

2006 AAHA Canine Vaccine Guidelines

In 2005, AAHA's Canine Vaccine Task Force met to re-examine and revise guidelines on the use of vaccines in dogs. The results of the Task Force's work are summarized and tabulated in this article and are published in their entirety on the AAHA website (www.aahanet.org). The 2006 AAHA Canine Vaccine Guidelines contain information on new technological developments in vaccines, an introduction to conditionally licensed vaccines, and detailed recommendations on the use of available vaccines. Perhaps the most noteworthy addition to the guidelines is a separate set of recommendations created for shelter facilities. Vaccines are classified as core (universally recommended), noncore (optional), or not recommended. The Task Force recognizes that vaccination decisions must always be made on an individual basis, based on risk and lifestyle factors.

Report of the American Animal Hospital Association (AAHA) Canine Vaccine Task Force:

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Executive Summary

Since the publication of the AAHA Canine Vaccine Guidelines in 2003, the profession and the biologics industry have moved in the direction advocated in that document by the Canine Vaccine Task Force. The profession has witnessed no negative medical ramifications to the recommendations issued by the Task Force, several well-documented studies have demonstrated the extended duration of immunity (DOI) and supported the extended vaccine intervals advocated by the guidelines, and the industry has responded in the main by supporting the use of products with extended DOI protocols. While a number of rabies vaccines have long been available as licensed for 3 years by the US Department of Agriculture (USDA), vaccines against other infectious diseases of dogs have generally been licensed as 1-year vaccines. At least one manufacturer has been successful in obtaining a 3-year license from the USDA Center for Veterinary Biologics (USDA/CVB).

This document was developed by the American Animal Hospital Association through a collaborative effort among Task Force members to aid practitioners in making decisions about appropriate care of their canine patients with respect to currently available vaccines. The Task Force included experts in immunology, infectious diseases, internal medicine, and medicine and clinical practice.

The guidelines are supported by professional, scientific and clinical evidence, as well as published and unpublished documentation.

These guidelines and recommendations should not be construed as dictating an exclusive protocol, course of treatment, or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to each individual practice setting. The guidelines are not intended to be an AAHA standard of care.

Please visit www.aahanet.org for a complete copy of this report.

In early 2005, the Canine Vaccine Guidelines Task Force was reconvened with the charge of updating the guidelines and developing a plan to simplify the revision process and make it more responsive to the emergence of new vaccines and developments. To that end, the guidelines will be published in their entirety electronically on the AAHA web site (www.aahanet.org), where they can be readily accessed by the profession.

The Task Force recognizes that individual readers will find some sections of immediate interest and others of background interest. However, practitioners are urged to read the entire document for reference, with special attention to certain key sections that have been revised and new sections that have been added.

Revised sections include those addressing the vaccine licensing process and the medical and legal implications of vaccine medicine. Because serologic interpretation in conjunction with or in lieu of vaccination is of major interest to the profession, the section addressing serologic testing has been expanded. The question is not the validity of serology but the application and indication for serologic testing.

A key section of the 2003 guidelines focused on vaccine adverse events and emphasized the importance of reporting adverse events to the appropriate agency. A vaccine adverse event is any undesirable or unintended outcome (including failure to achieve the desired result) that occurs in conjunction with vaccine administration. The section on vaccine adverse events has been updated to reflect recent developments in reporting procedures. The Task Force reiterates its recommendation that practitioners take the time to document and report all adverse events. As changes in protocols are adopted and innovative vaccines and vaccine technologies gain ground, such vigilance is even more essential.

Included in the 2006 guidelines is a section highlighting the science of vaccine development, specifically such technologies as live vectored, subunit, gene-deleted, and deoxyribonucleic acid vaccines. In adding this material, the Task Force's intent is to introduce its audience to new concepts and future technologies and to stimulate awareness of where the science of vaccine development is headed.

The Task Force has also introduced the subject of conditionally licensed vaccines in one of the several tables included in this update. These vaccines have demonstrated safety and purity and in preliminary studies have demonstrated a reasonable expectation of efficacy. Though only granted conditional licenses by the USDA/CVB, these products may have definite indications in individual animals and bear consideration in selected animals.

Another notable addition to these updated guidelines is a section devoted to shelter medicine. The impetus for separate shelter vaccination guidelines was the Task Force's recognition that this rapidly developing area of veterinary practice faces unique challenges. What best serves a clinical companion animal practice may not be ideal in an environment housing an ever-changing population. This section discusses some of the special considerations and issues confronting shelter medicine and provides tables listing vaccines that

are recommended, optional, and not recommended for the shelter environment.

For many readers, a highlight of the 2006 guidelines will be the recommendations for selecting appropriate vaccines to be administered to the individual patient. The vaccine type, optimal time of administration for puppies and adult dogs, and general comments are compiled in an easy-to-use table within the main guidelines. Vaccines are now categorized as *core*, *noncore* (or optional), and *not recommended*. Core vaccines are those that all dogs should receive in one form or other. Optional vaccines should be administered selectively, based on the animal's geographic and lifestyle exposure and an assessment of risk/benefit ratios. The table does not mention specific products or manufacturers; it is the position of the Task Force that all major manufacturers produce quality canine vaccines and that these decisions are best left to the clinician.

Even in their revised and updated form, the 2006 guidelines reflect the same underlying principles that imbued the 2003 edition:

- Vaccination is a medical decision and a medical procedure that should be individualized based on the risk and lifestyle of the individual animal.
- An extended vaccine interval is reasonable, safe, and effective in preventing most infectious diseases.
- Veterinary medicine must remain vigilant of emerging diseases, changes in incidence of known diseases, and adverse events associated with vaccine administration. It is incumbent on veterinarians to proactively report adverse events.
- Decisions surrounding vaccination of client-owned pets should include a discussion with clients and always be fully documented in the medical record.

Introduction

In 2003, the AAHA Canine Vaccine Task Force released its first set of guidelines specifically addressing canine vaccination.¹ The 2003 guidelines advocated a number of changes in the then generally accepted vaccine protocols of most practices. The guidelines undertook to increase awareness of the complexities involved in the development and licensing of a biologic product and emphasized the need for vigilance and the reporting of adverse events to appropriate agencies or the manufacturer.

Immunization was categorized as a medical procedure with definite benefits and risks, and one that should be undertaken only with individualization of vaccine choices and after input from the client. The guidelines specifically recommended that some vaccines be given to all dogs, some be given to a more select population, and some generally not be used because of a lack of demonstrated efficacy or indication of unacceptable risk of side effects. Additionally, the guidelines advocated for an extended interval between adult revaccination and stated that under typical conditions, protective revaccination intervals for the major viral diseases of normal adult dogs could safely be extended to 3 years.

Why Another Set of Guidelines Is Needed

The AAHA has chosen to revisit and update the canine vaccination guidelines for several reasons. The 3 years since the publication of the 2003 guidelines have seen many changes and advances in canine vaccination, necessitating revisions of several sections. Serologic testing, licensing of vaccine products, vaccine adverse event reporting, and vaccination from a medical and legal perspective have all been updated to reflect new information. In response to the profession's request, the number of citations has been expanded to enhance and enforce the guidelines as science-based.

Information on vaccine selection and administration has also been revised to reflect new thinking and the several years of experience gained from veterinarians following the 2003 guidelines. During that time, no increase in infectious diseases has been reported among adequately immunized dogs. Publications in refereed journals have demonstrated that the duration of immunity (DOI) provided by vaccines against major pathogens is at least 3 years.² Other than vaccines available for rabies immunization, as of this writing, only one product has obtained a U.S. Department of Agriculture (USDA) approved license for a DOI claim of 3 years following an initial vaccination series. However, many other vaccine manufacturers support their product as effective and protective when used in extended revaccination protocols. Furthermore, it is the opinion of the Task Force that vaccines against canine distemper virus (CDV), canine parvovirus (CPV), and canine adenovirus-2 (CAV-2) produced by major biologics manufacturers *all* produce excellent immune responses and can be soundly and reliably administered at the discretion of the clinician in extended duration of immunity protocols.^a Discretionary administration indicates that all of these vaccines can be used in extended interval vaccination programs. In response to these findings and other developments in canine vaccination, the Task Force has updated its guidelines and recommendations for core (recommended), noncore (optional), and not recommended vaccines for the general veterinary practice [Table 1].^{1,3,4,5,b}

In addition to revising and updating information, the Task Force has added material not included in the original guidelines. One section looks at the newly emerging technologies that provide options to the modified live and killed agents used in vaccines. These technologies include live vectored, subunit, gene-deleted, and deoxyribonucleic acid vaccines.

In one of the several tables that enrich this update, the Task Force also touches on novel products that most veterinarians might not consider as classical vaccines against infectious diseases as well as toxoids and agents that protect against conditions and diseases not generally considered infectious. Having demonstrated their safety and purity, these products have been issued conditional licenses by the USDA with a reasonable expectation of efficacy. At the end of the conditional license period, data obtained in support of product potency and performance will be evaluated to determine if the conditional licenses should be renewed or if regular product licenses may be issued.

Perhaps the most noteworthy of the additions to the 2006 update is a separate set of recommendations created for shelter facilities, an acknowledgment that shelter medicine presents unique challenges that may not be best served by general clinical recommendations. Therefore, the 2006 guidelines have been divided into two parts, with part 1 addressing vaccination in the general veterinary practice and part 2 focusing on vaccination in the shelter environment as well as specific issues associated with vaccination in a large and ever-changing population of dogs.

Disclaimer

The 2006 guidelines are built on a foundation of guidelines developed by the American Association of Feline Practitioners, American Veterinary Medical Association (AVMA), and the 2003 AAHA guidelines.

By their very nature as a consensus-built set of guidelines, these recommendations reflect a combination of expert opinion, personal experience, and scientific studies published and unpublished. The canine vaccination guidelines for the general veterinary practice and the shelter environment are neither designed as nor should they be interpreted to be a standard of care or set of legal parameters. They are intended to educate and inform the profession and to help veterinarians and shelter personnel make rational vaccine recommendations for an individual dog or, in the case of a shelter situation, a population of dogs.

Acknowledgment

AAHA wishes to acknowledge and thank the members of the 2006 Canine Vaccination Guidelines Task Force for their time and dedication. The Task Force is composed of practitioners, internists, infectious disease experts, and immunologists as well as those with a commitment to the growing concern of addressing the particular needs of shelter medicine. In addition, *AAHA wishes to acknowledge the openness, assistance, and encouragement of veterinary biologics manufacturers.*

PART 1 CANINE VACCINATION IN THE GENERAL VETERINARY PRACTICE

New Vaccine Technologies

The majority of vaccines currently in use for domestic animals (including dogs) consist of inactivated (killed) or modified live (attenuated) bacteria or viruses. Advances in immunology, molecular biology, genetics, microbiology, and the understanding of disease pathogenesis have resulted in innovative approaches to developing vaccines. Examples include live vectored vaccines and subunit vaccines, which are currently on the market. Other new approaches are also being investigated, including gene-deleted vaccines and vaccines that consist of only nucleic acid.⁶ In addition, new adjuvants are being developed and tested. Adjuvants are chemicals, microbial components, or mammalian proteins that enhance the immune response to vaccine antigens.⁷ New-generation adjuvants may be used to induce specific

Table 1
2006 AAHA Canine Vaccination Guidelines* for the General Veterinary Practice

Vaccine†	Initial Puppy Vaccination* (≤16 weeks)	Initial Adult Vaccination (>16 weeks)	Revaccination (Booster) Recommendation	Comments and Recommendations See the second page of the guidelines for definitions of core, noncore, and nonrecommended vaccines
Canine Parvovirus (CPV-2) (MLV)	Administer at 6-8 weeks of age, then every 3-4 weeks until 12-14 weeks of age.	Two doses, 3-4 weeks apart. One dose is considered protective and acceptable.	After a booster at 1 year (unless manufacturer label recommends otherwise), revaccination once every 3 years or more is considered protective.	<i>Core:</i> Although annual boosters are recommended by some vaccine manufacturers, studies have shown protection against challenge (DOI) up to 7 years postvaccination with MLV vaccine. ^{§,} Products with CPV-2, regardless of genotype (i.e., CPV-2, 2a, or 2b), all provide excellent protection against field isolates. <i>Not Recommended:</i> Killed parvovirus products have been shown to be susceptible to maternal antibody interference in puppies as old as 16-18 weeks. Multiple doses (2-5) may be required even in puppies older than 12 weeks.
Canine Parvovirus (CPV-2) (killed)				
Canine Distemper Virus (CDV) (MLV)	Administer at 6-8 weeks of age, then every 3-4 weeks until 12-14 weeks of age.	Two doses, 3-4 weeks apart. One dose is considered protective and acceptable.	After a booster at 1 year (unless manufacturer label recommends otherwise), revaccination once every 3 years or more is considered protective.	<i>Core:</i> Although annual boosters are recommended by some vaccine manufacturers, adult dogs challenged 7 years (Rockborn Strain) and 5 years (Onderstepoort Strain) following MLV vaccination were protected (DOI). [*]
rCanine Distemper Virus (rCDV)	Administer at 6-8 weeks of age, then every 3-4 weeks until 12-14 weeks of age.	Two doses, 3-4 weeks apart.	After a booster at 1 year (unless manufacturer label recommends otherwise), revaccination once every 3 years or more is considered protective.	<i>Core:</i> A suitable alternative to the MLV-CDV and may be used interchangeably with MLV-CDV vaccine. Recent unpublished studies have shown that compared with the MLV-CDV vaccines, the recombinant CDV vaccine is more likely to immunize puppies in the face of passively acquired maternal antibody (PAMA).
Distemper-Measles Virus (D-MV) (MLV)	One dose only between 4 and 12 weeks of age.	Never indicated in animals older than 12 weeks.	Never indicated in animals older than 12 weeks.	<i>Noncore:</i> Intended to provide temporary protection in young puppies because the measles vaccine is effective at providing immunity against CDV even in the presence of passively acquired maternal antibody (PAMA) to CDV. NOTE: Recent unpublished studies have shown that the recombinant CDV vaccine immunizes puppies in the face of PAMA. Therefore, D-MV is no longer the preferred option.

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Canine Adenovirus-1 (CAV-1) (MLV and killed)				<i>Not Recommended:</i> Significant risk of "hepatitis blue-eye" reactions is associated with CAV-1 vaccines. CAV-2 vaccines very effectively cross-protect against CAV-1 and are much safer.
Canine Adenovirus-2 (CAV-2) (MLV parenteral)	Administer at 6-8 weeks of age, then every 3-4 weeks until 12-14 weeks of age.	Two doses, 3-4 weeks apart. One dose is considered protective and acceptable.	After a booster at 1 year (unless manufacturer label recommends otherwise), revaccination once every 3 years or more is considered protective.	<i>Core:</i> Demonstrated cross-protection against canine hepatitis caused by CAV-1 as well as CAV-2, one of the agents known to be associated with infectious tracheobronchitis. Adult dogs challenged 7 years following CAV-2 MLV vaccination were found to be protected (DOI) against the more virulent CAV-1. ¹
Canine Adenovirus-2 (CAV-2) (killed or MLV-topical)				<i>Not Recommended:</i> CAV-2 (MLV parenteral) vaccines produce a more effective immune response than CAV-2 (killed parenteral) vaccines do. CAV-2 (MLV-parenteral) vaccine is commonly combined with CDV and CPV-2 parenteral vaccines, and in general, there is no advantage to administering both CAV-2 (MLV-parenteral) and CAV-2 (MLV-topical) vaccines.
Rabies 1-year (killed)	Administer one dose as early as 3 months of age.	Administer a single dose.	Annually. State, provincial, and/or local laws apply. The 1-year rabies vaccine may be used as a booster vaccine when dogs are required by statute to be vaccinated annually against rabies.	<i>Core:</i> State, provincial, and local statutes govern the frequency of administration for products labeled as "1-year rabies vaccines." The 1-year rabies vaccine is sometimes administered as the initial dose followed 1 year later by administration of the 3-year rabies vaccine. State, provincial, and local statutes may dictate otherwise. When given annually, 1-year rabies products should not be considered to cause fewer adverse reactions than 3-year rabies products. Route of administration may not be optional; see product literature for details.

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Rabies 3-year (killed)	Administer one dose as early as 3 months of age. Where authorized by local/state statutes, a 3-year rabies vaccine may be substituted as an alternative to a 1-year rabies vaccine for initial and subsequent doses.	Administer a single dose. Where authorized by local/state statutes, a 3-year rabies vaccine may be substituted as an alternative to a 1-year rabies vaccine for initial and subsequent doses.	The second rabies vaccination is recommended 1 year following administration of the initial dose, regardless of the animal's age at the time the first dose was administered. Booster vaccines should be administered every 3 years. State, provincial, and/or local laws apply.	Core: State, provincial, and local statutes govern the frequency of administration for products labeled as "3-year rabies vaccines." The 1-year rabies vaccine is sometimes administered as the initial dose followed 1 year later by administration of the 3-year rabies vaccine. State, provincial, and local statutes may dictate otherwise. Route of administration may not be optional; see product literature for details.
Parainfluenza Virus (CPIV) (MLV-parenteral)	Administer at 6-8 weeks of age, then every 3-4 weeks until 12-14 weeks of age.	One dose is adequate.	After a booster at 1 year (unless manufacturer label recommends otherwise), revaccination once every 3 years is considered protective.	Noncore: DOI by challenge has been shown to be at least 1 year (unpublished) for topical (intranasal) vaccine. Note: There is no evidence that parainfluenza vaccine produces any cross immunity to the recently reported canine influenza virus.
<i>Bordetella bronchiseptica</i> (killed bacterin)—parenteral	Administer one dose at 6-8 weeks and one dose at 10-12 weeks of age.	Two doses, 2-4 weeks apart.	Annually. Annually or more often in very high-risk animals not protected by annual booster.	Noncore: There is no known advantage to administering parenteral and intranasal <i>B. bronchiseptica</i> vaccines simultaneously. Vaccine should be administered at least 1 week prior to anticipated exposure.
<i>Bordetella bronchiseptica</i> (live avirulent bacteria) + Parainfluenza Virus (MLV)—topical (intranasal) application	Administer a single dose as early as 3 weeks of age (see product literature for specific age recommendations). For best results, a second dose should be given 2-4 weeks after the first.	A single dose is recommended by the manufacturer.	Annually. Annually or more often in very high-risk animals not protected by annual booster.	Noncore: Note: Transient (3-10 days) coughing, sneezing, or nasal discharge may occur in a small percentage of vaccinates. If animal has not been vaccinated within the previous 6 months, a booster is recommended 1 week prior to known exposure (e.g., boarding, showing).

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<i>Bordetella bronchiseptica</i> (cell wall antigen extract)—parenteral	Administer one dose at 8 weeks of age and one dose at 12 weeks of age.	Two doses, 4 weeks apart.	Annually (manufacturer). Annually or up to every 6 months in high-risk environments.	Noncore: DOI is approximately 9-12 months. There is no known advantage to administering parenteral and intranasal <i>B. bronchiseptica</i> vaccines simultaneously. Vaccine should be administered at least 1 week prior to anticipated exposure.
<i>Borrelia burgdorferi</i> (Lyme borreliosis) (killed whole bacterin) or <i>Borrelia burgdorferi</i> (rLyme borreliosis) (recombinant-Outer surface protein A [OspA])	Initial dose may be given at 9 or 12 weeks of age (depending on manufacturer recommendations) with a second dose 2-4 weeks later.	Two doses, 2-4 weeks apart.	Annually (manufacturer). Revaccinate just prior to start of tick season as determined regionally.	Noncore: Generally recommended only for use in dogs with a known high risk of exposure, living in or visiting regions where the risk of vector tick exposure is considered to be high, or where disease is known to be endemic. Minimum DOI based on challenge studies is 1 year.
Canine Coronavirus (CCV) (killed and MLV)				Not Recommended: Prevalence of clinical cases of confirmed CCV disease does not justify vaccination. Clinical disease rarely occurs and when seen is typically mild and self-limiting. Experience has shown no additional increase in infectious enteritis among adults or puppies subsequent to discontinuing CCV vaccine. Neither the MLV vaccine nor the killed CCV vaccines have been shown to significantly reduce disease caused by a combination of CCV and CPV-2. Only CPV-2 vaccines have been shown to protect dogs against challenge when these two viruses are used. DOI cannot be determined because in studies performed to date, neither vaccinates nor control dogs developed clinical evidence of disease following experimental virus challenge.

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<i>Leptospira interrogans</i> (combined with serovars canicola and icterohaemorrhagiae) (killed bacterin) (Also available with serovars grippityphosa and pomona)	Administer one dose at 12 weeks and one dose at 14-16 weeks. For optimal response, do not administer to dogs younger than 12 weeks.	Two doses, 2-4 weeks apart.	Annually (manufacturer). Annual boosters are not routinely recommended for all dogs. Vaccination should be restricted to use in areas where a reasonable risk of exposure has been established. Veterinarians are advised of anecdotal reports of acute anaphylaxis in toy breeds following administration of leptospiriosis vaccines. Routine vaccination of toy breeds should only be considered in dogs known to have a high exposure risk. Dogs determined to be at exceptionally high risk should be vaccinated at 12 and 16 weeks of age, and then at intervals of 6-9 months until the risk has been reduced.**	Noncore: Disease prevalence is likely to vary for each serovar. Vaccine recommendations are therefore difficult to make due to lack of information on prevalence of specific serovar infections in dogs in various geographic regions. Anecdotal reports from veterinarians and breeders suggest that incidence of postvaccination reactions (acute anaphylaxis) in puppies (<12 weeks of age) and small-breed dogs is high. Reactions are most severe in young puppies. Therefore, routine use of the vaccine should be delayed until dogs are 12 weeks of age. Minimum DOI based on challenge studies has been shown to be approximately 1 year for serovars <i>L. canicola</i> and <i>L. icterohaemorrhagiae</i> ; however, efficacy of the products can be low (<75%). DOI for serovars grippityphosa and pomona are assumed to be up to 1 year.
<i>Giardia lamblia</i> (killed)				Not Recommended: The vaccine may prevent oocyst shedding but does not prevent infection. There is insufficient data to warrant routine use of this vaccine. Infection in puppies and kittens is often subclinical. Most animal strains of <i>Giardia duodenalis</i> are not infective to an immunocompetent human host. Dogs can carry <i>Giardia</i> strains that are potentially infective for humans.†† Transmission to humans is most likely through fecal-oral contact with ingestion of cysts, or from contaminated water. Because the vaccine does not prevent infection, a minimum DOI based on challenge is not reported.

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<i>Crotalus atrox</i> Toxoid (rattlesnake vaccine)	Refer to manufacturer's label. Current administration is two doses 1 month apart to puppies as young as 4 months.	Refer to manufacturer's label. Current administration is two doses 1 month apart.	Refer to manufacturer's label. Annual boosters are currently recommended, especially at the beginning of rattlesnake "season" or when the animal is traveling into rattlesnake habitats.	Intended to protect dogs against the venom associated with the bite of the Western Diamondback Rattlesnake. Some cross-protection may exist against the venom of the Eastern Diamondback Rattlesnake. There is currently no evidence of cross-protection against the venom of the Mojave Rattlesnake. Because of a lack of experience and paucity of field validation of efficacy, the Task Force takes no position on the use of this vaccine. A reasonable expectation of efficacy does exist.
<i>Porphyromonas</i> sp. (periodontal disease vaccine)	See manufacturer's labeled directions.	See manufacturer's labeled directions.	See manufacturer's labeled directions.	Intended as an aid in prevention and control of periodontal disease in dogs. Because of a lack of experience and paucity of field validation of efficacy, the Task Force takes no position on the use of this vaccine. A reasonable expectation of efficacy does exist.

* The AAHA 2006 Canine Vaccine Guidelines are provided to assist veterinarians in developing a vaccination protocol for use in clinical practice. They are not intended to represent vaccination standards for all dogs.
 † MLV—modified live virus; r—recombinant.
 ‡ Route of administration is SQ (subcutaneous) or IM (intramuscular) unless otherwise noted by the manufacturer.
 § DOI—duration of immunity.
 \ American Animal Hospital Association Canine Vaccine Task Force. Report of the AAHA Canine Vaccine Task Force: executive summary and 2003 canine vaccine guidelines and recommendations. *J Am Anim Hosp Assoc* 2003;39:119–131.
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 †† Bowman D. Companion Animal Parasite Council Guidelines. North Am Vet Conf, Orlando, FL, 2004.

types of immunity or reduce vaccine-related adverse effects. The goal of these new vaccine technologies is to produce safer and more efficacious vaccines against both diseases for which vaccines are already available and diseases for which the conventional approach to developing vaccines has not been successful.

Live Vectored Vaccines

Live vectored vaccines are based on known protective antigens of an organism. The genes associated with those antigens are inserted into another organism—typically a virus—that then expresses the antigenic proteins upon infection of the host. The expressed proteins are then capable of inducing an immune response. Currently there is a live vectored canine distemper vaccine, in which the hemagglutinin and fusion genes have been inserted into a canarypox virus.⁸ When injected into a dog, the canarypox virus infects canine cells and expresses the hemagglutinin and fusion proteins intracellularly but does not replicate. Thus, humoral and T-cell-mediated immune responses similar to those induced by a modified live vaccine should occur. Another advantage to this type of vaccine is there is no opportunity for the virus to revert to virulence or to be virulent in an immunosuppressed animal because the vaccine consists only of genes from canine distemper, not the entire virus genome.

A potential advantage of live vectored vaccines is their ability to overcome inactivation by maternal antibodies. Maternal antibodies may prevent effective humoral and/or T-cell-mediated immune responses from occurring in response to conventional vaccines. The live vector carrying the genes may be able to induce protective immunity prior to the loss of maternal antibody protection. Potentially, diagnostic assays can be developed against inserted marker genes or antigens not found in the live vectored vaccine, allowing differentiation between natural infection and vaccine-induced immune responses.

Subunit Vaccines

Subunit vaccines contain a portion of the organism. As with vectored vaccines, subunit vaccines require information on the protective antigens of the infectious agents. Currently there is a subunit vaccine to an outer surface membrane protein, OspA, of *Borrelia burgdorferi*. Use of only the portion of the organism needed to induce a protective immune response precludes the necessity of using the entire organism. A study of dogs in a Lyme disease-endemic area found reduced infection rates in dogs vaccinated with OspA, compared with dogs not vaccinated with the protein.⁹ In order to produce efficacious subunit vaccines, the protective antigens must be identified and purified or, similar to a vectored vaccine, the genes for the antigens can be inserted into an expression system and the proteins produced in the laboratory for injection into the host.

An important advantage of subunit vaccines is the reduced levels of antigen required for immune stimulation due to the elimination of irrelevant antigens. Furthermore, large amounts of purified proteins can be produced for use in subunit vac-

cines, which can make the vaccines cost-efficient. However, for many diseases, more than one protein is required for protection against disease and the proteins are very specific; therefore, subunit vaccines often don't provide the necessary cross-protection because they induce an immune response to only the proteins contained in the vaccine. In addition, since the vaccine consists of a purified protein, no replication occurs within the host; thus, minimal T-cell activation occurs unless potent adjuvants are used.

Gene-Deleted Vaccines

Gene-deleted vaccines are produced from organisms that have been altered to either delete or inactivate a gene.¹⁰ The gene selected for deletion can't be responsible for proteins required for immune protection against disease. Gene-deleted vaccines can be generated for either live or killed vaccines. Gene deletion can be a mechanism by which organisms are attenuated and may occur naturally over time under laboratory conditions. Gene-deleted vaccines have been used successfully as marker vaccines in some (but not all) eradication programs. Some vaccinated animals can be differentiated from naturally infected animals by the presence of antibodies to the protein expressed from the deleted gene. Currently no gene-deleted vaccines are available for use in dogs.

Deoxyribonucleic Acid Vaccines

Deoxyribonucleic acid (DNA) vaccines are strands of DNA coding for the genes for protective antigens.¹¹ The genes are inserted into bacterial plasmids (circular pieces of DNA) and placed in their bacterial hosts where they replicate. The plasmid DNA is purified from the bacteria and can then be directly administered into hosts. A number of different mechanisms for administering the vaccines have been used including gene guns with DNA on gold microbeads, needle injection into the muscle with or without liposomes, and transdermally with needle-free bioinjectors. To be effective, the DNA must enter into the host cells, be transcribed into messenger ribonucleic acid, and then transcribed into proteins that can be presented to the immune system.

Potential advantages of naked DNA vaccines include vaccine stability, affordability, potential of overcoming maternal antibody interference, intracellular synthesis of protein antigens for presentation to cytotoxic T cells, and duration of immunity. The first DNA vaccine for use in animals was recently licensed for protecting horses from West Nile virus.¹² As of this writing, no DNA-based vaccines have been approved for use in dogs, but experimental canine DNA vaccines have been developed for CPV-2 and CDV.

The vaccines described here touch on only a few of the potential technologies that can and will be used to create better and more effective vaccines. The cutting-edge technologies used to develop vaccines typically have higher research and development costs. The ability to use these technologies requires detailed knowledge of the pathogen and the immune response required for control of infection and/or disease by each pathogen, further increasing the research costs for the

development of these vaccines. For many organisms, these factors remain unknown or are poorly understood. The availability of effective conventional vaccines typically reduces the incentive to develop improved vaccines unless it can be shown that these technologies increase the safety of conventional vaccines without loss of efficacy.

Licensing of Vaccine Products

*How Are Vaccines Licensed?*²ⁱ

In order to market a veterinary biological product, a firm must acquire both a product license and an establishment license from the USDA Center for Veterinary Biologics (CVB). To obtain the establishment license, the firm must establish the appropriateness of the facility for the product in question as well as the appropriateness of the qualifications of the personnel involved in developing and producing the product; in addition, the facility must be inspected by the CVB. To obtain the product license, a firm must complete the following steps:

1. Submit an application that includes an Outline of Production, which is a detailed analysis of the proposed production. Once the Outline of Production has been approved, the firm cannot deviate from it without CVB permission.
2. Identify the labeling to be used with the product, which must be reviewed against data submitted to and approved by the CVB.
3. Provide supporting data, including data from field studies and studies to support efficacy and safety. Prior to the initiation of the studies, the CVB reviews and approves protocols to ensure quality of design and acceptability of the data generated. The applicant firm must demonstrate to the satisfaction of the CVB that the proposed product is pure, safe, potent, and efficacious.
4. Provide three or more consecutive prelicensure serials for testing by the CVB. A serial is an identifiable, homogeneous quantity of the completed commercial product (i.e., it may be a blend of several production batches and/or antigen components). Each of these prelicensure serials must be produced according to the Outline of Production from separate batches of medium, cells, production serum, and other applicable production components. The purpose is to demonstrate commercial consistency of production.

Once the product and establishment are licensed, samples from each serial must be sent to the CVB, along with results of the firm's testing of it. The serial cannot be released for commercial sale until the firm is notified by the CVB.

What Is Required of a Vaccine Prior to Licensure?

Purity: Purity is the quality of a biological product (in its final form) that assures the product is free of extraneous microorganisms and extraneous material (organic or inorganic) that can adversely affect safety, potency, or efficacy.¹³ All product components and ingredients must meet

standards of purity and quality. Master seed, master cell stock, primary cells, ingredients of animal origin, and final products must be tested and shown to be free of extraneous microorganisms. If eggs are used in production of biological products, they must be acquired from flocks free of specific pathogens. Purity and identification of master seed and master cell stocks are confirmed by testing at the CVB Laboratory in Ames, Iowa.

In addition to testing of the first serials (batches of completed product) prepared under license, a random sample of serials is subjected to prerelease purity testing at the CVB Laboratory to verify the manufacturer's quality assurance/quality control on the final product. This testing assures to a reasonable level of confidence that all components of biological products are correctly identified and free of contaminating agents (pathogenic or not). The exact specifications of the testing performed depend to a great extent on the nature of the antigen or microorganism.

Safety: Safety in a vaccine is defined as freedom from properties causing undue local or systemic reactions when the vaccine is used as recommended or suggested by the manufacturer.¹⁴ As with purity, safety testing begins with evaluation of the master seed and concludes with testing of each serial prior to release. All master seeds and master cell stocks must be fully identified and characterized. Production passage levels (limits) beyond the master seed/cell stocks are established.

For modified live products, the master seed is evaluated to ensure that it does not revert to a virulent state. This is accomplished by administration and recovery of the vaccine strain in susceptible dogs through several passages and observation of characteristic clinical signs. This test is designed to detect the potential for reversion to virulence of an attenuated product. The ability of a modified live product to be shed and spread among animals is also evaluated.

Field safety studies are performed in which the final product (at the titer, dose, and route of administration for the commercially released product) is administered to a minimum of 600 animals, of which at least one third must be at the minimum age indicated for administration. The field safety studies are designed to detect relatively frequent safety issues. Relatively rare safety issues will be detected by postmarketing surveillance.

Additionally, each serial of product released to the market is tested for safety. For modified live products, the tests involve laboratory animal testing as well as the administration of a 10× dose to two animals of the target species followed by observation for 14 days. For inactivated products, laboratory safety tests are performed to confirm inactivation.

Potency: Potency is the relative strength of a biological product as determined by test methods or procedures established by the CVB or in the approved Outline of Production for a product.¹⁵ The purpose of potency testing is to assure that each serial of vaccine produced is equal to or more potent than a reference serial (equal to or more antigen than a reference) or the minimum antigenic content as specified

through licensure. Potency tests correlated to host animal vaccination and designed to measure the relative strength of each serial must be developed prior to licensure. In addition, each serial is formulated and tested prior to marketing to ensure effectiveness and reproducibility of activity (potency) according to standards set at the time of licensure. Generally, this is accomplished through established laboratory animal or *in vitro* minimum potency levels using microbiological counts or virus titrations. However, the type of potency assay used can be both product (antigen)-specific and firm-specific. Standard potency assay requirements for some established canine antigens can be found in the Code of Federal Regulations.¹⁶ As standard assays are developed for emerging antigens, the procedures should become available from the CVB.

Because of the heterogeneity of antigens required to protect the health of canine patients, a multitude of potency assay formats exist. These include laboratory animal-based *in vivo* tests, target animal-based *in vivo* tests, and *in vitro* tests. Regardless of the format, all potency assays must be approved by the CVB and correlated to efficacy. Making the reference vaccine a serial that was used to demonstrate efficacy generally allows a firm to make this correlation. This system of potency testing assures that each serial produced contains a minimum amount of antigen; however, no upper limits to antigen content currently exist. This oversight should be given further consideration because an excessive amount of antigen could result in both safety and efficacy concerns.

Efficacy: The efficacy of a biological product is the specific ability or capacity of the product to effect the result for which it is offered when the product is used under the conditions recommended by the manufacturer.¹⁷ In other words, efficacy is generally thought of as the ability of the product to stimulate the immune response required to provide protection from challenge (i.e., protective immunity). In contrast, immunogenicity is the ability of a product to elicit an immune response whether or not the response is correlated to protection.

All products must be shown to be effective according to the indication on the label. Efficacy and product immunogenicity are almost always demonstrated by statistically valid host animal vaccination-challenge studies. In some circumstances, where serology is well correlated to protection, serology may be used to demonstrate efficacy. However, in today's regulatory climate, it is difficult to license a product using serology alone to establish efficacy. The following general considerations are applied to efficacy studies:

- Immunogenicity studies must be conducted using minimum levels of antigen at the highest passage level from the master seed that is permitted for production.
- The product must be prepared in production facilities on a scale representative of normal production.
- Although challenge methods and criteria for evaluating protection will vary with the immunizing agent, tests are generally conducted under controlled conditions using seronegative animals of the youngest age recommended on the label.

- Duration of immunity data demonstrate efficacy to a specified date after vaccination, which could be 1 year, 3 years, or another time interval. The DOI data are required for only one existing product—the rabies vaccine. In the future, however, the minimum DOI must be demonstrated for all newly licensed antigens.
- Data are required for each species for which the product is recommended and for each route, dose, and regimen of administration.
- For products with two or more fractions (components), data are required demonstrating that there is no interference among antigens in eliciting a protective response.
- Stability studies are required to set the expiration date on the label.

Relevance: The clinical relevance of products is considered in the licensure process. The CVB will not issue licenses for products it believes are not warranted or clinically relevant. However, the CVB determination may or may not meet with general agreement within the profession or among experts. The decision to bring a vaccine to market is made by the manufacturer on the basis of perceived need, market, and relevance of the agent involved. Determining which products, among all of those approved, are appropriate for any individual patient should be based on careful consideration of the risk of infection, the severity of disease, and the efficacy of the products available. As with all medical care decisions, the client/owner should be included in these determinations.

How to Evaluate and Interpret a Vaccine Label

Labeling and Claims: Labeling is defined as the totality of the written, printed, or graphic material accompanying the final product container as it is sold in the marketplace. The labeling conveys important information about the product. The labeling and all the information conveyed therein must be approved by the CVB before use by a manufacturer.

What is considered a label "claim" is sometimes a source of confusion. This is understandable because the term is not an administrative term that has been defined by the CVB, and different people use it to convey various meanings. However, the CVB considers anything contained in the product labeling to be a claim for the product. Therefore, regardless of whether the information pertains to an indication, storage requirements, or duration of immunity, if it is contained in the labeling, it is a claim.

Proposed Labeling Policy Revision: The CVB has indicated it is developing sweeping changes in the content and presentation of information on the labeling of veterinary biologics. The veterinary biologics industry and the AVMA Council on Biologics and Therapeutic Agents have had extensive discussions and exchange of ideas about the information practitioners want to see conveyed via product labeling, the best approach to conveying such information, and the practical and legal constraints and parameters within which labeling policy must operate. These views have been

shared with the CVB. Because of the many federal regulations governing product labeling for biologics, the revision of the labeling policy must undergo the complex and lengthy process of formal federal rule promulgation. As a result, implementation likely will not be seen for years. However, it should be noted that the CVB has indicated a willingness to remove the annual revaccination recommendation from most products, leaving only data-driven revaccination recommendations.

Serologic Testing to Determine and Monitor Immunity to Canine Vaccines

Interpreting Results of Serologic Tests

Despite the confusion and controversy surrounding antibody titers, many practitioners are having large numbers of tests for antibodies performed on a routine basis at state diagnostic laboratories and commercial laboratories or with in-house diagnostics. Antibody titers are useful for monitoring immunity to CDV, canine parvovirus-2 (CPV-2), canine adenovirus-1 (CAV-1), and rabies virus and to ensure that an animal has responded to a specific vaccine.¹⁸⁻²⁹

Antibody assays for CDV and CPV-2—the two tests performed most often—are the tests of greatest benefit in monitoring immunity, especially after the puppy vaccination series. The serologic test considered the “gold standard” for CDV is virus neutralization (VN).^{30,31} Virus neutralization and hemagglutination inhibition (HI) are the gold standard tests for antibody to CPV-2.³² Although a few diagnostic laboratories use the gold standard tests, most laboratories use other methods such as immunofluorescence assays or enzyme immunoassays. During the past 2 or 3 years, most, if not all, laboratories have qualified and standardized their methodologies with samples that were tested by the gold standard methods.

Notwithstanding this development, results still vary among tests and between laboratories. Most diagnostic laboratories report classic titers, in which twofold dilutions of serum are made and the highest dilution that neutralizes the virus (CDV, CPV-2, CAV-1) or inhibits hemagglutination by the virus (CPV-2) or binds to viral antigen and is detected with a fluorescent or enzyme probe is reported. Using this standard twofold dilution technique, the amount of error is approximately a fourfold dilution. The titer of a single serum sample would be in the range of one doubling dilution below the reported value and one doubling dilution above the reported value. For example, a CDV virus neutralization titer reported at 128 in reality is between 64 and 256; similarly, a CPV-2 HI titer of 1280 is between 640 and 2560. Some laboratories simply report results of 5 or greater as positive and less than 5 as negative.³³

An in-house test that provides a positive or negative result was approved by the USDA in April 2005.^c A positive CDV result indicates that a serum sample has an antibody titer that is 32 or greater on the virus neutralization test. A positive result for CPV-2 indicates the serum sample has an antibody titer that is 80 or greater with the HI test. A negative test indicates that the animal has a titer less than these val-

ues or that it has no antibody.³³ Obviously, some dogs with a negative result on this test are immune, but these dogs may benefit from revaccination. After performing and comparing many serologic tests for thousands of dogs, researchers have found that approximately 15% ± 5% of dogs will have low (≤80 HI) or no antibody to CPV-2 and 10% ± 5% of dogs will have low (≤32 VN) or no titer to CDV.^b With CDV and/or CPV-2 tests, an animal with a negative result, regardless of the test used, should be considered as having no antibody and susceptible to infection with CDV and/or CPV-2.

What Are the Possible Applications of Serologic Testing?

On completion of a puppy series at 12 or more weeks of age with products containing CDV and CPV-2, an animal should have an antibody titer or positive test result, regardless of the serologic test performed, provided the serum sample is collected 2 or more weeks after vaccination.^{34,35} If the animal does not have an antibody titer, it should be revaccinated—perhaps using a different product—and then retested. If the titer is again negative, the individual animal should be considered a low responder or a nonresponder and possibly incapable of developing a protective antibody titer.

Such titer testing is the only way to ensure that a puppy has developed an immune response after vaccination. Young animals are at greatest risk to infection from CDV and CPV-2, and infections often lead to severe disease and death. Antibody titers are useful and recommended as a medical procedure to ensure the animal has developed an immune response to CDV and CPV-2 vaccines after the primary series of vaccinations. Vaccines can fail for various reasons.^{36,37} However, the following are the three main explanations for vaccination failure: (1) The puppy has a sufficient amount of passively acquired maternal antibody (PAMA) to block the vaccine, (2) the vaccine is not immunogenic, or (3) the dog is a poor or nonresponder (i.e., the immune system fails to recognize the antigenic determinants of the specific vaccine).

The most common reason for vaccination failure is the first. When the last dose of a vaccine containing CDV and CPV-2 is given at 12 or more weeks of age, however, PAMA should be at a level that will not block active immunization in most puppies (>95%) when a reliable product is used. At this point, the practitioner must consider the other two explanations for vaccine failure. If, after one or more attempts at revaccination with a product different than the one originally used, the animal fails to develop antibody response to CDV or CPV-2 by VN or HI test, the animal should be considered a transient or a permanent nonresponder. A negative on antibody tests other than VN and HI would indicate a low or nonresponder animal.^b

Because immunologic nonresponsiveness is genetically controlled in other species, certain breeds or families of dogs may be suspected to have a higher prevalence of low or nonresponders than the general canine population. It is believed by some (but not proven) that the increased susceptibility to CPV-2 recognized in certain Rottweillers and Dobermans during the early and mid-1980s (regardless of

their vaccination history) was due to an increased prevalence of nonresponders; it was also demonstrated, however, that some vaccination failures were attributable to the poor-quality vaccines available at that time. Today the two breeds seem to have no greater numbers of low or nonresponders than other breeds, possibly because the nonresponders died from CPV-2.^b

A high titer of antibody to CDV and/or CPV-2 as a result of active immunization from vaccination or from natural exposure protects from infection; therefore, no detectable virus replication occurs. Although a virus may be capable of replicating in a dog whose antibody titers have decreased, memory B and T cells should provide an anamnestic (secondary) humoral and cell-mediated immune response that limits virus replication and prevents disease.

Application of Serology to Evaluate Duration of Immunity

Antibody tests can also be used to demonstrate the DOI to vaccines or from natural immunization. Dogs have been shown to maintain antibody titers to the core viruses CDV, CPV-2, CAV-1, and CAV-2 in viral-free environments for many years.^{34,35} In a study reported in 1997, dogs vaccinated with a product containing CDV and then placed in an environment without CDV maintained antibody titers for at least 10 years.^{33,38} In a more recent controlled study of puppies vaccinated at 7 and 10 weeks of age (and housed with nonvaccinated dogs to ensure CDV, CPV-2, CAV-1, and CAV-2 were not present), it was shown that vaccinated dogs maintained antibody titers for more than 4 years.³⁹ These and other studies have clearly demonstrated that antibodies to the core vaccine viruses may persist in the absence of revaccination. In addition, it was demonstrated that antibody correlates with protection from infection and/or protection from disease since the vaccinated antibody-positive animals remained healthy after experimental challenge with virulent strains of the viruses.³⁹ In contrast, a vaccinated animal did not develop antibody to CDV and the unvaccinated control dogs became infected; some dogs developed disease and died.³⁹ Therefore, when antibody is absent (irrespective of the serologic test used to determine this fact) it should be assumed the animal may be susceptible to infection and disease and therefore should be revaccinated.

Application of Serology to Determine When to Vaccinate the Puppy

Antibody titers are also useful in determining the time to vaccinate a young puppy. Years ago nomographs were commonly used to estimate the decay of PAMA in a puppy and determine the age at which the puppy could be actively immunized with a given vaccine. Nomographs are rarely used today except in special circumstances, as when an estimate of when puppies can be immunized is important, e.g., in an infected kennel. Today's method of choice is to vaccinate puppies starting at 6 to 8 weeks of age, revaccinating every 3 to 4 weeks until the last dose of vaccine is given at 12 weeks of age or older.^{ii,40}

Application of Serologic Testing to Other Infectious Diseases

Antibody titers to additional vaccine antigens are sometimes determined, but the best correlations between antibody titer and protective immunity are for CDV, CPV-2, and CAV-1. Very sensitive and well-documented titers to rabies virus are done by a small number of laboratories. Though most widely used when shipping dogs to rabies-free countries, rabies titers are sometimes performed in dogs that have developed an adverse reaction to the vaccine.^{18,41,42} Antibodies to other vaccines have limited or no value because the antibody persists for a short time period (e.g., *Leptospira* products) or there is no correlation between serum antibody and protection (e.g., canine parainfluenza).

Currently a significant consideration in performing antibody tests is the cost and the time to obtain results. In response to these needs, more rapid, cost-effective tests are being developed. Practitioners will then have quick and simple in-office tests that can be performed at a reasonable cost to the pet owner.

Vaccine Adverse Events—Recognition and Response

Background

The National Childhood Vaccine Injury Act of 1986 mandated the reporting of certain adverse events following the vaccination of children to help ensure the safety of vaccines distributed in the United States. The act led to the establishment of the Vaccine Adverse Event Reporting System (VAERS) in November 1990 by the U.S. Department of Health and Human Services. Today, VAERS provides a database management system for the collection and analysis of data from reports of adverse events following vaccination of humans.

Currently no similar federal or uniform state mandate exists for veterinarians to report adverse events associated with animal vaccination.ⁱⁱⁱ Practitioner reports of known or suspected vaccine adverse events in animals may be voluntarily submitted to either the vaccine manufacturer or the CVB. Formerly, vaccine adverse events also could be submitted to the U.S. Pharmacopeia (USP) through the Veterinary Practitioners' Reporting Program. However, the USP terminated that program in 2003.

The federal regulatory structure for manufacturers' reporting of adverse events is in a state of change. The CVB is proposing to amend the regulations regarding adverse event record keeping and reporting. Under the required provisions of the Federal Administrative Procedures Act, amendment of the regulations is accomplished through the lengthy, cumbersome, and complex process known as "notice-and-comment rulemaking." It also requires multiple reviews within other areas of the administration, including the Office of Management and Budget. Initially, the CVB published a proposed rule in the Federal Register in January 2002 with a 60-day comment period.⁴³ The CVB received comments, which the agency was required by law to consider and address formally in the Federal Register.

In the process of comment review, the CVB determined that some comments had merit and should be incorporated into the proposed approach. The necessary changes were of sufficient magnitude that rather than incorporate the changes and finalize the earlier rule, the CVB withdrew the earlier rule and proposed a new rule. The new proposal was published in August 2005.⁴⁴ If enacted as proposed, it would require manufacturers to maintain detailed records of every adverse event reported to their companies and provide summary reporting to the CVB at 12-month intervals (6-month intervals in the first year of a product). The timeline to implementation of a final rule is uncertain, but the proposed new rule represents a positive step.

What Constitutes a Vaccine Adverse Event?

For purposes of this discussion, a vaccine adverse event is defined as any undesirable side effect or unintended effect (including lack of desired result) associated with the administration of a licensed biological product (vaccine). For vaccines administered to animals, adverse events are those involving the health of the treated animal and include the apparent failure to protect against a disease. An adverse event includes any injury, toxicity, or sensitivity reaction associated with the use of a vaccine, *whether or not the event can be directly attributed to the vaccine*. In other words, it is appropriate to report any known or suspected event associated with vaccination. A vaccine adverse event report may be defined as a communication concerning the occurrence of one or more suspected adverse events; the communication identifies the product(s) and animal(s) involved in the event(s) and the individual submitting the report.

Why Is Adverse Event Reporting Important?

Reporting field observations of unexpected vaccine performance is the most important means by which the manufacturer and the regulating agency are alerted to potential vaccine safety or efficacy problems that may warrant further investigation. The purpose of prelicensure safety studies is to detect relatively common adverse events. Relatively rare adverse events can be detected only by postmarketing surveillance through analysis of reported adverse events.

If a particular adverse event is well documented, reporting serves to provide a baseline against which future reports can be compared. In addition, reported adverse events can lead to detection of previously unrecognized reactions, detection of increases in known reactions, recognition of risk factors associated with reactions, identification of vaccine lots with unusual events or unexpected numbers of adverse events, and further clinical, epidemiological, or laboratory studies. Therefore, veterinarians are encouraged to report any clinically significant adverse event occurring during or after administration of any vaccine licensed in the United States. Reporting a vaccine adverse event is not an indictment against a particular vaccine. Reporting simply facilitates review of temporally associated conditions and adds to the safety database of the product.

How to Report a Known or Suspected Vaccine Adverse Event

The AVMA Council on Biologic and Therapeutic Agents believes the current adverse event reporting systems need significant improvement in the capture, analysis, and reporting of adverse events.⁴⁵ Veterinarians are encouraged to participate in the vaccine adverse event reporting process by reporting suspected and known adverse events to the vaccine manufacturer, usually through telephone communication with technical services [Table 2] or the CVB by toll-free call (800-752-6255). Reports made to the USDA are forwarded directly to the vaccine manufacturer.

What Information Is Required in a Vaccine Adverse Event Report?

A report of a known or suspected vaccine adverse event should include the following information:

1. Manufacturer's name
2. Product brand name, product code, product lot/serial number, and expiration date
3. The reporting practitioner's U.S. veterinary license number
4. Signalment (i.e., age, species, breed, gender) of the affected patient
5. A description of the clinical signs or diagnosis associated with administration of the vaccine should be provided. Specific reporting criteria are not defined for clinical events; however, the reporting of clinical signs associated with administration of a biological product should document the type of reaction and the length of time between administration of the vaccine and onset of the adverse event:
 - a. Local (injection-site) reactions occur exclusively at or around the site of inoculation. They may occur at the time of injection or several minutes, hours, or days later and may persist in duration from minutes (e.g., pruritus) to months (e.g., granuloma). Reports should include the route of administration, i.e., subcutaneous, intramuscular, or topical (oral, conjunctival, or nasal). Examples of local reactions following vaccination include pain, pruritus, swelling, injection-site alopecia, abscess formation, granuloma formation, and neoplasia. Infection and skin necrosis are rare but have been reported. Vaccines licensed for administration by the topical (oral, conjunctival, or intranasal) route have been associated with sneezing (persisting 3 days or longer), nasal and oral ulceration, ocular discharge, and cough (persisting 24 hours or longer).
 - b. Systemic reactions are events that involve the entire body or a defined location and/or region other than the injection site. Like injection-site reactions, systemic reactions typically don't occur at the time of injection, but can develop within minutes or hours and may persist for hours or days. Examples of systemic

Table 2
Contact Information for Biologics Manufacturers

Company Name	Address	Technical Services Phone
Boehringer Ingelheim Vetmedica Inc.	2621 North Belt Hwy. St. Joseph, MO 64506	800-325-9167
Delmont Laboratories Inc.	715 Harvard Ave. PO Box 269 Swarthmore, PA 19081	800-562-5541
Fort Dodge Animal Health	9225 Indian Creek Pkwy. PO Box 269 Overland Park, KS 66210	800-533-8536
Heska Corp.	3760 Rocky Mountain Ave. Loveland, CO 80538	888-437-5286
Intervet Inc.	29160 Intervet Lane PO Box 318 Millsboro, DE 19966	800-441-8272
Merial Ltd.	3239 Satellite Blvd. Duluth, GA 30096	888-637-4251 (ext. 3)
Pfizer Animal Health Inc.	812 Springdale Dr. Exton, PA 19341	800-366-5288
Schering-Plough Animal Health Corp.	1095 Morris Ave. Union, NJ 07083	800-224-5318

It is recommended that any vaccine adverse event also be reported to the U.S. Department of Agriculture Center for Veterinary Biologics by calling toll-free 800-752-6255.

reactions following vaccination include angioedema, especially involving the face, muzzle, and ears (most often reported in dogs); anaphylaxis and collapse; polyarthritis (lameness); vomiting with or without diarrhea (most often reported in cats); respiratory distress; fever; lethargy; and neurologic or behavioral changes. Severe events that may be vaccine-associated and involve long-term medical intervention and patient follow-up include immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, icterus, polyarthritis, renal failure, and glomerulonephritis.

- c. Vaccine-associated death, although rare, does occur. In dogs, anaphylactic shock is the most commonly reported adverse event leading to death. There has been no trend to suggest an association between anaphylaxis and a particular manufacturer's vaccine. Veterinarians are strongly encouraged to report to the vaccine manufacturer any death suspected or known to be associated with vaccination [Table 2].

Vaccination from a Medicolegal Perspective

As a general rule, the use of biological products by small animal veterinary practitioners is left to their professional judgment. Although the latitude afforded practitioners is broad, there are boundaries.

The analysis of the law governing use is complicated. The USDA CVB regulates the licensure and preparation of most veterinary biologics. The Virus-Serum-Toxin Act empowers the CVB to stop the sale, barter, or exchange of "any worthless, contaminated, dangerous, or harmful virus, serum, toxin, or analogous product." If a given discretionary veterinary use of a CVB-regulated product were viewed as unsafe, it could initiate an enforcement action; however, unless a safety issue is implicated, USDA historically has not considered such enforcement to be a priority. Additionally, some vaccines are licensed with specific restrictions regarding their use, which will be noted in their labeling.

Through its Center for Veterinary Medicine (CVM), the U.S. Food and Drug Administration also regulates some

products that most practitioners would consider biologicals. The jurisdictional gray zone between the two agencies is confusing, constantly blurred, and evolving. Products regulated by the CVM are covered by the Animal Medicinal Drug Use Clarification Act, which established specific rules for “extra-label” drug use.

What is the Potential of Liability Associated With Vaccine Administration?

Potential liability for medical decision making is a fact of life for any health care provider, including veterinarians. This potential professional liability encompasses all aspects of veterinary practice, including the selection and use of vaccines and other biological products. Generalizations about potential legal liability are as difficult to make as generalizations about medical practice. The range of possible legal liability theories used in litigation is broad and limited only by the creativity of the plaintiff’s attorney. To further complicate matters, legal statutes vary state by state. However, most lawsuits against practitioners are grounded in negligence theory, although other possible grounds include products liability, breach of express or implied contract, breach of express or implied warranty, guaranty, battery, and breach of fiduciary relationship. These principles apply to all aspects of professional veterinary practice, not simply vaccine or biological issues. The subsequent section discusses some types of negligence suits that could arise out of use of biological products.

Medical Negligence: Negligence actions involving veterinarians are usually cast as traditional “medical malpractice” cases. The law of professional medical negligence has evolved in the context of human medicine. Most jurisdictions apply the legal concepts developed in the litigation of physician malpractice cases to veterinary malpractice cases. The traditional elements of a medical malpractice lawsuit are the duty to conform to a certain standard of care, a failure to conform to the required standard, actual injury or damage, and a legally sufficient causal connection between the conduct and the injury.

The duty arises out of the veterinary-client-patient relationship and is typically stated as the duty to exercise reasonable care, i.e., the same level of care and competence as a reasonably prudent practitioner would, with the same or similar training, under the same or similar circumstances. This duty is often referred to as the “standard of care.” In this context, standard of care is a legal term and does not necessarily equate with professional practices or standards. With few exceptions, establishment of the relevant standard of care and whether a practitioner deviated from it must be established by competent expert testimony.

In practice, many medical negligence cases become a battle of experts. The plaintiff uses an expert witness to establish a standard of care and then presents the opinion that the practitioner failed to meet the standard and that such failure caused the plaintiff’s injury or damages. In turn, the defense offers differing expert testimony, establishing a different standard of care, and attests that the

defendant practitioner met the standard and that the defendant’s conduct did not legally cause the plaintiff’s injury or damage. Faced with conflicting evidence, the jury arrives at a verdict on the basis of innumerable variables, including the qualifications and presentation of the various experts and the defendant.

Malpractice as It Applies to Vaccine Decision Making: With regard to malpractice involving vaccination, the scenarios that could give rise to a lawsuit are as varied as the imagination allows. For example, a practitioner who chooses not to vaccinate an animal could potentially be sued for negligence if the animal contracts the disease for which vaccination was forgone. In such a case, the plaintiff would be required to have expert testimony that the defendant’s failure to vaccinate the animal was a departure from the standard of care and the cause of the injury to the animal. On the other hand, a practitioner who vaccinates an animal could potentially be sued for negligence if the animal experiences a complication from the use of the vaccine. In such a case, the plaintiff would be required to have expert testimony that the defendant’s vaccination of the animal was a departure from the standard of care and the cause of the injury to the animal. Whether a plaintiff prevails on such theories would depend on the facts of the individual case, the qualifications of the defendant and the experts, and the intangible factors that inevitably come into play in trials.

What Constitutes Informed Consent?

The legal doctrine of informed consent arises out of the obligation to obtain consent prior to providing care to a patient. The essence of informed consent is that a practitioner informs the client of the material risks of a proposed treatment or procedure and potential alternatives, including the risk of no treatment; the client/patient, having been informed, either gives or withholds consent. It is important to keep in mind that the goal is the *informed* consent of the client/patient, not simply the act of obtaining a signature on a form. One of the best deterrents to an informed consent lawsuit (or other legal action for that matter) is to communicate with (rather than talk at) clients and document the discussions.

The law governing this area developed as human medicine evolved from a paternalistic profession to one that recognizes the importance of a patient’s self-determination. Informed consent cases, common in human medical malpractice, can be used in suits against veterinarians as well. These cases are most often brought under negligence principles, reflecting the manner in which they developed in physician malpractice cases. In some jurisdictions, an informed consent case may be brought under other legal principles, such as battery. Most informed consent cases arise out of patient’s/client’s misunderstanding, misperception, and—from the practitioner’s perspective—sometimes unreasonable expectations.

A complicating factor is a split of authority on the standard by which a practitioner’s actions are judged in informed consent cases. Two primary standards are used, with a fairly even division between those states that use a practitioner-focused inquiry and those that use a patient/client-focused inquiry.

Thus, the standard by which a veterinarian's conduct is evaluated depends on the state in which he or she practices.

Under the practitioner-focused standard, the inquiry focuses on whether the defendant provided the information that a reasonable practitioner would disclose under the circumstances. The level of the required disclosure is established by expert testimony. Under the patient/client-focused standard, the inquiry is whether the practitioner provided sufficient information (in understandable terms) to allow a "reasonable person" to make decisions about the course of treatment. The real issue becomes what information would a reasonable person need in order to make informed, rational decisions. Regardless of which standard is employed, the other elements of a negligence case, including the causal connection, must be established in order for a plaintiff to prevail.

How Should Informed Consent Be Documented?

Whether the use of written consent forms deters informed consent cases is a matter of debate. Documentation of informed consent discussions is always helpful to the defense of an informed consent case. Such documentation ranges from a note in the chart (with or without co-signature by the client) to a generic consent form signed by the client to a very detailed document specific to the treatment or procedure contemplated. The more general the language used, the less helpful the documentation may prove in court; conversely, the more specific the language, the more helpful to the defense of a case.

It should be noted that in human medicine, most informed consent lawsuits have signed consent forms in the chart. While signed consent forms can be helpful, they do not preempt all lawsuits over consent issues. In fact, in some instances, consent documents can be harmful to the defense of a case. Some consent forms for vaccination estimate the odds of disease exposure or the chance of an adverse event occurring following vaccination. The practitioner should have a medically or scientifically defensible basis for making any such precise representations in a consent document. If precise numbers cannot be justified, then more general statements are preferable. For example, an appropriate statement would be one indicating that the true incidence of a particular adverse reaction is not known but is believed to be low or has been reported in the literature to be in the range of "X%–Y%." Additionally, a statement that the exact chances of exposure to a particular disease cannot be quantified but should be less where the animal is not exposed to other animals would be more defensible.

Such statements can be harder to craft, but may help a practitioner avoid the onerous burden of explaining to a jury that representations made to a client prior to a treatment or procedure were simply a "guesstimate," leaving the practitioner to justify on the stand any basis for statements made. Although there is room for professional judgment, very specific numbers based solely on experience or judgment will be harder to defend. Practitioners seeking the best approach to crafting consent forms for use in their practice

are advised to consult with an attorney who has defended informed consent cases in their state. He or she can provide invaluable assistance in understanding the law in a particular jurisdiction and crafting consent documents that best meet both local legal standards and the needs of the individual practice.

Comprehensive Individualized Care That Goes Beyond Vaccination

For many years, the practice of veterinary medicine has benefited from the annual administration of vaccines. By encouraging dog owners to bring their pets in yearly for vaccinations, veterinarians were able to recognize and treat disease earlier than might otherwise have been the case. In addition, the annual visit provided an opportunity to inform clients of important aspects of canine health care.

Unfortunately, many clients have come to believe that vaccination is the most important reason for annual veterinary visits. Veterinarians are justifiably concerned that a reduction in vaccination frequency will cause clients to forgo routine annual visits for their dogs and that the quality of care the animals receive will be diminished. To avoid this consequence, it is essential that veterinarians stress the importance of all aspects of a comprehensive individualized health care program. Clients should be informed that dogs with serious disease often appear healthy and that regularly scheduled health evaluations facilitate early detection. Emphasis should be placed on a comprehensive physical examination by the veterinarian and individualized patient care. The importance of dental care, proper nutrition, appropriate diagnostic testing, and the control of parasites and other zoonotic diseases should also be addressed during each patient evaluation. Behavior concerns should be discussed, as well as the necessity for more frequent examination of puppies and geriatric dogs.

Vaccinations as a Component of Comprehensive Individualized Care

Every patient's vaccination needs should be assessed at least yearly. The practitioner should explain to the client the types of vaccines available, their potential benefits and risks, and their applicability to the particular dog, given its lifestyle and risk of exposure. The regional incidence and risk factors for various infectious diseases should also be discussed. With a focus on the welfare of the patient, these discussions should take place even with clients who choose to vaccinate their pets themselves or have them vaccinated by individuals other than the primary care veterinarian. Ways to reduce the impact of acquired disease (e.g., avoiding overcrowding, improving nutrition, and restricting access to infected animals) should also be reviewed.

Vaccinations should be considered as only one component of a comprehensive preventive health care plan individualized based on the age, breed, health status, environment (potential exposure to harmful agents), lifestyle (contact with other animals), and travel habits of the dog.

Age

Obviously age has a significant effect on the preventive health care needs of any given individual. Puppy programs have traditionally focused on vaccinations, parasite control, and sterilization. Today, opportunity exists to incorporate behavior counseling and zoonotic disease management as well. For aging pets, tiered senior care programs are increasingly popular. Nutritional, dental disease, and parasite control assessment and counseling should take place on an individualized basis throughout the life of the pet.

Breed

It is well known that certain breeds are predisposed to various diseases. Early detection and management of breed-associated disease can significantly improve the quality of the dog's entire life.

Health Status

Dogs with chronic medical conditions such as diabetes mellitus, hypothyroidism, heart disease, renal failure, hyperadrenocorticoidism, hypoadrenocorticoidism, glaucoma, and keratoconjunctivitis sicca warrant periodic scheduled medical progress examinations and testing designed to monitor the progression of the diseases and provide for therapeutic adjustments. Dogs receiving certain medications also warrant therapeutic monitoring of blood levels and/or organ systems. The development of recheck protocols for chronic diseases and medications, which can be included in reminder systems, can greatly improve client compliance and, accordingly, patient care.

Environment

The environment in which a pet resides can profoundly affect the pet's health status. Exposure to trauma (automobiles, animal fights, high rise syndrome), weather (heat stroke, frostbite), water (drowning), toxins (antifreeze, human medications, poisonous plants, household and industrial toxins), sunlight (solar dermatitis), as well as internal and external parasites should be assessed during annual health care visits in order to define risk factors and develop appropriate preventive measures.

Lifestyle

By determining the extent to which dogs come in contact with other animals either in controlled or unobserved circumstances, veterinarians can assess the need for noncore vaccinations. Dogs that visit kennels, grooming salons, common areas, and wooded, tick-infested areas are potentially at greater risk from certain infectious diseases than dogs that do not frequent these areas.

Travel Habits

Just as the human population has become much more mobile, so has the canine population, resulting in potential exposure to infectious agents, parasites, and environmental hazards not found in the home environment. Determining past and anticipated future travel of dogs during each preventive care

visit allows for greater individualization of preventive care and diagnostic testing plans.

Medical Record Documentation (AAHA Accreditation Standards)

At the time of vaccine administration, the following information should be recorded in the patient's permanent medical record:

- date of vaccine administration,
- identity (name, initials, or code) of the person administering the vaccine,
- vaccine name, lot or serial number, expiration date, and manufacturer, and
- site and route of vaccine administration.

The use of peel-off vaccine labels and stamps that imprint the medical record with the outline of a dog facilitates this type of record keeping. Adverse events should be recorded in a manner that will alert all staff members during future visits. Informed consent should be documented in the medical record in order to demonstrate that relevant information was provided to the client and that the client authorized the procedure. At the very least, this notation should indicate that a discussion of risks and benefits took place prior to vaccination.

PART 2 CANINE VACCINATION IN THE SHELTER ENVIRONMENT

Introduction

The first edition of the AAHA Canine Vaccination Guidelines and Recommendations, published in 2003, did not specifically address vaccination of dogs entering or residing in an animal shelter environment. This omission was more a consequence of the lack of published information than oversight. Since 2003, however, additional publications and presentations have focused on management strategies for mitigating the risk of infectious diseases in animal shelters. This new information has provided the impetus to create a section specifically addressing canine vaccination guidelines in the shelter environment.

Why Shelters Need Separate Vaccination Guidelines

The Canine Vaccination Task Force created these shelter vaccination guidelines and accompanying vaccination tables to aid individuals responsible for purchasing vaccines, administering vaccines, or establishing vaccination policy for dogs presented to and maintained in a shelter environment. These guidelines reflect the Task Force's acknowledgment that many of the fundamental principles of vaccination, infection control, and health risk assessment routinely followed in clinical companion animal practice may not apply in the shelter environment. To practice shelter medicine is to practice in an environment where eradication of infectious diseases is not an attainable goal. It is possible, however, to minimize the spread of diverse infections within a high-density, high-risk population and maintain the

health of those individuals that have not become the target of an infectious disease.

When the overall purpose is to place healthy pets into welcoming homes, the time and effort dedicated to controlling infectious disease is only one of many variables in the complex shelter medicine and husbandry equation. The recommendations provided here attempt to address some shelter-unique issues as they pertain to vaccination and control of infectious diseases. The Task Force recognizes that other variables in the shelter environment may benefit from the application of scientific study and strategic management methods. These guidelines then represent—not the final word—but a first step in addressing the unique concerns of the shelter environment.

Disclaimer

These shelter vaccination guidelines are intended as recommendations only and do not constitute standards; there is no mandate or requirement for any facility to adopt these guidelines in part or in their entirety. However, the Task Force emphasizes that it is in the best interest of the individual shelter to establish policy regarding the administration of recommended vaccines and to assure such policy is communicated to all professional and nonprofessional staff in the facility.

Definition of a Shelter Environment

The proper interpretation and use of these guidelines requires a clear understanding of what is meant by a “shelter.” An animal shelter is a holding facility for homeless animals, usually awaiting adoption, rescue, or reclaim by owners. In general, animal shelters are characterized by a random source population with a largely unknown vaccine history, high population turnover, and significant potential for relatively high levels of infectious disease risk.

Within this broad definition, however, there is wide variation. The term “shelter” encompasses situations ranging from sanctuaries that possess a stable population to facilities that admit dozens or even hundreds of animals per day to rescue and foster homes that care for multiple litters or individuals at any given time. Just as the appropriate vaccine strategy varies with each individual pet, there is no one-size-fits-all strategy for vaccinating shelter animals. Shelters should interpret these guidelines in light of the infectious disease risk and turnover rate within their own populations.

Special Consideration of a Shelter Vaccination Program

The relatively high likelihood of disease exposure in most shelters and the potentially devastating consequences of infection necessitate a clearly defined shelter vaccination program with exacting requirements. It is necessary to define not only *what* antigens are appropriate, but also *when* vaccines should be administered with respect to shelter entry, *which animals* are candidates for vaccination, and *how and by whom* vaccines will be administered, including record keeping and documentation of adverse events. For vaccines that offer significant protection against common and severe infectious

diseases, the appropriate vaccination program may be one that is more aggressive than is generally indicated in private practice. Such a program may include, for example, vaccinating animals at the short end of the suggested intervals.

With the use of vaccines in an expanded population, it is also important to minimize the vaccine antigens given to those that are clearly indicated by the immediate circumstances. Vaccines are often administered to stray dogs not legally belonging to the shelter and may be given by lay staff under indirect veterinary supervision. These considerations make it even more crucial to develop a vaccine program that minimizes the risk of vaccine-induced adverse reactions. Furthermore, cost differences that are trivial for one individual become significant when multiplied by thousands of doses. Therefore, only those antigens that demonstrate a clear benefit against common and significant shelter diseases should be used. Adopters should be encouraged to discuss an individually tailored vaccination program with their own veterinarian following adoption.

General Vaccine Guidelines for Shelters

Vaccines Recommended for the Shelter Environment

Those vaccines deemed most important for all dogs housed in a shelter environment are categorized as recommended vaccines rather than core vaccines [Table 3].⁴⁶⁻⁵¹ The Task Force acknowledges the fact that frequent introduction of healthy and sick dogs, seasonal variations in population density, and variable risk of exposure among shelters makes it impractical to define specific core vaccines that will equally serve all facilities at all times.

It is the opinion of the Task Force that all vaccines categorized in Table 3 as recommended be administered at the time of admission to all dogs older than 6 weeks (4 weeks in cases of disease outbreaks). It is strongly recommended that immediate vaccination on entry be made a priority in all shelters. Delaying vaccination, even by a few hours, may increase the risk of infection subsequent to exposure.⁵² Failing to immediately vaccinate an animal on entry could compromise an effective disease prevention program and possibly lead to sustained, shelter-wide outbreaks of an infectious disease.

Vaccines Categorized as Optional for the Shelter Environment

Because of the variation in vaccine selection and use of canine vaccine among animal shelters, an alternative selection of optional vaccines for use in shelters is provided in Table 4. It is recommended that a 1-year rabies vaccine be administered to all dogs, according to the appropriate age guidelines, at the time of discharge from the shelter. Recommendations for rabies vaccine administration may be different for “sustained stay” shelters [Table 4].

Vaccines NOT Recommended for the Shelter Environment

In the opinion of the Task Force, several vaccines licensed for use in the United States are not indicated for dogs residing in

Table 3
Schedule of Recommended Canine Vaccination for the Shelter Environment

Recommended Vaccines in Various Combinations*	Initial Vaccine Series for Puppies (<16 weeks of age)	Initial Vaccine Series for Adults (>16 weeks of age)	Comments
<p>NOTE: All of these products may fit into a recommended shelter protocol provided all core diseases are protected against. Also refer to Table 1.</p>			
<p>Canine Distemper Virus + Canine Adenovirus-2 + Canine Parvovirus (MLV) Combination product is administered SQ or IM according to manufacturer recommendations. NOTE: Parainfluenza virus is recommended. If not administered parenterally, it should be administered as an intranasal vaccine.</p>	<p>Administer one dose on admission. Repeat at 2-week intervals until 16 weeks of age if animal is still in the facility. NOTE: Where CDV and/or parvovirus infection rates are high, the CDV vaccine may be safely administered as early as 4 weeks of age.</p>	<p>Administer one dose on admission. Repeat in 2 weeks.</p>	<p>Ideally puppies should be vaccinated beginning at 6 weeks of age. Nursing history is not always available. In the face of an outbreak, vaccination as early as 2-3 weeks (for distemper) or 5 weeks (for parvovirus) may be indicated.[†] Passively acquired maternal antibodies (PAMA), if present, can interfere with immunization.</p>
<p>rCanine Distemper Virus + Canine Adenovirus-2 + Canine Parvovirus (rCDV + MLV) Combination product is administered SQ or IM according to manufacturer recommendations. NOTE: Parainfluenza virus is recommended. If not administered parenterally, it should be administered as an intranasal vaccine.</p>	<p>Administer one dose on admission. Repeat at 2-week intervals until 16 weeks of age if animal is still in the facility. NOTE: Where CDV and/or parvovirus infection rates are high, the rCDV vaccine may be safely administered as early as 4 weeks of age.</p>	<p>Administer one dose on admission. Repeat in 2 weeks.</p>	<p>Ideally puppies should be vaccinated beginning at 6 weeks of age. In the face of an outbreak, vaccination as early as 2-3 weeks (for distemper) or 5 weeks (for parvovirus) may be indicated.[†] The rCDV vaccine has been shown to demonstrate immunogenicity that is the same as MLV vaccines.[‡] NOTE: The rCDV vaccine has been shown to immunize puppies despite the presence of PAMA.[‡]</p>
<p>Canine Distemper Virus + Canine Adenovirus-2 + Parainfluenza Virus + Canine Parvovirus (MLV) Combination product is administered SQ or IM according to manufacturer recommendations. NOTE: Multivalent core vaccines are available without MLV parainfluenza virus. Also, MLV parainfluenza vaccine is available in combination with all <i>B. bronchiseptica</i> approved for intranasal administration.</p>	<p>Administer one dose on admission. Repeat at 2-week intervals until 16 weeks of age if animal is still in the facility. NOTE: Where CDV and/or parvovirus infection rates are high, vaccine may be administered as early as 4 weeks of age.</p>	<p>Administer one dose on admission. Repeat in 2 weeks.</p>	<p>Ideally puppies should be vaccinated beginning at 6 weeks of age. Nursing history is not always available. In the face of an outbreak, vaccination as early as 2-3 weeks (for parvovirus) may be indicated.[†] Passively acquired maternal antibodies (PAMA), if present, can interfere with immunization.</p>
<p>rCanine Distemper Virus + Canine Adenovirus-2 + Parainfluenza Virus + Canine Parvovirus (rCDV + MLV) Combination product is administered SQ or IM according to manufacturer recommendations. NOTE: Multivalent core vaccines are available without MLV parainfluenza virus. Also, MLV parainfluenza vaccine is available in combination with all <i>B. bronchiseptica</i> approved for intranasal administration.</p>	<p>Administer one dose on admission. Repeat at 2-week intervals until 16 weeks of age if animal is still in the facility. NOTE: Where CDV and/or parvovirus infection rates are high, vaccine may be administered as early as 4 weeks of age.</p>	<p>Administer one dose on admission. Repeat in 2 weeks.</p>	<p>Ideally puppies should be vaccinated beginning at 6 weeks of age. In the face of an outbreak, vaccination as early as 2-3 weeks (for distemper) or 5 weeks (for parvovirus) may be indicated.[†] The rCDV vaccine has been shown to demonstrate immunogenicity that is the same as MLV vaccines.[‡] NOTE: The rCDV vaccine has been shown to immunize puppies despite the presence of PAMA.[‡]</p>

(Continued on next page)

Table 3 (cont'd)
Schedule of Recommended Canine Vaccination for the Shelter Environment

Recommended Vaccines in Various Combinations*	Initial Vaccine Series for Puppies (<16 weeks of age)	Initial Vaccine Series for Adults (>16 weeks of age)	Comments
<i>Bordetella bronchiseptica</i> (avirulent live bacterin) + Parainfluenza Virus (MLV) If parenteral parainfluenza vaccine is not administered, this product is highly indicated. For intranasal use only. Parenteral administration MUST BE avoided.	Administer a single dose as early as 3 weeks of age. For best results, if administered prior to 6 weeks of age, an additional dose should be given after 6 weeks of age.	Two doses 2-4 weeks apart are recommended.	Intranasal (avirulent live) vaccine is preferred to parenteral vaccine in puppies because it can safely be administered to puppies younger than 6 weeks. Additionally a single dose may be protective. [§]
<i>Bordetella bronchiseptica</i> (available as killed bacterin or antigen extract) Intranasal	Administer one dose at time of admission. Administer a second dose 2-4 weeks later.	Two doses 2-4 weeks apart are recommended.	Topical vaccination is not superior to parenteral administration in adult dogs or puppies older than 16 weeks. [†] With the possible exception of vaccinating puppies, topical vaccination is not necessarily superior to parenteral vaccination when administering parenteral vaccine to adult dogs. This is especially true when administering booster vaccination to adult dogs. ^{‡,¶}
<i>Bordetella bronchiseptica</i> (available killed bacterin or antigen extract) For parenteral administration only	Administer one dose at the time of admission. A second dose is required 2-4 weeks following the first dose.	Not stipulated; however, two doses 2-4 weeks apart are recommended.	Topical vaccination is not superior to parenteral administration in adult dogs or puppies older than 16 weeks. [†] With the possible exception of vaccinating puppies, topical vaccination is not necessarily superior to parenteral vaccination when administering parenteral vaccine to adult dogs. This is especially true when administering booster vaccination to adult dogs. ^{‡,¶}

* IM—intramuscular; MLV—modified live virus; r—recombinant; SQ—subcutaneous.

† Greene CE, Schultz RD. Immunophylaxis and immunotherapy. In: Infectious Diseases of the Dog and Cat. 3rd ed. Philadelphia: WB Saunders, 2005:1069-1119.

‡ Schultz RD. Canine Distemper and Vaccination. Duluth, GA: Merial, 2005.

§ Edinboro CH, Ward MP, Glickman LT. A placebo-controlled trial of two intranasal vaccines to prevent tracheobronchitis (kennel cough) in dogs entering a humane shelter. Prev Vet Med 2004;62(2):89-99.

† Glickman LT, Appel MJ. Intranasal vaccine trial for canine infectious tracheobronchitis (kennel cough). Lab Anim Sci 1981;31(4):397-399.

¶ Bey RF, Shade FJ, Goodnow RA et al. Intranasal vaccination of dogs with live avirulent *Bordetella bronchiseptica*: correlation of serum agglutination titer and the formation of secretory IgA with protection against experimentally induced infectious tracheobronchitis. Am J Vet Res 1981;42 (7):1130-1132.

Ellis JA, Krakowka GS, Dayton AD et al. Comparative efficacy of an injectable vaccine and an intranasal vaccine in stimulating *Bordetella bronchiseptica*-reactive antibody responses in seropositive dogs. J Am Vet Med Assoc 2002;220(1):43-48.

Table 4
Optional Vaccines for Use in the Shelter Environment

Vaccine*	Initial Vaccine Series for Puppies (<16 weeks of age)	Initial Vaccine Series for Adults (>16 weeks of age)	Comments
Canine Distemper-Measles Combination (MLV) Intramuscular administration only	Administer one dose between 4 and 12 weeks of age.	NEVER indicated in animals older than 12 weeks.	Indicated to provide temporary protection against canine distemper virus in puppies 12 weeks of age or younger when passively acquired maternal antibodies (PAMA) are more likely to occur. There is evidence that recombinant distemper vaccine will break through PAMA and so may be a superior product.
Rabies 1-year (killed) NOTE: Route of administration may not be optional. See product literature for details.	Administer one dose as early as 12-16 weeks of age depending on local regulations. Administer at the time of release from the facility. If a long-term shelter stay is anticipated (as in a legal case, sanctuary, or long-term care facility), a single dose of a 1-year vaccine should be administered at the time of admission.	Administer one dose at the time of release from the shelter. If a long-term shelter stay is anticipated (as in a legal case, sanctuary, or long-term care facility), a single dose of a 1-year vaccine should be administered at the time of admission.	Booster vaccination is required 1 year later. Local statutes apply. There is NO medical indication to vaccinate against rabies at the time of admission to the shelter unless the dog is being admitted for a long-term stay at the facility. Separate regulations may apply to dogs being held in rabies quarantine.
Rabies 3-year (killed) NOTE: Route of administration may not be optional. See product literature for details.	Normally, rabies vaccine labeled as 3 year would not be indicated in puppies because revaccination is required 12 months later. However, the 3-year vaccine may be used as an alternative to a 1-year vaccine for additional and subsequent doses. Local, state, and provincial statutes may apply. Do not administer to dogs younger than 3 months.	In some situations, the 3-year rabies vaccine may be used as an alternative to the 1-year vaccine for initial and subsequent doses. Local, state, and provincial statutes may apply. Do not administer to dogs younger than 3 months.	Booster vaccination is required 1 year later unless documentation is available that confirms previous vaccination. Local statutes apply. There is NO medical indication to vaccinate against rabies at the time of admission to the shelter unless the dog is being admitted for a long-term stay at the facility. Separate regulations may apply to dogs being held in rabies quarantine.

* MLV—modified live vaccine.

Table 5**Vaccines NOT RECOMMENDED for Use in the Shelter Environment**

Vaccine	Comment
<i>Borrelia burgdorferi</i> (rLyme borreliosis) (recombinant—Outer Surface Protein A [OspaA]) Limited use in endemic regions	Most shelters should not routinely administer Lyme borreliosis vaccine. Risk of exposure/infection in the individual dog is best determined after placement.
<i>Borrelia burgdorferi</i> (Lyme borreliosis) (killed, whole cell bacterin) Limited use in endemic regions	Most shelters should not routinely administer Lyme borreliosis vaccine. Risk of exposure/infection in the individual dog is best determined after placement.
Leptospirosis (<i>L. canicola</i> combined with <i>L. icterohaemorrhagiae</i>) (killed bacterin)	Vaccine is not generally recommended without knowledge that infection is known to occur in the community. The cost:benefit value to shelters has not been established. The risk of exposure/infection within the shelter to leptospirosis is sufficiently low that vaccination at the time of admission is not generally indicated. In communities with very high incidence of leptospirosis or when dogs are admitted to long-term holding facilities, it may be indicated.
Leptospirosis (<i>L. canicola</i> , <i>L. icterohaemorrhagiae</i> combined with <i>L. grippityphosa</i> , <i>L. pomona</i>) (killed bacterin)	Vaccine is not generally recommended without knowledge that infection is known to occur in the community. The cost:benefit value to shelters has not been established. The risk of exposure/infection within the shelter to leptospirosis is sufficiently low that vaccination at the time of admission is not generally indicated. In communities with very high incidence of leptospirosis or when dogs are admitted to long-term holding facilities, it may be indicated.
Canine Adenovirus-1 (CAV-1) (MLV)*	Do not use products containing CAV-1. They may cause ocular or renal insults. Though not often used, CAV-1 vaccines are still available through over-the-counter sources. Donated vaccines should be checked closely to assure quality, consistency, and safety of vaccines used.
<i>Giardia lamblia</i> (bacterin)	Though demonstrated to reduce shedding of organisms, the vaccine does not prevent infection. The value of vaccinating against <i>Giardia</i> has not been demonstrated in shelters.
Canine Coronavirus (MLV or killed)	Canine coronavirus vaccine is not indicated. Because there is no practical way of diagnosing the disease, the incidence and significance of the disease are unknown. The clinical syndrome attributed to coronavirus is not sufficiently severe enough to warrant routine vaccination. There is no demonstrated value to vaccinating against coronavirus. Routine vaccination has not resulted in a decrease in diarrheal disease in dogs, and when vaccination is discontinued, no corresponding increase in diarrheal disease is seen. Routinely vaccinating against coronavirus in shelters is not cost effective.
<i>Crotalus atrox</i> Toxoid	Though this conditionally licensed product has a reasonable likelihood of efficacy, there is no indication for its use in shelters.
<i>Porphyromonas</i> sp. Vaccine	Though this conditionally licensed product has a reasonable likelihood of efficacy, there is currently no indication for its use in shelter situations.

* MLV—modified live virus.

an animal shelter. In addition to representing an unnecessary expense, the vaccines listed in this category are for diseases that do not represent a significant threat to the population of dogs residing in shelters, have limited efficacy against clinical disease, and/or may represent potential harm or injury to the individual dog. The vaccines not recommended for shelter use are listed in Table 5.

Vaccination Recommendations for Specific Cases in the Shelter Environment

Dogs with a Documented Vaccination History at Time of Admission

There is no compelling reason to administer vaccines to an individual dog at the time of admission to a shelter *if clear documentation of vaccination is provided*. The following is the minimum information acceptable as documenting proof that a valid vaccination has been administered:

- proprietary name of product,
- manufacturer name,
- serial/lot number,
- date vaccine was administered (at least month and year),
- expiration date of vaccine administered, and
- signature of a licensed veterinarian.

This information should be associated with a medical record that clearly describes the dog in question. If any of this information is not available at the time of admission or cannot be associated with a formal record for the dog, then immediate vaccination is indicated.

Dogs Held Long Term in Shelters

Historically, shelters have been thought of as short-term holding facilities for animals. However, as the number of dogs entering shelters has decreased in recent years, many shelters are holding some dogs for extended periods. Whether a dog is undergoing behavioral or physical rehabilitation, being held for legal reasons, awaiting adoption, or being held in permanent sanctuary, special considerations apply when determining a vaccination program for these animals. Unique infection control challenges exist because of the extended time individual dogs reside in the facility and the increased opportunity for exposure to infectious pathogens.

Implementing an effective vaccination program for dogs held on a long-term basis poses significant additional challenges, both economical and immunological. At this time, the Task Force recommends that all dogs entering a long-term care facility (or any dog entering a shelter for which a long-term stay is anticipated) be inoculated with all recommended vaccines, *plus rabies vaccine*, at the time of admission to the facility. If a dog is routinely exposed to the outdoors, then optional vaccines should be considered (as for pet animals), depending on the dog's risk profile.

Because it can be difficult or impossible to determine whether young dogs (under 4 months of age) have received any vaccines at all, implementation of an initial series, beginning as early as 6 weeks of age, may be indicated. When it is the decision of the facility to initiate the entire "initial

series" (i.e., "puppy shots") to an individual dog, then the recommended vaccines should be administered at 2-week (rather than 3- or 4-week) intervals until the animal reaches the age of 16 weeks.

In the event that an individual dog resides in the facility long enough to justify booster vaccination, it is recommended that the revaccination schedule recommended for individual pets be followed [see Table 1].

Pregnant Dogs

Shelter personnel may be faced with the dilemma of whether to vaccinate a pregnant dog upon admission to a facility. Historically, vaccination in pregnancy has been advised against in small animal medicine. This is due in part to the paucity of data concerning vaccine safety and efficacy during gestation and partly to the accepted belief that no substance should be administered unnecessarily during pregnancy. When the immunity of the dog is unknown, however, the risk of maternal, fetal, and neonatal infection must be weighed against the risk of vaccination.

According to the Centers for Disease Control and Prevention,⁵³ the risk to a developing fetus from vaccination of the mother during pregnancy is primarily theoretical, no evidence exists of risk from vaccinating pregnant women with inactivated viral or bacterial vaccine or toxoids, and the benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high. Further research in vaccination of pregnant dogs is needed, but extrapolating from the human field is advised at this time. The typical shelter environment provides an example of likely disease exposure. Therefore, unless the shelter has excellent isolation facilities, pregnant dogs should be vaccinated upon admission with CDV, parvovirus, and *Bordetella bronchiseptica* (intranasal). If available, inactivated, subunit, recombinant, polysaccharide conjugate vaccines should be selected for use in the pregnant dog.

Sick Dogs

As with pregnant dogs, veterinary medicine has advised against vaccination during illness, due to concerns about suboptimal seroconversion, or worse, conversion of vaccine to disease. The decision to administer or delay vaccination because of a current illness depends on the severity of symptoms and the etiology of the disease. Vaccines can be administered to dogs with minor acute illness or injury (e.g., diarrhea, mild upper respiratory tract infection with or without fever); reports of lower rates of seroconversion are limited. Moderate doses of steroids or surgery and anesthesia have *not* been shown to lead to increased vaccine-induced disease or failure to seroconvert.^{54,55}

The shelter environment does not usually permit the luxury of isolating animals and delaying their vaccination until concurrent illness is resolved. Therefore, vaccination with distemper virus, parvovirus, and *Bordetella bronchiseptica* is advised upon admission for dogs with mild illness or injuries. Vaccination of dogs with severe signs of disease ideally

should be delayed until recovery to avoid superimposing adverse effects of the vaccine on the underlying illness and the (undocumented) risk of causing vaccine-induced disease. It should be recognized, however, that these dogs are at high risk for developing severe infections superimposed on the current clinical problem if they are not carefully isolated.

Recommended Additional Reading on Shelter Recommendations

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Endnotes

¹Information on statutes, implementing regulation, and administrative agency guidance materials relative to the regulatory review and governmental oversight of veterinary vaccines can be found at 21 U.S.C. § 151 *et. seq.* (commonly known as the Virus-Serum-Toxin Act or VSTA), 9 CFR § 101 *et. seq.* and <http://www.aphis.usda.gov/vs/cvb/regsandguidance.htm>. The relative hierarchy of these materials begins with the statute established by Congress and signed by the president. All other regulatory materials must relate back to the authority conveyed in the statute. Such statutes are typically broad and generally worded. For example, the VSTA empowers the secretary of agriculture to prevent the preparation, sale, barter, or exchange of worthless, contaminated, dangerous, or harmful virus, serum, toxin, or analogous material for use in the treatment of domestic animals. Administrative regulations, promulgated via notice-and-comment rulemaking by an agency delegated the authority conveyed in the statute, carry the force of law and provide further detail to the general language in the statute. For example, the CVB changes the negative language of the statute to state positively that biologics are required to be pure, safe,

potent, and effective. Such rules are published in the Code of Federal Regulations, or CFR, and must derive their authority from the statute. Finally, to offer even further detail, an agency can provide guidance documents. The CVB calls these guidance documents Memoranda, Public Notices, or Supplementary Assay Methods. These documents do not carry the force of law. They are intended to communicate and provide additional detail regarding acceptable practices and methods. They do not necessarily represent the only way to satisfy the statutory and regulatory requirements (although some would say they are often implemented by agencies in this fashion).

ⁱⁱ In the spring of 2005, CPV-2 disease was prevalent in puppies in a number of states throughout the United States. Observation and serologic studies showed that the majority of infections were seen in puppies during the periods of initial vaccination or within 1 to 2 weeks after the last vaccination in the puppy series (e.g., 6–16 weeks of age). Dogs older than a year were generally not affected. Although mutant strains of virus were suspected and suggested as the cause of these outbreaks, viruses isolated from diseased puppies were unable to infect dogs vaccinated with commercial vaccines containing CPV-2. Vaccines containing the original canine parvovirus genotype (CPV-2) or those vaccines with the CPV-2b genotype were equally effective in providing protective immunity. To date, a mutant of CPV-2 that is capable of infecting dogs immunized with current commercial vaccines has not been demonstrated. Infection in these dogs was occurring at an age when the PAMA did not prevent infection but the puppies were not actively immunized and thus were susceptible to infection and disease.

The cause of similar outbreaks of CDV at shelters in Chicago, Los Angeles, and elsewhere were suggested to be mutants of CDV not controlled by current CDV vaccines. However, studies with viral isolates obtained from diseased and dead dogs in the Chicago shelter showed that commercial CDV vaccines containing Rockborn virus, Onderstepoort virus, or the canarypox recombinant CDV provided immunity that prevented infection and disease when the viruses were used to experimentally challenge the vaccinated animals. It should be noted that the studies in Chicago showed that approximately 65% of the dogs entering the shelter had no antibody to CDV and thus were susceptible to infection. The CDV outbreak was controlled when dogs were vaccinated at time of capture or immediately upon arrival at the shelter. A direct correlation was found between antibody and protection in the outbreak, and absence of antibody correlated with susceptibility to infection with or without disease. (Schultz RD. Information presented at Central Veterinary Conf, Kansas City, Mo., 2005.)

ⁱⁱⁱ Although there is no federal requirement imposed on veterinarians to report adverse events, individual states may have reporting requirements. For example, Texas requires any person using a veterinary biologic to report suspected adverse events to the Texas Animal Health Commission. 4 TAC § 34.2 (d).

Footnotes

- ^a Ford R, personal communication.
- ^b Schultz RD, personal communication of unpublished study.
- ^c TiterChek,[®] Synbiotics Corp., San Diego, CA 92127-1706 USA.

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