine, is a type of RNA vaccine. Instead of a fixed dose of mRNA encapsulated in lipid nanoparticles, as in most vaccines used during the COVID pandemic, Nobivac NXT is a variation of self-amplifying RNA vaccines, which have been successfully used to reduce disease associated with influenza virus infections in swine and poultry.[5-8] As the name implies, in the self-amplifying approach, there is transcription of multiple copies of the mRNA encoding for the hemagglutinin 3 (*H3*) gene of CIV, which reduces the immunizing dose to 0.5 mL and reportedly extends the duration of immunity.[8]

Nobivac NXT consists of viral replicon particles that are produced by using the Venezuelan equine encephalitis virus (VEEV) genome as a backbone. Basically, the vaccine is made by transfecting producer cells with 3 RNA species.[6-8] The "replicon RNA" contains only the genes for the VEEV RNA-dependent RNA polymerase (RdRp) and the gene for CIV H3. RdRp is an enzyme necessary for the transcription of multiple copies of CIV H3 mRNA. Of note, the replicon RNA lacks the genes for VEEV structural proteins (capsid and envelope glycoproteins), thereby making it "replication-defective" and therefore safe for use.

Two helper RNAs are also transfected into the same producer cells; one encoding for the VEEV capsid and the other for the VEEV envelope glycoproteins E1 and E2. The helper mRNAs are translated into the 3 VEEV structural proteins but are not encapsulated into the viral replicon particles. The VEEV structural proteins assemble around the replicon RNA to form the viral replicon particles, which are then purified to make the final vaccine. The envelope VEEV glycoproteins protrude from the viral replicon particle membranes, as in the parent virus, enabling them to bind and enter cells in the dog via receptor-mediated endocytosis.

This process is similar to what happens with the lipid nanoparticles in conventional mRNA vaccines; neither RNA vaccine type requires an adjuvant. Because the genes for the VEEV structural proteins are not present in the replicon RNA and the helper RNAs are not packaged into the viral replicon particles, the viral replicon particles are noninfectious beyond the first cell they enter in the vaccinated dog; in other words, they cannot make new, infectious particles.[5,6]

Mechanisms of Action

TruCan Ultra CIV H3N2/H3N8

Much like the vaccines previously used against influenza viruses in humans, most CIV vaccines, including TruCan Ultra, have been inactivated whole-virus vaccines. Immunologically, this means that they are skewed toward production of antibodies[8] because B cells recognize epitopes making up whole proteins, such as the CIV H3 molecule, and develop into antibody-secreting plasma cells. In addition, vaccine virus is engulfed by dendritic cells and other antigen-presenting cells, processed via the exogenous antigen pathway, and resulting peptides are presented on major histocompatibility complex (MHC) class II molecules to $CD4^+$ helper T cells, which secrete a variety of cytokines, including those that support the growth and differentiation of B cells, and interferon γ.[9]

Nobivac NXT Canine Flu H3N2

In many ways, RNA vaccines in their various iterations act like conventional modified-live vaccines. Hemagglutinin translated following the "instructions" from the transcribed vaccinal mRNA can be secreted, shed from the cell surface, or released at cell death and stimulate B cells and CD4 T cells as with inactivated virus. In addition, because of the intracellular or endogenous synthesis directed by the mRNA, the resulting H3 is also processed in endosomes, and peptides are presented on MHC class I molecules to $CD8^+$ killer T cells, a response similar to that of an infected cell. Thus, engagement of both the exogenous and endogenous pathways leads to a broader immune response, albeit one that is directly against only the H3 protein.[8,10]

Clinical immunity to influenza virus infections, especially in individuals that have not been repeatedly exposed or vaccinated, is primarily serotype specific; neutralizing (hemagglutination-inhibiting) antibodies are the best predictor of protection. Although CIV-specific T-cell responses in dogs are poorly documented, they are undoubtedly relevant to overall immunity to influenza virus infections, especially during recovery from infection.[11,12]

Efficacy

To the author's knowledge, no peer-reviewed data

documenting the efficacy of TruCan Ultra have been published. There are accessible data on file with the USDA that were used to obtain licensure for both TruCan Ultra and Nobivac NXT.[5,9]

TruCan Ultra CIV H3N2/H3N8

For TruCan Ultra, 2 heterologous (i.e., with different isolates than in the vaccine) challenges were performed, 1 each with H3N8 and H3N2 isolates, both in 7-week-old puppies 3 weeks after 2 doses of vaccine or (unidentified) placebo administered subcutaneously 3 weeks apart.[9] No details have been provided about the challenge dose or method of challenge. The primary outcome variable assessed was percentage (total) of abnormal (consolidated) lung.

In the CIV H3N8 challenge, pulmonary lesions were detected in 4/19 vaccinees and 10/18 controls; percentage involvement was 2.15% to 6.07% (median 0) among vaccinees and 0.3% to 32.5% (median 0.96%) among controls.[9] In the CIV H3N2 challenge, pulmonary lesions were detected in 0/20 vaccinees and 14/18 controls; percentage involvement was 0.5% to 44.1% (median 4%) among controls, and no lesions in vaccinees were reported.[9]

To the author's knowledge, no peer-reviewed data have been published that provide details concerning clinical responses, CIV shedding, or statistical analyses. In promotional material, the manufacturer claims that the vaccine induced antibodies that mediated "100% neutralization of current field isolates"; however, those data are "on file," with no further details provided.[4] Also reported in the USDA file are the results of a field safety study of 688 dogs, 244 of which were <7 weeks of age, vaccinated twice 3 weeks apart, and then monitored for 14 days after each vaccination. Of the 688 enrolled dogs, 155 had at least 1 of the listed transient adverse events; the total number reported was 350.[9]

Nobivac NXT Canine Flu H3N2

For Nobivac NXT, in addition to the USDA data on file, there is a detailed peer-reviewed published manuscript.[5,6] Nineteen 8-week-old, CIV H3N2-seronegative puppies were vaccinated twice subcutaneously, 3 weeks apart, and then challenged intranasally with a heterologous H3N2 isolate 3 weeks after the second vaccination. At day 10 after challenge, 5/19 vaccinees had lung lesions with 0% to 1% involvement (median 0); whereas, significantly more (12/20) controls had lung lesions with 0.2% to 22.6% involvement (median 7.2). Among vaccinees, clinical signs, including coughing, were significantly reduced compared with controls, as was the duration and amount of nasal viral shed. The disease-sparing response was associated with significantly higher concentrations of hemagglutination-inhibiting antibodies after vaccination and challenge in the vaccinees. In a field safety study, 654 dogs (217 at 8 weeks of age; 437 at various ages) were monitored for 14 days after a second vaccination. During the observation period, minor adverse events associated with the vaccine, notably lethargy, were observed in 32 dogs (2.5%); adverse events not associated with the vaccine were noted for 14 dogs (1.1%).[6]

Overall, based on available data, both new CIV vaccines seem to be safe and efficacious for reducing typical pulmonary sequalae to CIV H3N2 (and CIV H3N8) infection.

Overall, based on available data, both new CIV vaccines seem to be safe and efficacious for reducing typical pulmonary sequalae to CIV H3N2 (and CIV H3N8) infection. Clinical signs, virus shedding, and transmission of CIV can also be expected to be reduced but may not be completely prevented in vaccinated dogs. Despite what may be claimed,[10] the disclaimer in the USDA data files should be noted: "Do not use the following studies to compare one product to another. Slight differences in study design and execution can render the comparisons meaningless."[5,9] Currently, there are no published direct comparative (challenge) studies to establish superiority of any CIV vaccine or published field trials to assess the efficacy of responses to natural CIV challenge in vaccinated versus nonvaccinated dogs.

Use of CIV Vaccines

Despite being capable of causing severe disease, CIVs are not currently considered as core antigens, and thus core vaccines, for dogs.[13] This is primarily because, to date, CIV-associated disease has occurred in sporadic nonsustaining outbreaks,[1,2,13] precluding a recommendation for routine CIV vaccination of all dogs.[13] The situation for dogs differs from that for humans, most likely due to differences in host population dynamics, not in the pathogenicity of CIVs per se.[1,2] Use of CIV vaccines should be based on risk assessment, essentially addressing the question: "Is CIV circulating in the practice area or in an area to which the dog may be traveling?" Updated surveillance data to help answer this question are accessible online (go.navc.com/4iAeTpB).

CIV vaccines are like most other vaccines used in veterinary practice and require boosting in the initial series. Although not formally tested, inhibition by maternal antibodies is likely not a practical concern, given the current low prevalence of CIV exposure or previous use of alphavirus particle vaccines. There are no data related to the duration of immunity; however, annual boosters may be considered in at-risk dogs. Although CIV H3N8 is not currently circulating in North America, a bivalent whole inactivated virus vaccine may be better than a monovalent H3N2 vaccine for inducing cross-reactive immune responses, which could include potentially protective antibody and cell-mediated immune responses against more than just the H3 protein (e.g., against the neuraminidase envelope glycoprotein).[11,12] Although untested in dogs, it may be immunologically beneficial, in terms of cross-reactive immunity, to use the 2 new vaccines in a "prime-boost" protocol: priming with the bivalent vaccine and boosting with viral replicon particle vaccine in the initial series.[14,15]

Using CIV vaccines during an outbreak among dogs that have already been exposed to the virus may be of limited use as the incubation and transmission of CIV are likely more rapid than the development of vaccine-induced immunity.[16]

Summary

In 2025, two new CIV vaccines were introduced: TruCan Ultra by Elanco and Nobivac NXT by Merck. TruCan Ultra is a purified, reduced-dose, bivalent (H3N2/H3N8) whole inactivated virus vaccine, which can be expected to stimulate robust antibody responses. Nobivac NXT is a self-amplifying RNA vaccine that stimulates antibody and cytotoxic lymphocyte responses to the H3 glycoprotein of the virus. Both new vaccines confer significant disease-sparing responses, as measured by reduction in CIV-induced pulmonary lesions in experimentally infected dogs. Use of CIV vaccines should be based primarily on assessment of anticipated risk for exposure to circulating CIVs; other considerations should be based on breed predilection or comorbidity risks. TVP

References

1. Wasik BR, Rothschild E, Voorhees IEH, et al. Understanding the divergent evolution and epidemiology of H3N8 influenza viruses in dogs and horses. *Virus Evol*. 2023;9(2):vead052. doi:10.1093/ve/vead052
2. Wasik BR, Damodaran L, Maltepes MA, et al. The evolution and epidemiology of H3N2 canine influenza virus after 20 years in dogs. *Epidemiol Infect*. 2025;153:e47. doi:10.1017/S0950268825000251
3. Ly H. Highly pathogenic avian influenza H5N1 virus infection of companion animals. *Virulence*. 2024;15(1):2289780. doi:10.1080/21505594.2023.2289780
4. Elanco receives USDA approval for TruCan™ Ultra CIV H3N2/H3N8 (canine influenza vaccine) bringing to market a high standard of respiratory protection. Elanco. July 9, 2025. Accessed November 15, 2025. https://investor.elanco.com/press-releases/press-releases-details/2025/Elanco-Receives-USDA-Approval-for-TruCan-Ultra-CIV-H3N2-H3N8-Canine-Influenza-Vaccine-Bringing-to-Market-a-High-Standard-of-Respiratory-Protection/
5. Summary of studies supporting USDA product licensure: Merck Animal Health Canine Influenza Vaccine, H3, RNA Particle. USDA APHIS. Accessed November 15, 2025. https://www.aphis.usda.gov/veterinary-biologics/product-summaries/165a-15p5r0.pdf
6. Classe HM, Dant JC, Mogler M, et al. Efficacy and safety in dogs following administration of an alphavirus RNA particle canine influenza H3N2 vaccine. *Vaccines (Basel)*. 2024;12(10):1138. doi:10.3390/vaccines12101138
7. Pushko P, Parker M, Ludwig GV, Davis NL, Johnston RE, Smith JF. Replicon-helper systems from attenuated Venezuelan equine encephalitis virus: expression of heterologous genes invitro and immunization against heterologous pathogens in vivo. *Virology*. 1997;239(2):389-401. doi:10.1006/viro.1997.8878
8. Blakney AK, Ip S, Geall AJ. An update on self-amplifying mRNA vaccine development. *Vaccines (Basel)*. 2021;9(2):97. doi:10.3390/vaccines9020097
9. Summary of studies supporting USDA product licensure: TruCan Ultra CIV H3N2/H3N8 - Elanco US Inc. USDA APHIS. Accessed November 15, 2025. https://www.aphis.usda.gov/veterinary-biologics/product-summaries/196-15q520.pdf
10. Ghattas M, Dwivedi G, Lavertu M, Alameh MG. Vaccine technologies and platforms for infectious diseases: current progress, challenges, and opportunities. *Vaccines (Basel)*. 2021;9(12):1490. doi:10.3390/vaccines9121490
11. Topham DJ, DeDiego ML, Nogales A, Sangster MY, Sant A. Immunity to influenza infection in humans. *Cold Spring Harb Perspect Med*. 2021;11(3):a038729. doi:10.1101/cshperspect.a038729

12. Krammer F. The human antibody response to influenza A virus infection and vaccination. *Nat Rev Immunol*. 2019;19(6):383-397. doi:10.1038/s41577-019-0143-6
13. Ellis J, Marziani E, Aziz C, et al. 2022 AAHA canine vaccination guidelines. *JAAHA*. 2022;58(5):2132-2130. doi:10.5326/JAAHA-MS-Canine-Vaccination-Guidelines
14. Kardani K, Bolhassani A, Shahbazi S. Prime-boost vaccine strategy against viral infections: mechanisms and benefits. *Vaccine*. 2016;34(4):413-423. doi:10.1016/j.vaccine.2015.11.062
15. Van Reeth K, Mancera Gracia JC, Trus I, et al. Heterologous prime-boost vaccination with H3N2 influenza viruses of swine favors cross-clade antibody responses and protection. *NPJ Vaccines*. 2017;2:11. doi:10.1038/s41541-017-0012-x
16. Newbury S, Godhardt-Cooper J, Poulsen KP, Cigel F, Balanoff L, Toohey-Kurth K. Prolonged intermittent virus shedding during an outbreak of canine influenza A H3N2 virus infection in dogs in three Chicago area shelters: 16 cases (March to May 2015). *JAVMA*. 2016;248(9):1022-1026. doi:10.2460/javma.248.9.1022

Author

John A. Ellis

Dr. Ellis received his DVM degree from the University of Illinois in 1979 and a subsequent PhD degree in comparative pathology from Colorado State University in 1984. He is a diplomate of the American College of Veterinary Pathologists and the American College of Veterinary Microbiology (ACVM). After veterinary school, he worked as a staff veterinarian and instructor in animal science at the Navajo Community College in Arizona and a research associate in Peru for the U.S. Agency for International Development. He was a postdoctoral fellow and subsequently a visiting scientist at the International Laboratory for Research on Animal Disease in Nairobi, Kenya, where he worked on bovine cellular immunology. In addition, Dr. Ellis was previously a diagnostic pathologist and on the faculty of the department of veterinary science at the University of Wyoming. Since 1992, Dr. Ellis has been in the department of veterinary microbiology at the University of Saskatchewan's Western College of Veterinary Medicine in Saskatoon, Saskatchewan, Canada, where he teaches virology and immunology. He has published extensively in peer-reviewed journals, textbooks, and conference proceedings. One of his primary research interests has been the development and efficacy testing of intranasal and parenteral vaccines for respiratory infections. He was recognized by the ACVM as the Distinguished Veterinary Microbiologist for 2024.