The 2006 American Association of Feline Practitioners Feline Vaccine Advisory Panel Report

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The report provided here was developed by the AAFP Feline Vaccine Advisory Panel to aid practitioners in making decisions about appropriate care of patients with respect to currently available vaccines. The Advisory Panel included experts in immunology, infectious disease, internal medicine, and clinical practice. As much as possible, the information reported here was based on information from studies in peer-reviewed publications. When such information was not available, the Advisory Panel depended on clinical experience, technical judgments, and results of unpublished studies. Although the information contained herein is intended to be accurate, thorough, and comprehensive, it is subject to change in light of developments in research, technology, and experience. As such, this document should not be construed as dictating exclusive protocols, courses of treatment, or procedures. Other techniques and procedures may be warranted on the basis of the needs of the patient, available resources, and limitations unique to the setting.

The AAFP thanks the members of the Feline Vaccine Advisory Panel for their devotion to this project. The AAFP also appreciates the openness and assistance provided by manufacturers of feline vaccines.

Abbreviations

AAFP	American Association of Feline Practitioners
MDA	Maternally derived antibody
FPV	Feline parvovirus
FHV-1	Feline herpesvirus-1
FCV	Feline calicivirus
FIP	Feline infectious peritonitis
DOI	Duration of immunity
IN	Intranasal
CVB	Center for Veterinary Biologics
MLV	Modified-live virus
SPF	Specific pathogen-free
SARSS	Suspected adverse reaction surveillance scheme
URD	Upper respiratory tract disease
CPV-2	Canine parvovirus type 2
VS-FCV	Virulent systemic-FCV
IFA	Immunofluorescent antibody
FCoV	Feline coronavirus
ADE	Antibody-dependent enhancement
TNR	Trap-neuter-return

Introduction

Vaccination programs for cats have been major topics of discussion among veterinarians in recent years, primarily because of concerns about vaccine safety, the number of commercially available vaccines, and an incomplete knowledge of the duration and extent of protection provided by certain vaccines.

Vaccines play an important role in the control of infectious diseases. However, some vaccines do not induce complete protection from infection or disease, and they do not induce the same degree of protection in all cats. Exposure to infected animals and infectious agents should be minimized, even in vaccinated cats. The risk of infection and subsequent disease varies with the age and health of the cat, extent of its exposure to the infectious agent and to other cats, and the geographic prevalence of infection. Factors that negatively affect an individual cat's ability to respond to vaccination include interference from MDA, congenital or acquired immunodeficiency, concurrent disease or infection, inadequate nutrition, and immunosuppressive medications. When practical, every effort should be made to ensure that cats are healthy prior to vaccination.

Kittens are generally more susceptible to infection and typically develop more severe diseases than adult cats. Thus, kittens represent the principal target population for vaccination. As part of a routine health care program, the vaccination needs of all cats, including adults, should be assessed at least yearly and, if necessary, modified on the basis of an assessment of a cat's risk.

Vaccination is a medical procedure, and the decision to vaccinate, even with vaccines considered as core vaccines, should be based on a risk-benefit assessment for each cat and each vaccine. Vaccination may indeed be beneficial, but it is not innocuous, and the benefit of vaccinating a cat (ie, the induction of clinically meaningful immunity) must be balanced against the risk of adverse events associated with vaccination. The overall objectives of vaccination, then, are to vaccinate the greatest number of cats in the population at risk; vaccinate each cat no more frequently than necessary; vaccinate each cat only against infectious agents to which it has a realistic risk of exposure, infection, and subsequent development of disease; vaccinate a cat only when the potential benefits of the procedure outweigh the potential risks; and vaccinate appropriately to protect public health.

Core, noncore, and not generally recommended vaccines—Core vaccines are recommended for all cats. The Advisory Panel believes vaccines against FPV, FHV-1, FCV, and rabies virus fall into this category. Noncore vaccines should be administered to cats in specific risk categories as outlined in the section on vaccine antigens. The Advisory Panel believes vaccines against FeLV, FIV, *Chlamydophila felis*, and *Bordetella bronchiseptica* fall into this category. Not generally recommended vaccines are those that the Advisory Panel believes have little or no indication; these vaccines have not been found to induce a clinically meaningful immune response in most cats and circumstances, or they may be associated with adverse events out of proportion to their usefulness. The Advisory Panel believes vaccines against FIP and *Giardia* spp fall into this category.

The Advisory Panel commends veterinary biologics manufacturers for responding to many of the concerns and recommendations in the 2000 report,[1] such as inclusion of vaccine antigens in multivalent products on the basis of similar vaccine target populations (ie, similar exposure and infection risks) and similar DOI induced by vaccination (eg, FHV-1/FCV combinations); creation of appropriate monovalent products (eg, FPV vaccines); attempts to develop vaccines that create less inflammation at injectable vaccination sites (eg, nonadjuvanted FeLV and rabies virus vaccines and

nonadjuvanted inactivated FPV vaccines); development of novel methods of vaccine administration (eg, transdermal application); development of products with a lower required dosage (eg, IN administered FHV-1/FCV vaccines and recombinant FeLV vaccines); funding of studies to investigate the DOI; licensing of vaccines with DOI > 1 year; exploration of novel vaccine technologies (eg, recombinant vaccines); and desire to work with regulatory agencies to improve vaccine labels and the manner by which adverse events are reported.

Immune Response to Vaccination and Infection

Two major types of immunity prevent or limit infectious diseases: natural (innate) immunity and acquired (adaptive) immunity. Innate immunity, including but not limited to skin, hair, tears, normal microbial flora, mucus, acidity of the stomach, type 1 interferons, neutrophils, macrophages, natural killer cells, and age, prevents most pathogens from infecting and causing disease in animals. Innate immunity is the first line of defense; thus, it is already active or immediately activated in response to inherent or elaborated chemical substances of the infectious agent.[2-6]

Acquired immunity is characterized by specificity and memory and is stimulated when an animal is vaccinated or exposed to an infectious agent or other antigen. The acquired immune system consists of humoral immunity and cell-mediated immunity. In humoral immunity, differentiated B lymphocytes, called plasma cells, produce the primary feline immunoglobulin classes IgG, IgM, IgA, and IgE.[7] Phagocytic cells and effector molecules, such as complement, also play an important role in providing vaccinal immunity. Cell-mediated immunity comprises T lymphocytes, including T helper, T regulatory, and T cytotoxic cells; macrophages; and a number of products of those cells, called cytokines, which all help to provide vaccinal immunity.[2,3,7]

When a cat is infected or vaccinated, B and T lymphocytes specific for a multitude of antigenic epitopes on viruses, bacteria, and parasites are stimulated to proliferate and differentiate into effector cells. In addition to effector B and T cells that develop and survive for short periods after vaccination, memory B and T cells usually develop to provide long-term immunity. Most of the effector cells themselves are short lived, often surviving only days or weeks after initial stimulation. Memory cells, on the other hand, survive for years, sometimes for the life of a cat. It has been discovered that certain cells continue to produce antibodies for long durations after initial antigenic stimulation such as vaccination. These cells, called long-lived plasma cells or memory effector B cells, persist in the bone marrow for many years and contribute to long-term humoral immunity.[8] Similarly, long-lived T-effector cells, or memory effector T cells, probably persist after vaccination or infection with certain pathogens in the absence of overt antigenic stimulation.[9] Memory B and T cells and antibodies produced by memory effector B cells cooperate to provide protection from infection at a later time in the life of a vaccinated cat. Immunologic memory is the basis for protective vaccines.[10] Cell-mediated immunity and humoral immunity are stimulated in minutes to hours (anamnestic response) when a vaccinated cat is exposed, whereas it often takes days to weeks (primary response) for immunity to be stimulated in a nonvaccinated, immunologically naive cat.[10-13]

Whether cell-mediated or humoral responses are most important for mediation of protection varies with the specific pathogen, the route of infection, and the colonization and replication of the infectious agent. For instance, many pathogens of the respiratory or gastrointestinal tract require generation of mucosal cellular or humoral immune responses, with IgA being the most effective and abundant antibody class on mucosal surfaces of cats.[14] On the other hand, systemic infections are controlled or prevented primarily by IgG and circulating effector T cells.[5,9]

If vaccination prevents subsequent infection, the animal is considered to have sterilizing immunity, the ultimate form of immunity because disease cannot develop. This form of immunity may develop after immunization against FPV and rabies virus. When vaccination does not prevent infection (eg, FHV-1 and FCV), systemic and local cell-mediated immunity and humoral immunity, including local IgA antibodies, play important roles in preventing or reducing the severity of disease.[2,5,9]

Duration of Immunity

Few independent studies investigate the DOI induced by feline vaccines (for additional information, see the section on vaccine antigens). In immunologic terms, DOI is the duration that immunologic memory persists to provide protection from infection or disease at the time of natural challenge. In regulatory terms, establishing DOI means demonstrating to the satisfaction of a regulatory agency that efficacy is demonstrated when challenge occurs at a specific point in time after vaccination. The USDA CVB requires manufacturers to perform efficacy studies that correlate with the time frame referenced on the label for rabies vaccines and all novel antigens, which are antigens that were not licensed prior to 1994. This requirement does not apply to most feline vaccines currently in use. In the absence of DOI information for each product, veterinarians may rely on guidelines for each vaccine, such as those provided here. In the European Union, a minimum DOI must be determined for each product on the basis of controlled experimental challenge and field trials.[15]

Tests to predict immunity—Measurement of specific systemic immune responses to an infectious agent may potentially predict resistance to infection or disease and determine whether vaccination is required in an individual cat, provided the appropriate immune response can be accurately measured.[16] In most infections in cats, the presence of serum antibodies against an infectious agent indicates that the cat has the immunologic memory required for a rapid anamnestic immune response if the cat is subsequently exposed. In

many mucosal (eg, respiratory or gastrointestinal tract) infections, local immune responses, particularly the presence of secretory IgA antibody, are most effective at preventing infection or disease.[14] Unfortunately, mucosal immune responses cannot be easily determined in a clinical setting, and direct determination of cell-mediated immune responses cannot be currently performed in a clinical setting. However, detection of serum antibodies against an infectious agent is an indirect measure of memory B and T cells and memory effector B cells that are required for protective immunity because responses to all complex vaccine antigens require both B- and T-cell activation.[2,3,5,17]

Information relating vaccine-induced serum antibody responses with resistance to infection has been collected primarily for FPV, FHV-1, and FCV. For FPV, serum antibody titers as determined by validated viral neutralization, hemagglutination inhibition, or ELISA techniques can be used to predict resistance to both infection and disease.[18-21] Results of 2 studies[20,21] indicate that all cats with antibodies against FPV as a result of vaccination within the previous 7 years were protected against the USDA challenge strain and dose of FPV. However, because vaccination for FCV and FHV-1 does not prevent infection, but only lessens the severity of clinical disease when exposure to virulent virus occurs, the predictive value of serum antibody titers for determination of vaccination need is less clear than for FPV. In cats vaccinated with a commercially available modified-live agent product or a killed agent product 30 to 36 months earlier, detection of virus-specific antibodies against FCV and FHV-1 (as determined by virus neutralization and ELISA) was predictive of disease resistance following challenge with USDA challenge viruses.[20] In that study,[20] all cats with detectable antibodies against FCV and most cats with detectable antibodies against FHV-1 (91.3% via virus neutralization; 90.5% via ELISA) had > 50% reduction in magnitude of clinical signs, compared with unvaccinated control cats.

Virus neutralization antibodies against FeLV can be measured (although tests are not commercially available), but their presence in a vaccinated cat does not always predict resistance to infection; presence in a nonvaccinated cat indicates that the cat either was or is infected.

For most cats, the Advisory Panel recommends using revaccination intervals as described herein rather than measuring antibody titers. However, if antibody testing is used in lieu of set revaccination intervals for FPV, FCV, and FHV-1, the following points should be considered:

- If previous vaccination history is not available, core vaccines should be given.
- Antibody test results from all laboratories cannot be assumed to be equivalent; practitioners are cautioned to only use laboratories that have validated their test results.
- Virus neutralization assays document in vitro inactivation of the specific virus by serum antibodies. An ELISA can be designed to measure antibodies against viral antigens, but positive results do not necessarily indicate that the antibodies neutralize the virus. Thus, only tests for which results have been found to predict protection should be used.
- Serologic testing for assessment of vaccine need should be reserved for previously vaccinated adult cats. If circumstances require measurement of antibodies in kittens younger than 16 weeks of age, a sample should be collected on the day of vaccination and a second sample should be collected 2 or more weeks later. An increase in antibody titer indicates that vaccination induced an immune response.
- Detection of serum antibodies against FPV, FCV, and FHV-1 by validated assays appears to predict resistance to disease in most cats. Failure to detect serum antibodies does not necessarily indicate susceptibility, but it would, in most cases, be an indication that the cat may benefit from revaccination.

Types of Vaccines

The immune response induced by natural infection depends on the type of antigen, route of entry, primary site of infection, and pathogenic mechanisms. These same factors must be considered when a vaccine is given to induce an effective immune response.

Various types of feline vaccines are commercially available (**Table 1**). The most common vaccines currently in use are infectious vaccines, which include modified-live agent vaccines and live virus-vectored recombinant vaccines, and noninfectious vaccines, which include inactive (killed) whole-organism vaccines and subunit vaccines.

Modified-live agent vaccines consist of avirulent or attenuated organisms that infect the host. In cats, some are formulated to be given by injection; others are designed to be administered IN. Modified-live agent vaccines are capable of stimulating serum antibodies, local mucosal antibodies, and systemic and local cell-mediated immune responses, depending on the route of administration, and create immunity similar to that induced by recovery from natural infection.[4,5,10,23,24]

The USDA currently recognizes 3 categories of recombinant vaccines for use in veterinary medicine: category 1 products comprising inactivated recombinant organisms or purified antigens derived from such organisms (eg, subunit vaccines), category 2 products comprising live organisms with deleted genes (eg, gene-deleted vaccines), and category 3 products comprising live vectors expressing heterologous genes for immunizing antigens (eg, live virus-vectored vaccines).[23] Chimera is an additional term soon to be applied to certain recombinant veterinary vaccines.[25] All vaccines rely on antigen presentation by antigen-presenting cells (eg, macrophages and dendritic cells) to initiate an immune response. With category 3 recombinant vaccines, nonpathogenic virus vectors replicate in a limited way and cause antigen-presenting cells to express products of genes (specific proteins unique to the pathogenic virus or bacteria) inserted into the vector's genome, thereby inducing an immune response to an organism. Recombinant vaccines may or may not contain adjuvant; however, none of the virus-

vectored vaccines currently licensed for cats by the USDA are adjuvanted.

Killed agent vaccines frequently contain adjuvant (usually a chemical in companion animal vaccines) to enhance the immune response. Adjuvanted FeLV and rabies virus vaccines have been associated with local inflammatory reactions at injection sites, with the degree of inflammation varying among products.[a] The potential role of local inflammatory reactions in the genesis of vaccine-associated sarcomas remains controversial (see section on adverse events and reporting). In general, the response to killed agent vaccines is slower than that induced by infectious vaccines[24]; however, studies indicating that this is true for all feline vaccines are lacking. The immunity induced by killed agent vaccines is predominantly, but not exclusively, systemic antibody with little or no IgA antibody on mucosal surfaces, and cell-mediated immunity is limited to type 1 T–helper cell immunity. Immunity induced by killed agent vaccines is therefore less likely to provide effective levels of secretory IgA or complete cell-mediated immune protection at mucosal surfaces in the respiratory and gastrointestinal tracts.[5,14]

Each vaccine type has advantages and disadvantages in addition to those aforementioned. For example, properly manufactured killed agent vaccines (eg, not contaminated with live agents) cannot cause the diseases for which they are designed to prevent; inactivated agent vaccines may therefore be preferable in disease-free colonies, such as research facilities housing SPF cats. Although infectious agents in modified-live agent products have been attenuated, normal host immune responses are required if vaccinates are to resist disease from attenuated organisms. Thus, attenuated agents in severely immunosuppressed or genetically susceptible hosts may result in the disease for which the vaccine was designed to prevent. In the early 1980s, several cats vaccinated with attenuated rabies virus vaccines developed rabies.[26,27] Furthermore, a live attenuated agent may revert to virulence, causing disease even in cats that are not immunosuppressed. On the other hand, some inactivated agent vaccines are more highly associated with inflammatory reactions at vaccine sites than are modified-live agent vaccines.[15]

Although multiple manufacturers may produce a vaccine designed to protect against a specific disease, vaccines are not all the same. A careful review of individual labels and package inserts is necessary to distinguish 1 vaccine type from another.

Routes of Administration

Numerous routes are approved for administration of feline vaccines. For some infectious agents (eg, FPV, FHV-1, and FCV), vaccines administered via injection and IN routes are available in some parts of the world. Depending on the properties of the infectious agent and the situation in which the product will be applied, a particular route of vaccine administration may be advantageous. Vaccines must be administered by routes stipulated by the manufacturer in the package insert; the consequences of administering a vaccine by any route not evaluated and recommended by the manufacturer may impair the health of the patient.

Injection—Most injectable feline vaccines are licensed for administration by SC or IM injection. There is no evidence that the risk of vaccine-associated sarcomas is decreased in cats vaccinated by the IM route; in fact, development of a sarcoma in muscle may delay detection. Additionally, although 1 manufacturer may offer the option of either SC or IM administration, it should not be assumed that these routes apply to a vaccine containing the same antigens but produced by a different manufacturer.

IN administration—Immunity against many pathogens of the respiratory or gastrointestinal tract requires generation of mucosal cellular or humoral immune responses. However, this varies by agent. Viruses and bacteria that effectively replicate in the respiratory tract will generally produce an effective local and systemic immune response. Feline calcivirus, FHV-1, and *B bronchiseptica* replicate locally in the respiratory tract, and vaccines designed for IN administration are available for each of these agents. Vaccines administered IN are also available for FPV and FIP; the reader is referred to the section on vaccine antigens for additional discussion.

Transdermal administration—A recombinant canarypox-vectored FeLV vaccine licensed in the United States is only approved for administration by use of the manufacturer's transdermal administration system; SC or IM administration of this vaccine by use of needle and syringe is expected to result in a suboptimal immune response. This is in contrast to a recombinant FeLV vaccine available in the European Union that is given by SC injection.

Special Considerations

Many factors can negatively influence a cat's ability to respond to vaccines. Routine physical examination and FeLV and FIV testing prior to administration of vaccines is important to determine such factors as age, preexisting illness or infection, and alterations of immune status, all of which should be considered when developing a vaccination protocol. The level of challenge dose may also influence the efficacy of a vaccine in an individual. Thus, additional vaccinations might be considered in situations where, for example, a previously low-risk cat enters a high-risk situation.

Age

Kittens—Immunity existing at an early age includes innate immunity (which is often not as effective in young kittens), MDA, and actively acquired humoral and cell-mediated immunity induced by effective vaccination or recovery from natural infection.

Although the immune response may not be as robust in young kittens, it is important to vaccinate kittens at an early age in an attempt to induce immunity prior to their first exposure to the pathogen. An important cause of vaccine failure in kittens is the presence of MDA. In most situations and most diseases, MDA in most kittens is lost by 9 to 12 weeks of age. However, in some cases in which maternal antibody titers are low or in which there was inadequate transfer of colostrum, kittens may lose their MDA by 6 weeks of age or earli-

Table 1—Feline vaccines currently available in the United States.

FPV

Brand name	Company	Description		
		FPV	Adjuvant	Route of administration
Continuum Feline P*	Intervet Inc	MLV	No	Injection
Felocell P	Pfizer Animal Health	MLV	No	Injection
Panagen	Schering-Plough Animal Health	K	No	Injection

FCV and FHV-1

Brand name	Company	Description			
		FCV	FHV-1	Adjuvant	Route of administration
Feline UltraNasal FVRC	Heska Corp	MLV	MLV	No	IN only
Continuum Feline HC*	Intervet Inc	MLV	MLV	No	Injection
PUREVAX Feline Respiratory 2	Merial Ltd	MLV	MLV	No	Injection
Felocell FVR C	Pfizer Animal Health	MLV	MLV	No	Injection
Felocell FVR C (IN)	Pfizer Animal Health	MLV	MLV	No	IN only
FVR C	Schering-Plough Animal Health	MLV	MLV	No	Injection

FCV, FHV-1, and *Chlamydophila felis*

Brand name	Company	Description				
		FCV	*C felis*	FHV-1	Adjuvant	Route of administration
PUREVAX Feline Respiratory 3	Merial Ltd	MLV	AL	MLV	No	Injection
Felocell FVR C Ch	Pfizer Animal Health	MLV	AL	MLV	No	Injection

FPV, FCV, and FHV-1

Brand name	Company	Description				
		FPV	FCV	FHV-1	Adjuvant	Route of administration
Fel-O-Guard Plus 3	Fort Dodge Animal Health	MLV	MLV	MLV	No	Injection
Fel-O-Vax PCT	Fort Dodge Animal Health	K	K	K	Yes	Injection
Feline UltraNasal FVRCP	Heska Corp	MLV	MLV	MLV	No	IN only
Continuum Feline HCP*	Intervet Inc	MLV	MLV	MLV	No	Injection
Protex-3	Intervet Inc	MLV	MLV	MLV	No	Injection
PUREVAX Feline 3	Merial Ltd	MLV	MLV	MLV	No	Injection
Felocell 3	Pfizer Animal Health	MLV	MLV	MLV	No	Injection
Eclipse 3	Schering-Plough Animal Health	MLV	MLV	MLV	No	Injection
FVR C-P	Schering-Plough Animal Health	K	MLV	MLV	No	Injection

FPV, FCV, FHV-1, and rabies virus

Brand name	Company	Description					
		FPV	FCV	FHV-1	Rabies	Adjuvant	Route of administration
Continuum Feline HCP + R*	Intervet Inc	MLV	MLV	MLV	K	Yes	Injection
PUREVAX Feline 3/Rabies	Merial Ltd	MLV	MLV	MLV	V	No	Injection

FPV, FCV, FHV-1, and FeLV

Brand name	Company	Description					
		FPV	FCV	FHV-1	FeLV	Adjuvant	Route of administration
Fel-O-Guard Plus 3+Lv-K	Fort Dodge Animal Health	MLV	MLV	MLV	K	Yes	Injection
Fel-O-Vax Lv-K III	Fort Dodge Animal Health	K	K	K	K	Yes	Injection
Eclipse 3+FeLV	Schering-Plough Animal Health	MLV	MLV	MLV	K	Yes	Injection

FPV, FCV, FHV-1, and *C felis*

Brand name	Company	Description					
		FPV	FCV	FHV-1	*C felis*	Adjuvant	Route of administration
Fel-O-Guard Plus 4	Fort Dodge Animal Health	MLV	MLV	MLV	K	Yes	Injection
Fel-O-Vax IV	Fort Dodge Animal Health	K	K	K	K	Yes	Injection
Protex-4	Intervet Inc	MLV	MLV	MLV	AL	No	Injection
PUREVAX Feline 4	Merial Ltd	MLV	MLV	MLV	AL	No	Injection
Felocell 4	Pfizer Animal Health	MLV	MLV	MLV	AL	No	Injection
Eclipse 4	Schering-Plough Animal Health	MLV	MLV	MLV	AL	No	Injection

FPV, FCV, FHV-1, *C felis*, and rabies virus

Brand name	Company	Description						
		FPV	FCV	FHV-1	*C felis*	Rabies	Adjuvant	Route of administration
PUREVAX Feline 4/Rabies	Merial Ltd	MLV	MLV	MLV	AL	V	No	Injection

FPV, FCV, FHV-1, *C felis*, and FeLV

Brand name	Company	Description						
		FPV	FCV	FHV-1	*C felis*	FeLV	Adjuvant	Route of administration
Fel-O-Guard Plus 4+Lv-K	Fort Dodge Animal Health	MLV	MLV	MLV	K	K	Yes	Injection
Fel-O-Vax Lv-K IV	Fort Dodge Animal Health	K	K	K	K	K	Yes	Injection
Eclipse 4+FeLV	Schering-Plough Animal Health	MLV	MLV	MLV	AL	K	Yes	Injection

Table 1—Feline vaccines currently available in the United States (continued).

FeLV

Brand name	Company	Description		
		FeLV	Adjuvant	Route of administration
Fel-O-Vax Lv-K	Fort Dodge Animal Health	K	Yes	Injection
PUREVAX Recombinant Leukemia	Merial Ltd	V	No	Transdermal only†
Leukocell 2	Pfizer Animal Health	K	Yes	Injection
Fevaxyn FeLV	Schering-Plough Animal Health	K	Yes	Injection

FIP

Brand name	Company	Description	Adjuvant	Route of administration
Felocell FIP (IN)	Pfizer Animal Health	MLV	No	IN only

Bordetella bronchiseptica

Brand name	Company	Description	Adjuvant	Route of administration
Protex Bb‡	Intervet Inc	AL	No	IN only
Continuum Feline Bb‡	Intervet Inc	AL	No	IN only

C felis

Brand name	Company	Description	Adjuvant	Route of administration
Continuum Feline Cp	Intervet Inc	AL	No	Injection

Giardia lamblia

Brand name	Company	Description	Adjuvant	Route of administration
Fel-O-Vax Giardia	Fort Dodge Animal Health	K	Yes	Injection

FIV

Brand name	Company	Description	Adjuvant	Route of administration
Fel-O-Vax FIV	Fort Dodge Animal Health	K	Yes	Injection

FeLV and FIV

Brand name	Company	Description	Adjuvant	Route of administration
Fel-O-Vax LVK/FIV	Fort Dodge Animal Health	K	Yes	Injection

Rabies virus

Brand name	Company	Description					
		Type	1 year	3 year	4 year	Adjuvant	Route of administration
Rabvac 1	Fort Dodge Animal Health	K	X			Yes	Injection
Rabvac 3	Fort Dodge Animal Health	K		X		Yes	Injection
Rabvac 3 TF	Fort Dodge Animal Health	K		X		Yes	Injection
Continuum Rabies	Intervet Inc	K			X§	Yes	Injection
Prorab-1	Intervet Inc	K	X			Yes	Injection
Imrab 1	Merial Ltd	K	X			Yes	Injection
Imrab 1 TF	Merial Ltd	K	X			Yes	Injection
Imrab 3 TF	Merial Ltd	K		X		Yes	Injection
Imrab 3	Merial Ltd	K		X		Yes	Injection
PUREVAX Feline Rabies	Merial Ltd	V	X			No	Injection
Defensor 1	Pfizer Animal Health	K	X			Yes	Injection
Defensor 3	Pfizer Animal Health	K		X		Yes	Injection
Rabdomun 1	Schering-Plough Animal Health	K	X			Yes	Injection
Rabdomun	Schering-Plough Animal Health	K		X		Yes	Injection

*This product is labeled for use every 3 years. Use in this manner is supported by challenge data.[22] †Administration by use of Vetjet device only. ‡Protex Bb and Continuum Bb are the same product but sold under different labels. §This product carries a 4-year label for cats; in states and municipalities in which feline rabies vaccination is required, veterinarians must follow applicable statutes.

K = Killed virus. V = Vectored recombinant. AL = Avirulent live.

er and thus be capable of responding to vaccination at this early age. In kittens born to queens with high antibody titers (eg, through natural exposure), MDA may last for as much as 16 weeks; results of 2 studies[28,b] suggest that some kittens will not be protected by a final vaccine given at 12 to 14 weeks of age. Although studies indicating the age at which all vaccinates will be protected have not been performed, it is prudent to ensure that the final vaccine in the initial series be given to kittens no sooner than 16 weeks of age. In most situations, revaccinating every 3 to 4 weeks until kittens attain that age is sufficient.

There is no evidence that vaccination of kittens every 2 weeks results in an impaired immune response, and although such frequent revaccination of kittens is not necessary or cost effective in most cases, kittens in high-risk environments (eg, panleukopenia-endemic shelters or catteries) may benefit from being vaccinated this frequently as long as they remain in the environment or until 16 weeks of age, whichever comes first. A single dose of modified-live agent vaccine should, in theory, suffice for initial vaccination of cats older than 16 weeks of age. Nonetheless, to increase the likelihood of immunization in this group of cats, the Advisory Panel recommends that 2 doses of vaccine, whether killed agent or modified-live agent, be administered. The 2 doses should be given at an interval of 3 to 4 weeks and not < 2 weeks.

Analysis of data from the SARSS[15] in the United Kingdom found that kittens < 6 months old were overrepresented for adverse events associated with vaccination, compared with older cats.[15] This may be a real effect or it may reflect a high reporting rate by owners. It may also be attributable in part to the coincidental onset of age-related diseases or infection with naturally occurring viruses.

Other potential causes of vaccine failure in kittens include stressors such as early weaning and changes in environment, concurrent illnesses, parasites, nutritional inadequacies, and exposure to high numbers of pathogens in multiple-cat environments (eg, shelters and breeding catteries). However, the true impact of these stressors is not known.

Senior cats—Whether older cats respond in the same manner to vaccination as do younger cats has not been adequately studied. In the absence of data, the Advisory Panel recommends that healthy older cats and those with chronic but stable disease conditions receive vaccines in the same manner as young adults.

Breed

In the United Kingdom, analysis of the SARSS database revealed that pedigree cats, especially Burmese and semilonghair cats (a category that includes Birmans and Maine Coons), were overrepresented for vaccine adverse events, compared with nonpedigree cats.[15] This could be a real effect, with some breeds being more predisposed than others to reactions after vaccination. However, it may also reflect greater use of vaccines in pedigree cats than nonpedigree cats, with pedigree cat owners being more inclined to report any reactions seen. Similar information is not available for cats in the United States.

Vaccination in breeding catteries

Vaccine schedules reported here are appropriate in most cats. Queens in which the vaccination status is not adequate or that have a prior history of infection with FHV-1 or FCV may receive booster vaccines prior to breeding or parturition to maximize delivery of MDA to kittens.[29,30] Unless specifically stated on the label, vaccines are not evaluated by manufacturers for safe use in pregnant queens, and routine vaccination of pregnant cats should be avoided. However, the benefits of vaccinating a pregnant queen may outweigh the risks in some circumstances (eg, catteries with endemic URD). If vaccination is determined to be essential, use of killed agent vaccines may be preferable. Use of products labeled for IN administration in kittens in shelters (see section on vaccination in shelters) is appropriate in catteries with endemic viral URD.

Vaccination of lactating queens

Lactation is not known to interfere with the immune response to vaccines. However, administration of any vaccine may stress the queen, even in the absence of vaccine-associated adverse events, and may result in a temporary deterioration of mothering ability and milk production. Thus, in general, use of vaccines in lactating queens should be avoided. In shelter environments, however, it is advisable to vaccinate all cats with modified-live agent vaccines, including lactating queens, at the time of admission, as the benefits of vaccination (protection of the queen from disease) likely outweigh the risks of vaccine-induced disease (eg, possible FPV vaccine virus shedding to kittens younger than 4 weeks old).

Vaccination of cats with preexisting illness

Manufacturers evaluate vaccine efficacy in healthy cats and, accordingly, vaccines are labeled for use in healthy cats only. However, the Advisory Panel acknowledges that in certain circumstances, vaccination of a cat with chronic but stable illness may be justified. Whether a vaccine should be administered to an ill patient is at the discretion of the veterinarian.

Cats with acute illness, debilitation, or high fevers should not be vaccinated. However, in shelters or other multiple-cat environments in which delaying vaccination may lead to increased susceptibility to infection, vaccination in the face of illness may be indicated. Vaccination of cats in shelters with injuries or mild to moderate illness (such as URD or dermatophytosis) with FPV, FHV-1, and FCV is advised on admission. Vaccination of cats not in shelters, yet with severe disease, should ideally be delayed until the cat has recovered from the illness.

Vaccination of retrovirus-infected cats

Retrovirus-infected cats should be housed indoors and isolated from unvaccinated cats to diminish their likelihood of infecting others and to reduce their exposure to other infectious agents or trauma. The Advisory Panel recommends that core vaccines (FPV, FHV-1, FCV, and rabies virus) be administered to FeLV-infected cats; noncore vaccines should be given only if the risk of patient exposure justifies their use. Cats infected with FeLV may not be able to mount adequate immune responses to vaccination against rabies virus and perhaps to other vaccines as well.[c] Therefore, protection induced by vaccines in FeLV-infected cats may not be comparable to that achieved in uninfected cats.

Experimental evidence indicates that FIV-infected cats are capable of mounting immune responses to administered antigens, except during the terminal phase of infection, although these responses may be delayed or diminished.[31-35] Results of studies[32,36] to determine whether immune stimulation (eg, vaccination) accelerates the course of FIV-induced immunodeficiency are conflicting, but a potential trade-off to protection from disease by vaccination is progression of FIV infection secondary to increased viral production. The Advisory Panel recommends that core vaccines be administered to FIV-infected cats, but noncore vaccines should be given only if the risk of patient exposure justifies their use. In 1 study,[37] cats experimentally infected with FIV developed vaccine-induced panleukopenia when given modified-live FPV vaccines. Whether cats naturally infected with FIV are at increased risk of developing vaccine-induced disease from residual virulence of infectious vaccines is not known; however, administration of noninfectious vaccines is preferred whenever available.

In shelter environments, cats destined to be group housed with other cats should be appropriately tested for FeLV and FIV prior to inclusion.[38] Retrovirus-infected cats should be housed separately from uninfected cats and sent off-site for more appropriate care (such as spaying or neutering) as soon as possible. Because of their high risk of exposure, FIV- and FeLV-infected cats should receive killed FPV, FHV-1, and FCV vaccines when maintained in a shelter. Rabies virus vaccine should be administered to all cats that are placed at the time they are discharged from the shelter.

Concurrent use of corticosteroids

Depending on dosage and duration of treatment, corticosteroids may cause functional suppression of immune responses, especially cell-mediated responses; however, studies examining vaccine effectiveness and safety in cats receiving corticosteroids are lacking. In dogs, corticosteroids do not appear to result in ineffective immunizations when given for short durations at low to moderate doses.[39] Comparable studies have not been performed in cats; nonetheless, concurrent use of corticosteroids at the time of vaccination should be avoided if practical.

Vaccination of cats with prior vaccine-associated adverse events

Vaccination of cats with prior vaccine-associated adverse events should be undertaken only after serious consideration of the risks and benefits. In such patients, vaccination may be more life threatening than omitting vaccination altogether. Determination of antibody titer would be useful to assess immunity to core vaccines.

The clinical signs of allergic reactions in cats are different from those in dogs. Of those reported to the US Pharmacopoeia Veterinary Practitioners' Reporting Program during the time it was operational, 66% involved the gastrointestinal tract (usually vomiting, with or without diarrhea), 22% involved the respiratory tract (eg, dyspnea), and 12% involved the skin (eg, urticaria). These signs may progress to hypotension and cardiovascular collapse if untreated. No trend suggesting an association between anaphylaxis and any particular brand or type of vaccine was evident.[40]

In cats that have had vaccine-associated sarcomas, if practical, injectable vaccines should not be administered again. Cats having developed anaphylaxis with prior vaccination should not receive the same product again, but the extent to which the risk of severe reactions is mitigated by use of a different product, type, or route is not known. If revaccination is determined to be more beneficial than harmful, only 1 vaccine should be administered. If other vaccines are to be administered, they should be given no sooner than 3 weeks later and only 1 vaccine should be given at each time. The cat should then be monitored in the hospital for 4 to 6 hours after vaccination. For mild reactions, the Advisory Panel suggests that antihistamines (eg, diphenhydramine HCl administered at a dose of 2 mg/kg, IM) and corticosteroids (eg, dexamethasone administered at a dose of 5 mg, IM) be administered 20 minutes prior to vaccination; however, the ability of these medications to blunt an adverse reaction has not been adequately investigated.

Rabies virus vaccines are particularly problematic if previously associated with an adverse event because in many parts of the world, the law requires them. In situations in which vaccination is legally mandated yet may endanger the health of the cat, a certificate of exemption may be signed by the client and veterinarian in lieu of vaccination. A copy of the certificate should be given to the client and a copy maintained in the patient's permanent record. Text used in New York State is included as an example (**Appendix 1**).

Suggested vaccination intervals

Studies addressing minimum and maximum vaccination intervals for cats receiving the initial vaccination series have not been published. The Advisory Panel recommends the following:

Primary vaccination of kittens—Vaccines should be administered at intervals of 3 to 4 weeks until kittens are 16 weeks old. In general, the series is started at 8 to 9 weeks of age; however, under mitigating circumstances (eg, in shelters and catteries with endemic URD), vaccination may begin as early as 6 weeks of age. The minimum vaccination interval during the primary series is 2 weeks, and the maximum recommended interval is 4 weeks. Kittens presented for booster vaccination 6 weeks or longer following administration of the previous dose of vaccine should receive at least 2 doses of vaccine, 3 to 4 weeks apart.

Rabies virus vaccines should be administered in accordance with local or state statutes. In locations in which rabies virus vaccination is not required, the Advisory Panel suggests that kittens receive a single dose of rabies virus vaccine between 12 and 16 weeks of age (as early as 8 weeks of age, depending on vaccine type); a booster vaccine should be administered 1 year later.

Primary vaccination of adult cats—Cats older than 16 weeks of age that are evaluated for initial vaccination should receive 2 doses of vaccine at an interval of 3 to 4 weeks and not < 2 weeks.

Booster vaccination—Recommended vaccination intervals for cats receiving booster vaccines are summarized (**Table 2**). Once the initial vaccine series has been completed, the Advisory Panel believes a single dose is sufficient for cats evaluated for revaccination beyond the suggested interval for booster vaccination.

Vaccine Antigens

FPV

Agent—Feline panleukopenia is an often fatal disease found worldwide and caused by FPV infection. Clinical signs of disease include lethargy, anorexia, vomiting, diarrhea, fever, and sudden death. Disease is often accompanied by a profound panleukopenia, and mortality rates are high in young, susceptible cats.[41] In utero infection with FPV can cause cerebellar hypoplasia,[42] and as cerebellar development continues during the first 2 weeks after birth, infection in young neonates may also occasionally result in the condition. Feline parvovirus is highly contagious, remains stable

Table 2—Summary of vaccination of cats in general practice.

Vaccine	Primary series: kittens (≤ 16 weeks old)	Primary series: adolescent/adult (> 16 weeks old)	Booster	Comments
Panleukopenia virus (FPV) MLV, nonadjuvanted Injectable	Begin as early as 6 weeks of age, then every 3 to 4 weeks until 16 weeks of age.	Administer 2 doses, 3 to 4 weeks apart.	A single dose is given 1 year following the last dose of the initial series, then no more frequently than every 3 years.	Core • Use of MLV vaccines is not recommended in pregnant cats, kittens < 4 weeks of age, and FeLV- or FIV-infected cats.
FPV Killed virus, adjuvanted[a] Killed virus, nonadjuvanted Injectable	Begin as early as 6 weeks of age, then every 3 to 4 weeks until 16 weeks of age.	Administer 2 doses, 3 to 4 weeks apart.	A single dose is given 1 year following the last dose of the initial series, then no more frequently than every 3 years.	Core • Killed virus vaccines are generally preferred for use in pregnant cats (and only if absolutely necessary) and in FeLV- or FIV-infected cats. • Killed virus vaccines may be more appropriate in disease-free colonies because there is no risk of spread or reversion to virulence.
FPV MLV, nonadjuvanted IN[b]	Begin as early as 6 weeks of age, then every 3 to 4 weeks until 16 weeks of age.	Administer 2 doses, 3 to 4 weeks apart.	A single dose is given 1 year following the last dose of the initial series, then no more frequently than every 3 years.	Core • Intranasal vaccination may not be as effective as injectable vaccination in high-risk environments in which exposure thereafter may occur soon after vaccination and is not recommended for routine use in kittens housed in shelter environments.
FHV-1 and FCV MLV, nonadjuvanted Injectable	Begin as early as 6 weeks of age, then every 3 to 4 weeks until 16 weeks of age.	Administer 2 doses, 3 to 4 weeks apart.	A single dose is given 1 year following the last dose of the initial series, then every 3 years.[c]	Core • MLV FHV-1 and FCV vaccines are invariably combined with each other, either as bivalent products or in combination with additional vaccine antigens.
FHV-1 and FCV Killed virus, adjuvanted[a,d] Injectable	Begin as early as 6 weeks of age, then every 3 to 4 weeks until 16 weeks of age.	Administer 2 doses, 3 to 4 weeks apart.	A single dose is given 1 year following the last dose of the initial series, then every 3 years.[c]	Core • Killed virus FHV-1 and FCV vaccines are invariably combined with each other, either as bivalent products or in combination with additional vaccine antigens. • Killed virus vaccines are generally preferred for use in pregnant cats (and only if absolutely necessary) and in FeLV- or FIV-infected cats. • Killed virus vaccines may be more appropriate in disease-free colonies because there is no risk of spread or reversion to virulence.
FHV-1 and FCV MLV, nonadjuvanted IN	Begin as early as 6 weeks of age, then every 3 to 4 weeks until 16 weeks of age.	Administer 2 doses, 3 to 4 weeks apart.	A single dose is given 1 year following the last dose of the initial series, then every 3 years.[c]	Core • Clinical signs of URD are more commonly seen following IN vaccination. • FHV-1/FCV vaccines for IN administration are invariably combined with each other, either as bivalent products or in combination with FPV.

Table 2—Summary of vaccination of cats in general practice (continued).

Vaccine	Primary series: kittens (≤ 16 weeks old)	Primary series: adolescent/adult (> 16 weeks old)	Booster	Comments
Rabies virus[e] Canarypox virus-vectored recombinant (rRabies), nonadjuvanted Injectable	Administer a single dose as early as 8 weeks of age, with revaccination 1 year later.	Administer 2 doses, 12 months apart.	Annual booster is required.	Core • In states and municipalities in which feline rabies virus vaccination is required, veterinarians must follow applicable statutes. • Booster vaccination with a 1-year rabies virus vaccine is only appropriate in states and municipalities where permitted by law. • Any rabies virus vaccine can be used for revaccination, even if the product is not the same brand previously administered.
Rabies virus[e] 1-year killed virus, adjuvanted[a] Injectable	Administer a single dose as early as 12 weeks of age, with revaccination 1 year later.	Administer 2 doses, 12 months apart.	Annual booster is required.	Core • In states and municipalities in which feline rabies virus vaccination is required, veterinarians must follow applicable statutes. • Booster vaccination with a 1-year rabies virus vaccine is only appropriate in states and municipalities where permitted by law. • Any rabies virus vaccine can be used for revaccination, even if the product is not the same brand previously administered.
Rabies virus[e] 3-year killed virus, adjuvanted[a] Injectable	Administer a single dose as early as 12 weeks of age, with revaccination 1 year later.	Administer 2 doses, 12 months apart.	Every 3 years or as required by state or local ordinance.	Core •In states and municipalities in which feline rabies virus vaccination is required, veterinarians must follow applicable statutes. • Any rabies virus vaccine can be used for revaccination, even if the product is not the same brand previously administered. • No laboratory or epidemiologic data exist to support the annual or biennial administration of 3-year vaccines following the initial series.
FeLV Canarypox virus-vectored recombinant (rFeLV), nonadjuvanted Transdermal	Administer an initial dose as early as 8 weeks of age; a second dose should be administered 3 to 4 weeks later.	Administer 2 doses, 3 to 4 weeks apart.	When indicated, a single dose is given 1 year following the last dose of the initial series, then annually in cats determined to have sustained risk of exposure.[f]	Noncore • Booster inoculation is recommended only in cats considered to be at risk of exposure.[f] • FeLV vaccination is highly recommended for all kittens. • In the United States, the 0.25-mL rFeLV vaccine dose may only be administered via the manufacturer's transdermal administration system.[g] • Only cats testing negative for FeLV should be vaccinated; FeLV testing prior to vaccine administration is recommended. • Cats should be tested for FeLV infection before their initial vaccination and when there is a possibility that they have been exposed to FeLV since they were last vaccinated.

Table 2—Summary of vaccination of cats in general practice (continued).

Vaccine	Primary series: kittens (≤ 16 weeks old)	Primary series: adolescent/adult (> 16 weeks old)	Booster	Comments
FeLV Killed virus, adjuvanted[a] Injectable	Administer an initial dose as early as 8 weeks of age; a second dose should be administered 3 to 4 weeks later.	Administer 2 doses, 3 to 4 weeks apart.	When indicated, a single dose is given 1 year following the last dose of the initial series, then annually in cats determined to have sustained risk of exposure.[f]	Noncore • Booster inoculation is recommended only in cats considered to be at risk of exposure.[f] • FeLV vaccination is highly recommended for all kittens. • Only cats testing negative for FeLV should be vaccinated; FeLV testing prior to vaccine administration is recommended. • Cats should be tested for FeLV infection before their initial vaccination and when there is a possibility that they have been exposed to FeLV since they were last vaccinated.
FIV Killed virus, adjuvanted[a] Injectable	Three doses are required: the initial dose is administered as early as 8 weeks of age; 2 subsequent doses should be administered at an interval of 2 to 3 weeks.	Three doses are required: each dose is administered 2 to 3 weeks apart.	When indicated, a single dose is given 1 year following the last dose of the initial series, then annually in cats determined to have sustained risk of exposure.[h]	Noncore • FIV vaccine should be restricted to cats at high risk of infection.[h] • Vaccination induces production of antibodies indistinguishable from those developed in response to FIV infection and interferes with all antibody-based FIV diagnostic tests for at least a year following vaccination. • Cats with positive FIV antibody assay results may have antibodies as a result of vaccination, infection, or both. • Antibodies against FIV are passed from vaccinated queens to their kittens in colostrum. Colostrum-derived antibodies interfere with FIV diagnosis past the age of weaning in most kittens, but this interference appears to wane by 12 weeks of age. • Cats should test negative for antibodies against FIV immediately prior to vaccination. • Permanent identification of vaccinated cats (eg, microchip) will help clarify vaccination status but will not indicate that such cats are free of infection.
FIP (FCoV) MLV, nonadjuvanted IN	Administer a single dose at 16 weeks of age and a second dose 3 to 4 weeks later.	Administer 2 doses, 3 to 4 weeks apart.	Annual booster is recommended by the manufacturer.	Not generally recommended • According to the limited studies available, only cats known to be negative for antibodies against FCoV at the time of vaccination are likely to develop some level of protection. • Vaccination of cats living within households in which FIP is known to exist or cats that are known to be positive for antibodies against FCoV is not recommended.

Table 2—Summary of vaccination of cats in general practice (continued).

Vaccine	Primary series: kittens (≤ 16 weeks old)	Primary series: adolescent/adult (> 16 weeks old)	Booster	Comments
C felis Avirulent live organism, nonadjuvanted Injectable	Administer the initial dose as early as 9 weeks of age; a second dose is administered 3 to 4 weeks later.	Administer 2 doses, 3 to 4 weeks apart.	Annual booster is indicated for cats with sustained exposure risk.	Noncore • Vaccination is generally reserved as part of a control regime for cats in multiple-cat environments in which infections associated with clinical disease have been confirmed. • Inadvertent conjunctival inoculation of vaccine has been reported to cause clinical signs of infection.
C felis Killed organism, adjuvanted[a] Injectable	Administer the initial dose as early as 9 weeks of age; a second dose is administered 3 to 4 weeks later.	Administer 2 doses, 3 to 4 weeks apart.	Annual booster is indicated for cats with sustained exposure risk.	Noncore • Vaccination is generally reserved as part of a control regimen for cats in multiple-cat environments in which infections associated with clinical disease have been confirmed.
B bronchiseptica Avirulent live organism, nonadjuvanted IN	Administer a single dose IN as early as 8 weeks of age.	Administer a single dose IN.	Annual booster is indicated for cats with sustained risk.	Noncore • Vaccination may be considered in cases in which cats are likely to be at specific risk of infection.[i]
Feline *G lamblia* Killed organism, adjuvanted[a] Injectable	Administer a single dose at 8 weeks of age; a second dose is administered 2 to 4 weeks later.	Administer 2 doses, 2 to 4 weeks apart.	Annual booster is recommended by the manufacturer.	Not generally recommended • There are insufficient studies available to support the role of *G lamblia* vaccination in preventing clinical disease in cats. • Whether the *G lamblia* vaccine is an effective therapeutic agent in naturally infected cats is currently not known.

Core vaccines are recommended for all cats. Noncore vaccines should be administered to cats in specific risk categories. Not generally recommended vaccines are those that the Advisory Panel believes have little or no indication.

[a]Injectable adjuvanted vaccines have been associated with local inflammatory reactions at injection sites, with the degree of inflammation varying among products. The potential role of local inflammatory reactions in the genesis of vaccine-associated sarcomas remains controversial. [b]Only available in combination with modified-live FHV-1 and FCV vaccines for IN administration. [c]In unusual circumstances, if a cat is going to be placed in a known high-risk situation, an additional booster vaccination shortly before such risk is encountered may be considered. [d]In the European Union, a combination modified-live FHV-1 and killed (but nonadjuvanted) FCV vaccine has been approved for use in cats. [e]All rabies virus vaccines must be administered in accordance with the specifications of the product label or package insert and with state or local regulations. [f]Cats allowed outdoors, residing in open multiple-cat environments, living with FeLV-infected cats, and residing in households with cats of unknown FeLV-infection status or in which introduction of new cats is common. Booster inoculation is not generally recommended for cats housed strictly indoors. [g]A recombinant FeLV vaccine available in Europe is designed to be administered by SC injection; this product differs from the one licensed in the United States. [h]For example, outdoor cats that fight and cats that are not infected with FIV living with FIV-infected cats. [i]For example, prior to confinement in multiple-cat environments such as rescue shelters, boarding facilities, or catteries in which bordetellosis has been confirmed.

and infectious for months to years in the environment, and is primarily spread via the fecal-oral route. Fomites (eg, cages, food bowls, litter boxes, and health care workers) play an important role in transmission of the organism, as can buildup of the virus in a contaminated environment.

Canine parvovirus type 2 emerged as a canine pathogen probably from mutation of FPV or another closely related parvovirus. Canine parvovirus type 2 initially lacked the ability to infect cats, but CPV-2 variants have now emerged (CPV-2a, CPV-2b, and CPV-2c) that have largely replaced the original CPV-2, and these do have the ability to infect cats and, in some cases, to cause clinical parvoviral disease.[43,44] Results of cross-neutralization and challenge studies[43,45,46,d] suggest that FPV vaccination affords good protection against these CPV-2 variants; however, further studies are needed to confirm these observations.

Diagnosis of infection—A presumptive diagnosis of FPV infection is often made on the basis of appropriate clinical signs with profound leukopenia detected on CBC. Detection of a rise in antibody titer during a 2-week period may help to confirm the diagnosis, as may the detection of virus, viral antigen (as determined via ELISA), or viral genetic material (as determined via PCR assay) in fecal samples.[e] Histologic examination of tissues usually reveals characteristic lesions in the small intestine, which are virtually pathognomonic, and viral inclusion bodies may be detected in infected cells.

Vaccination—Immunity conferred by FPV vaccines is considered to be excellent, and most vaccinated cats are completely protected from clinical disease. Both antibody titer and challenge exposure data indicate that an FPV vaccine for administration via injection induces immunity that is sustained for at least 7 years.[19,21] Modified-live and inactivated FPV vaccines for injectable administration and, in some countries, MLV vaccines for IN administration are available and effective. Results of studies indicate that IN administration of CPV-2 vaccines to puppies is less effective than parenteral administration in overcoming maternal antibody interference,[f] possibly resulting from fewer virus particles reaching and replicating in lymphoid tissue. Although similar studies have not been performed in cats, the same phenomenon could occur in this species as well. Experience with naturally occurring disease suggests IN vaccination may not be as effective as SC vaccination in high-risk environments in which exposure may occur soon after vaccination.[f,g]

Maternally derived antibody may interfere with immunization when antibody titers are high during the neonatal period, and kittens will be at greatest risk of infection in the period between waning MDA and effective vaccine-induced immunity. Maternally derived antibody titers generally wane sufficiently to allow immunization by 8 to 12 weeks of age.[47,48] However, there is considerable interindividual variation,[28] and no single vaccination schedule will be appropriate for all kittens. A proportion of kittens will have low to no MDA titers and may respond to vaccination at 6 weeks of age[28]; thus, early vaccination may be appropriate, especially in situations of high risk and questionable MDA status (eg, rescue catteries). Nevertheless, some cats will have sufficient MDA to prevent effective vaccination before 12 weeks of age or possibly older in some situations. In 1 study,[28] only 67% of kittens were protected after receiving 2 to 3 FPV vaccines before 12 weeks of age because of MDA. In another study,[b] 75% of kittens with preexisting MDA that received a modified-live FPV vaccine at 8, 11, and 14 weeks of age developed protective titers by 17 weeks of age.

Adverse events associated with vaccination—Serious adverse events associated with FPV vaccines are rare. Vaccination of pregnant queens with modified-live FPV vaccines may result in neurologic disease in developing fetuses; the same concern applies to kittens vaccinated at 4 weeks of age.[49,50] Therefore, the use of modified-live FPV vaccines should be avoided in pregnant queens and kittens < 4 weeks old,[51,52] although use of modified-live FPV vaccines in pregnant cats in rescue shelters may be beneficial (see section concerning vaccination in shelters).

Advisory Panel recommendations—Because of its ubiquitous nature and serious disease-causing potential, FPV vaccines should be considered as core vaccines. Following the initial series of vaccinations (beginning as early as 6 weeks of age and repeated every 3 to 4 weeks until 16 weeks of age), cats should be revaccinated 1 year later. Thereafter, cats should be vaccinated no more frequently than once every 3 years.

Shelter considerations—Feline parvovirus vaccines should be considered as core vaccines in shelters. Kittens should be vaccinated beginning at 4 weeks of age during an outbreak and at 6 weeks of age otherwise.[28] The Advisory Panel recommends that modified-live FPV vaccines be used instead of inactivated vaccines because of their quick onset of immunity and greater efficacy at overcoming maternal antibody.[53] Feline parvovirus vaccines administered via injection should be used in a shelter environment instead of or in addition to vaccines administered IN, as they provide more consistent protection in a contaminated environment and may be better at overcoming MDA interference.[53] Although concerns have been raised regarding reversion to virulence when many vaccinated cats share a litter box, this has never been documented.[24] Modified-live FPV vaccines should be given by injection to cohoused cats and kittens, regardless of the number of animals housed together. Vaccination should be repeated every 3 to 4 weeks (every 2 weeks in high-risk environments) in kittens until 16 weeks of age. If adult cats are ill or otherwise compromised at the time of initial vaccination, consider repeating the vaccine once when the cat is in good health (no sooner than 2 weeks after administration of the initial vaccine).

FHV-1

Agent—Feline herpesvirus-1 is an important cause of URD in cats.[54,55] Feline herpesvirus-1 occurs worldwide, and it is likely that most cats will be exposed to infection. There is only 1 serotype of the virus, and genetically, all isolates are similar. Typically, FHV-1 induces mild to severe URD. The disease is generally self-limiting, although some cats may develop chronic clinical signs of URD. Occasionally, generalized disease may develop, particularly in young or immunosuppressed cats. In addition, the role of FHV-1 in various forms of ocular disease and skin lesions is increasingly being recognized and evaluated.[56-59]

All ages of cats are susceptible, although disease may be more severe in young kittens. Upper respiratory tract disease is common in groups of cats, such as in some boarding facilities, pedigree catteries, and rescue shelters, in which stress may lead to virus reactivation and spread from carrier cats; in addition, rapid, high-dose exposure may lead to a shorter incubation period and severe clinical signs.[55,60,61] In breeding colonies, disease tends to be seen in young kittens following the decline of MDA. This generally develops by 9 weeks of age but may develop earlier.[28,55]

Virus is shed in the oropharyngeal, conjunctival, and nasal secretions of infected cats. Transmission is mainly by direct cat-to-cat contact, but indirect transmission may occur via contamination of the environment or fomites.[54,55] However, the virus is relatively labile in the environment, remaining infectious for 24 hours. Aerosol transmission is not of major importance, although sneezed macrodroplets may transmit infection over short distances. Acutely infected cats shed virus for 1 to 3 weeks, after which most, if not all, become lifelong, latently infected carriers. In a proportion of such carriers, reactivation can occur following periods of stress or corticosteroid treatment, and these

cats may then transmit infection.[54,55] During such episodes, carrier cats may have clinical signs of disease.

Diagnosis of infection—Diagnosis of FHV-1 infection has classically been confirmed by virus isolation in cell culture from oropharyngeal or conjunctival swab specimens, although immunofluorescence has also been used. Increasingly, PCR assay is being used because it is significantly more sensitive than traditional methods[59,62-65]; however, test sensitivity varies greatly.[66] In addition, because FHV-1 can be shed both by clinically normal cats as well as cats with disease, viral detection by PCR assay (or other techniques) will not necessarily confirm the cause of disease.[66]

Vaccination—Modified-live and inactivated FHV-1 vaccines for injection are commercially available, and in some countries, MLV vaccines for IN administration are also available. Both MLV and inactivated virus vaccines provide reasonable protection against disease but do not prevent infection or viral latency. Inactivated virus vaccines may be more appropriate in disease-free colonies because there is no risk of spread or reversion to virulence.

Maternally derived antibody in most kittens is undetectable by 9 weeks of age, but there is considerable interindividual variation, and in some individuals, MDA may still be at interfering concentrations at 12 to 14 weeks of age.[28,b] A proportion of kittens will have low to no MDA titers and may respond to vaccination at 6 weeks of age[28]; thus, early vaccination may be appropriate, especially in situations of high risk and questionable MDA status (eg, rescue catteries). Vaccines for IN administration offer rapid (2 to 6 days) onset of protection in naïve cats and can be useful for cats entering a high-risk situation, such as a boarding facility or shelter.[54,55,67] Although not licensed for such use, where disease is endemic, vaccines for IN administration have been advocated in kittens younger than 6 weeks old, and results of several studies[28,68] indicate that vaccines for injectable administration may be effective starting at 5 to 6 weeks of age.[28,68] Results of 1 study[69] indicate that vaccination during pregnancy can help protect kittens by prolonging MDA; vaccination in this manner is not generally recommended but may be considered in multiple-cat environments with endemic URD and housing pregnant cats (eg, some breeding catteries and shelters).

Results of serologic and challenge studies[19-21,70] indicate that there is likely to be reasonable protection in most cats for as much as 3 years or longer after vaccination. However, protection is not always complete immediately following vaccination and may decline as the vaccination interval increases.[18,21]

Adverse events associated with vaccination—Modified-live FHV-1 vaccines for injectable administration, invariably used in combination with FCV vaccines, are generally safe, although mild clinical signs may occasionally develop after their use.[15] In some cases, this may result from accidental oronasal exposure to vaccine virus (eg, a cat licking the injection site or when an aerosol is made with the syringe).[71-73] However, such cats may be undergoing coincidental infection with naturally occurring virus.

Clinical signs of URD are more commonly seen following IN vaccination than after injectable vaccination. In a recent study,[74] although no clinical signs were seen in SPF cats, 30% of client-owned cats had transient sneezing after combined FHV-1/FCV/FPV vaccination.[74]

Advisory Panel recommendations—Feline herpesvirus-1 vaccines should be considered as core vaccines because infection is highly prevalent and easily transmitted and because disease may occasionally be severe and, in some cases, may lead to chronic clinical signs. Following the initial series of vaccinations (beginning as early as 6 weeks of age and repeated every 3 to 4 weeks until 16 weeks of age), cats should be revaccinated 1 year later. Thereafter, cats should be vaccinated once every 3 years. In unusual circumstances, if a cat is going to be placed in a known high-risk situation, an additional booster vaccination shortly before such risk is encountered may be considered.

Shelter considerations—Feline herpesvirus-1 vaccines should be considered as core vaccines in shelters. Intranasal vaccination in addition to or in lieu of vaccines for injectable administration may be preferable in high-risk shelters to induce a more rapid immune response in potentially naïve cats. Although most pet cats are seropositive for FHV-1, the same cannot be assumed for the population of cats entering a shelter.[20,75] For shelters that retain resident cats for only a short duration or that do not routinely treat upper respiratory tract infections, the major benefit of reduced disease severity will be seen by adopters and rescue groups. This benefit should not be underestimated, as it may lead to a positive adoption experience and a much-needed increase in the number of adoptions and community support. Cats vaccinated against FHV-1 are significantly less likely to shed virus than unvaccinated cats, which may improve population health.[76]

FCV

Agent—Feline calicivirus is an important cause of URD and oral disease in cats.[54,55] Feline calicivirus occurs worldwide, and it is likely that most cats will be exposed. Phylogenetically, FCV comprises 1 genogroup, although there is considerable variation within this group.[77-79] There appears to be no distinct geographic associations with particular strains, although there is some evidence for Japanese genotypes.[80] The numerous strains of FCV vary in antigenicity and induce a spectrum of diseases; acute infection may be subclinical or may result in combinations of oral and respiratory disease and lameness. Recently, outbreaks of a severe acute systemic disease with high mortality rates have been reported (VS-FCV disease).[81-84]

Virus is shed in oropharyngeal, conjunctival, and nasal secretions of infected cats. Fecal and urinary shedding may also occur but are probably not of major epidemiologic importance. Transmission is mainly by direct cat-to-cat contact, but indirect transmission may occur via contamination of the environment or fomites.[54,55] The virus survives better than FHV-1 in the environment (approx 1 week) but is still relatively

labile. Aerosol transmission is not of major importance, although sneezed macrodroplets may transmit infection over short distances. Acutely infected cats generally shed virus for as long as 2 to 3 weeks. However, some cats shed virus persistently for periods varying from months to years,[55] and reinfection also commonly occurs. Such carrier cats are widespread in the population.

All ages of cats are susceptible, although classic oral and respiratory tract disease may be more severe in young kittens. Interestingly, disease caused by VS-FCV appears to be more severe in older cats. In general, FCV infection tends to be common in groups of cats, such as in boarding catteries, rescue shelters, and breeding colonies.[55,85,86] Disease tends to be seen in young kittens following the decline of MDA. Maternally derived antibody generally lasts as long as 10 to 14 weeks, but subclinical infection may develop prior to this time.[54,55]

Diagnosis of infection—Diagnosis of FCV infection has classically been confirmed by virus isolation in cell culture from oropharyngeal or conjunctival swab specimen. Real-time PCR assays have been developed but are not widely used for FCV diagnosis largely because strain variation may lead to variable sensitivity.[87,88] Polymerase chain reaction assays and sequencing are useful for distinguishing between isolates in investigating the epidemiology of the disease and between vaccine and naturally occurring strains.[89]

Vaccination—An important consideration for FCV vaccines is the question of strain variation. Several FCV strains are used in commercially available vaccines, such as F9 and 255. Most of these strains appear to protect against most isolates but not as well against all, including some of the VS-FCV isolates.[83] It has also been suggested that the profile of naturally occurring FCV strains may be changing with time,[90-93] although this may depend on the sampling strategy used for the strains tested. Some evidence suggests that multivalent FCV vaccines may increase the proportion of strains neutralized.[94,95]

Modified-live and inactivated FCV vaccines for injection are commercially available, and in some countries, MLV vaccines for IN administration are also commercially available. Both modified-live and inactivated FCV vaccines are reasonably effective against disease, but do not prevent infection or the carrier state. Results of serologic and challenge studies[19-21,70] indicate that reasonable protection in most cats for as much as 3 years or longer after vaccination is likely. Although immunity is reasonably good following vaccination, it is not always complete in all cats and may decline slightly as the vaccination interval increases.[18,21] In addition, the DOI of FCV will be affected by strain variation and whether homologous or heterologous protection is being considered.

Maternally derived antibody may persist for 10 to 14 weeks, but there is considerable interindividual variation.[28,b] A proportion of kittens will have low or no MDA titers and may respond to vaccination at 6 weeks of age[28]; thus, early vaccination may be appropriate, especially in situations of high risk and questionable MDA status (eg, rescue catteries). Compared with injectable products, vaccines administered IN offer more rapid (2 to 6 days) onset of protection and can be useful for cats entering a high-risk situation, such as a boarding facility or shelter.[54,67] Although not licensed for such use, where disease is endemic, vaccines for IN administration have been advocated in kittens younger than 6 weeks of age, and results of 1 study[28] indicate that vaccines administered via injection may be effective starting at 6 weeks of age. Results of another study[69] indicate that vaccination during pregnancy can help protect kittens by prolonging MDA; vaccination in this manner is not generally recommended but may be considered in multiple-cat environments with endemic URD and housing pregnant cats (eg, some breeding catteries and shelters).

Adverse events associated with vaccination—Modified-live FCV vaccines for administration via injection, invariably used in combination with FHV-1 vaccines, are generally safe, but mild clinical signs of URD and, in some cases, lameness may occasionally develop after their use.[15,89,96,97] Although many such vaccine reactions are results of coincidental infection with naturally occurring virus, sequencing has confirmed that some are caused by vaccine virus.[89,98,99] Inactivated vaccines may therefore be preferable in disease-free colonies, such as research facilities housing SPF cats.

Clinical signs of URD are more commonly seen following IN vaccination. In 1 study,[74] although no clinical signs were seen in SPF cats, 30% of client-owned cats had transient sneezing after combined FHV-1/FCV/FPV vaccination.

Advisory Panel recommendations—Feline calicivirus vaccines should be considered as core vaccines because infection is highly prevalent and easily transmitted and because disease may occasionally be severe. Following the initial series of vaccinations (beginning as early as 6 weeks of age and repeated every 3 to 4 weeks until 16 weeks of age), cats should be revaccinated 1 year later. Thereafter, cats should be vaccinated once every 3 years. In unusual circumstances, if a cat is going to be placed in a known high-risk situation, an additional booster vaccination shortly before such risk is encountered may be considered.

Shelter considerations—Feline calicivirus vaccines should be considered as core vaccines in shelters. Intranasal vaccination in addition to or in lieu of vaccines for administration via injection may be preferable in high-risk shelters to induce a rapid immune response in potentially naïve cats. Vaccination against FCV does not prevent infection or shedding but may mitigate severity of signs. As with FHV-1 vaccination, the benefit of reduced disease severity may lead to increased adoptions and community support.

Rabies virus

Agent—Rabies is transmitted when virus is introduced into bite wounds, open cuts in the skin, or onto mucous membranes from saliva or other potentially infectious material such as neural tissue. With an estimated 45,000 to 60,000 human deaths worldwide

attributed to rabies virus infection each year, rabies virus ranks among the most serious zoonotic agents.[100] Although bites from rabid dogs still cause most human infections in the world today, widespread rabies inoculation of dogs in North America has reduced the threat of rabies transmission from dogs to humans since the early 1950s.[101,102] In the United States, rabid bats are recognized as the most important threat of rabies virus infection in humans.[103] Rabies in cats, however, continues to be confirmed in the United States and has, every year since 1982, been diagnosed more often than rabies in dogs.[101,104]

All instances of suspected or known rabies virus infection in cats and dogs must be reported to local health department officials. Treatment for rabies in cats is not effective and should not be attempted under any circumstances. Proper handling precautions and quarantine procedures are published annually.[105,106]

Vaccination—Presently, the following types of rabies virus vaccines for cats are licensed in the United States and several other countries: recombinant virus, nonadjuvanted, canarypox-vectored vaccine licensed to be administered annually by injection and killed virus, adjuvanted vaccines licensed to be administered either annually or triennially by injection.

Statutes governing the administration of rabies virus vaccines to cats vary considerably throughout the world. In the United States, several states do not require rabies virus vaccination of cats; however, local statutes may override state requirements and mandate vaccination. In certain regions of the United States, a 3-year licensed rabies vaccine may be administered triennially subsequent to administration of an initial dose 1 year previously. The individual veterinarian must understand and comply with state or local laws pertaining to the type of rabies vaccine required and the frequency of vaccine administration.

Every effort should be made to change laws that require rabies virus vaccination more often than every 3 years (when using a 3-year approved product) after vaccination as kittens and 1 year later. Annual revaccination by use of 3-year approved products induces no greater protection than that achieved with triennial administration and can increase the possibility of adverse events associated with vaccination.

In cases in which rabies virus vaccination may potentially endanger the life or health of a cat, the client and veterinarian may sign a certificate of exemption in lieu of vaccination (Appendix 1). A copy of the certificate should be given to the client and a copy maintained in the patient's permanent record.

Adverse events associated with vaccination—Adverse events associated with injectable rabies virus vaccination include local swelling or pain, transient lethargy or fever, and granuloma formation after vaccination (see section on adverse events and reporting). Accidental human exposure to rabies virus vaccine, either recombinant or killed, is not considered a human rabies exposure.

Advisory Panel recommendations—Because of the public health risk associated with susceptible domestic cats becoming infected following exposure to rabid wild animals, rabies virus vaccines should be considered as core vaccines in the United States and in all countries in which rabies is endemic and should be administered in accordance with local or state regulations. Primary vaccination should occur at 12 to 16 weeks of age (as early as 8 weeks, depending on vaccine brand), with revaccination 1 year later. Annual or triennial vaccination should then follow, depending on the type of vaccine and applicable legal requirements. State or local statutes regarding vaccination type and interval should be adhered to when applicable.

Shelter considerations—Although not contraindicated, there is little benefit to rabies virus vaccination at the time of admission to a shelter in which cats are not held long term. Vaccination on admission will not protect against an infection acquired prior to shelter entry and therefore will not mitigate concern for human health should a cat with an unknown history bite a person during its shelter stay. However, rabies virus vaccination at the time of adoption is advisable to help ensure compliance with vaccination requirements. All cats entering a long-term care facility, or any cat for which a long-term shelter stay is anticipated, should be vaccinated against rabies at the time of admission.

FeLV

Agent—Feline leukemia virus infects domestic cats throughout the world and frequently results in death in persistently viremic cats. Prevalence in the general pet cat population in North America is < 5% in adult cats, regardless of whether they are owned or feral.[107] Transmission is thought to be primarily through transfer of virus in the saliva or nasal secretions resulting from prolonged intimate contact (eg, mutual grooming), biting, or sharing of food and water utensils. The virus may also be transmitted by transfusion of blood from an infected cat, in utero, or through milk.[108] The virus is extremely labile; thus, exposure to virus persisting in the environment, on fomites, or in aerosolized secretions is not an efficient means of viral transmission. Clinical signs of FeLV infection primarily result from immunosuppression, neoplasia, or anemia.

Acquired immunity to FeLV is based on humoral and cell-mediated immune responses.[109] Kittens and young adult cats are the most susceptible to infection; results of 1 experimental challenge study[110] indicate that resistance increases with maturity. However, age-related resistance to infection is not absolute, and adult cats may be vulnerable to infection. In several studies[111-113] involving experimental challenge of vaccinated and nonvaccinated control cats, at least 50% of adult control cats became infected.

Diagnosis of infection—Available tests include patient-side immunochromatographic tests (eg, ELISA) that detect FeLV antigen in whole blood, serum, plasma, or saliva; IFA tests that detect viral antigen in circulating WBCs and platelets; virus isolation; and PCR assays that detect viral RNA or proviral DNA.[38,114]

Vaccination—Several adjuvanted inactivated FeLV vaccines for injection, a nonadjuvanted recombinant FeLV vaccine designed to be given transdermally (available in the United States), and a nonadjuvanted recombinant FeLV vaccine designed to be given SC (a different preparation from the US product and available in Europe) are commercially available. A review[115] of independent studies of vaccine efficacy indicates that the ability of any particular vaccine brand to induce an immune response sufficient to resist persistent viremia varies considerably between studies. Results of several studies[112,116] indicate that FeLV vaccine-induced immunity persists for at least 12 months following vaccination, although it is likely immunity would persist longer than 12 months.

Because protection is not induced in all vaccinates, vaccination against FeLV does not diminish the importance of testing cats to identify and isolate those that are viremic. Therefore, the FeLV infection status of all cats should be determined.[38] In addition, cats should be tested for FeLV infection before initial vaccination and when there is a possibility that they have been exposed to FeLV since they were vaccinated. There is no value in administering FeLV vaccines to individuals confirmed to be infected.

Adverse events associated with vaccination—Adverse events associated with vaccination against FeLV include local swelling or pain, transient lethargy or fever, and granuloma formation after vaccination.

Advisory Panel recommendations—Feline leukemia virus vaccines should be considered as noncore vaccines and are recommended for cats at risk of exposure (eg, cats permitted outdoors, residing in multiple-cat environments in which incoming cats are not tested prior to entry, living with FeLV-infected cats, and residing with cats in which FeLV infection status is not known or in which introduction of new cats is common). However, vaccination of all kittens is highly recommended because they may subsequently be at risk of FeLV exposure even if not currently at risk. Kittens are also more likely than adult cats to become persistently viremic if exposed.

When FeLV vaccination is determined to be appropriate, a 2-dose primary series is recommended, with the first dose administered as early as 8 weeks of age followed by a second dose administered 3 to 4 weeks later. A single booster vaccination should be administered 1 year following completion of the initial series. Presently, the Advisory Panel is not aware of any studies supporting DOI beyond 1 year in a natural setting or controlled study design. Therefore, it is the Panel's opinion that FeLV booster vaccinations be administered annually in cats at risk of exposure.

Shelter considerations—Vaccination is generally not recommended in shelters in which cats are individually housed because of the low risk of viral transmission. In such shelters, resources are generally better spent on testing, and the decision to vaccinate is best left to the adopter based on the cat's risk profile in its new home. In facilities in which cats are group-housed, such as in some shelters and foster homes, FeLV vaccination is recommended.

FIV

Agent—Feline immunodeficiency virus is a lentivirus discovered in 1986 in a group of cats with signs of immunodeficiency. Feline immunodeficiency virus is commonly classified into 5 subtypes (A, B, C, D, and E) based on genetic variation within 1 section of the virus envelope gene. Subtypes A and B are the predominant subtypes in the United States. Substantial genetic variation exists both within and between the various subtypes (also called genotypes or clades). The virus is present worldwide, with prevalence of infection ranging from 0% to 44%, depending on age, sex, lifestyle, physical condition, and geographic location. Prevalence in the general cat population in North America is < 5% in adult cats, regardless of whether they are owned or feral.[107] Unlike other infections in cats, kittens do not appear to be more susceptible to FIV infections than adult cats. Transmission is primarily via bite wounds from infected cats; therefore, most infections are diagnosed in adult males.

Diagnosis of infection—Unlike the case of FeLV, circulating viral antigens are not detectable in FIV-infected cats. Lentiviral infection is considered to be lifelong; for this reason, detection of FIV-specific antibodies in blood is considered to be a reliable indicator of infection. Patient-side immunochromatographic antibody tests (eg, ELISA) are commonly used for screening cats, and western blot or IFA tests are recommended for confirmation of infection. Antibody tests are complicated in kittens that have acquired anti-FIV antibodies by passive transfer in colostrum. It is not common for kittens to become infected from their mothers or from other cats; therefore, initial positive test results in most kittens will eventually become negative when their maternal antibody wanes by 5 to 6 months of age. Some cats do not produce detectable antibodies against FIV following infection, and these cats will have false-negative results on antibody tests. Virus culture is an extremely accurate method of diagnosis but is not commercially available.[117] The sensitivity and specificity of PCR assays for FIV are reportedly inadequate, and these assays are not reliable for the diagnosis of FIV infection.[117]

Vaccination—Feline immunodeficiency virus has proven to be a difficult agent to immunize against, in part because experimental FIV vaccines do not induce cross-protective immunity against viruses from other strains or clades. Only a single vaccine is currently available for prevention of FIV infection in the United States and Canada. The vaccine is a whole-virus, dual subtype (clades A and D), inactivated product combined with an adjuvant. The vaccine is licensed for the vaccination of healthy cats 8 weeks of age or older as an aid in the prevention of infection with FIV. In licensing trials required by the USDA, when cats were challenged with a heterologous clade A FIV subtype 1 year after the initial vaccination series, the vaccine yielded a preventable fraction (defined as the proportion of cats protected by vaccination in excess of the proportion that is naturally resistant) of 82%. Results of 2 subsequent studies[118,119] indicate 100% protection against infection with 2 subtype B FIV strains. In 1 natural

exposure study[118] in which vaccinated cats and control cats were housed with infected cats for more than a year, 4 of 8 control cats became infected, compared with 0 of 6 vaccinated cats. In a study[119] in which cats were experimentally challenged IV with subtype B virus, 9 of 9 control cats became infected, compared with 0 of 8 vaccinated cats. Results of a third study[120] in which cats were challenged IM or IP with subtype A FIV indicated that all vaccinated cats and control cats became infected.

Vaccination results in the production of antibodies that are indistinguishable from those produced in response to FIV infection and interferes with all antibody-based FIV diagnostic tests (ELISA, other immunochromatographic tests, western blot, and IFA) for at least a year following vaccination.[121] Presently, there are no commercially available tests that can reliably determine the FIV infection status of cats with positive results for antibodies against FIV, as these cats may have antibodies as a result of vaccination against FIV, infection with FIV, or both. Positive tests results caused by FIV vaccination complicate identification, isolation, and requisite specialized care of infected cats, which have long been the mainstays of FIV control. Antibodies against FIV are also passed from vaccinated queens to their kittens in colostrum. Vaccine-induced FIV antibodies delivered to kittens via colostrum interfere with the diagnosis of FIV past the age of weaning in most kittens, but this interference appears to wane by 12 weeks of age.[122]

Adverse events associated with vaccination—In a licensing field trial,[123] 689 cats receiving 2,051 vaccine doses were monitored for acute reactions. Twenty-two doses (1%) were associated with mild reactions, including signs of pain on injection (n = 9), lethargy (5), fever (4), vomiting or diarrhea (3), and anorexia (1).[123]

Advisory Panel recommendations—Feline immunodeficiency virus vaccines should be considered as noncore vaccines, with use restricted to cats at high risk of infection (eg, outdoor cats that fight) and cats not infected with FIV living with FIV-infected cats. An initial series of 3 doses is administered SC 2 to 3 weeks apart; annual revaccination is recommended subsequent to the initial series if the risk of infection continues.

Clients should be informed that vaccinated cats will develop false-positive FIV test results, and the decision to vaccinate should be reached only after careful consideration of this implication. If the decision falls in favor of vaccination, cats should test negative immediately prior to vaccination. Permanent identification of vaccinated cats (eg, by use of a microchip) will help clarify vaccination status but will not indicate that such cats are free of infection. It will also increase the likelihood of a lost cat being returned home if taken to a shelter and lessen the risk that a positive FIV antibody test result will lead to euthanasia.

Shelter considerations—Vaccination is not generally recommended because of the low risk of FIV transmission in typical single-cat housing, and FIV vaccines are thus considered as noncore vaccines. Resources of time and money are generally better spent on testing prior to cohousing; the decision to vaccinate is best left to the adopter based on a cat's risk profile in its new home.

FCoV

Agent—Feline coronaviruses vary considerably in pathogenic potential. Strains that cause FIP are serologically and genetically indistinguishable from less virulent strains and represent virulence variants of the same virus rather than separate virus species.[124] Results of studies[125-127] indicate that primarily avirulent FCoV replicates in enterocytes. In some instances, however, a mutation occurs in a certain region of the FCoV genome,[125-127] leading to the ability of the virus to replicate to high titers within macrophages, a key pathogenic event in the development of FIP. Population densities > 5 cats/household increase the risk of virus mutation.[128]

Feline coronaviruses are widespread in feline populations, with antibodies present in as many as 90% of cats in catteries and 50% of those in single-cat households.[129-132] In environments in which FCoV infection is endemic (eg, almost all multiple-cat households), 35% to 70% of cats will be shedding FCoV in feces at any given time.[133,134] However, even in multiple-cat households, only approximately 5% of FCoV-infected cats develop FIP; the number is much lower (0.01% to 1%) in single-cat environments.[129,130,135,136] Kittens are at highest risk of developing FIP, but the disease develops in cats of all ages. A genetic predisposition has been suggested, with a higher incidence of disease in certain genetic lines.[125,137,138]

Diagnosis of infection—Tests for the detection of antibody against FCoV are widely available. Although positive test results are indicative of FCoV exposure, detection of antibody alone is insufficient to diagnose FIP. Patient signalment, history, physical examination findings, and laboratory test results may yield a presumptive diagnosis of FIP; however, definitive diagnosis requires detection of FCoV within macrophages in effusions or within lesions detected in affected tissues.[139]

Vaccination—Only 1 vaccine is currently available, and considerable controversy surrounds its ability to protect against FCoV infection or to prevent development of disease. Results of 2 studies[140,141] indicate protection from disease; results of other studies[142,143] indicate little benefit from vaccination. Discrepancies between study results are likely attributable to differences in the experimental setting of the challenge trials (eg, strain and dose of challenge virus or genetic predisposition of study cats). In a field study[144] of 138 cats from 15 cat breeders in which virtually all cats had antibodies against FCoV, no difference was detected in the development of FIP between vaccinated cats and cats receiving the placebo. Thus, vaccination in households with known cases of FIP or in FCoV-endemic (and thus high-risk) environments is not effective. There may be certain circumstances (eg, a cat that has never been exposed to FCoV enters an FCoV-endemic environment) in which the vaccine may induce some

level of protection. In placebo-controlled double-blind trials in groups of cats that were not exposed to FCoV before vaccination, a small but significant reduction in the number of cats that developed FIP was detected.[144-146] As the vaccine is not effective in cats with prior exposure to FCoV, antibody testing before vaccination is advisable; seropositive cats would not be expected to benefit from vaccination.

Adverse events associated with vaccination— Antibody-dependent enhancement leading to faster development of disease in vaccinates has been detected in experimental challenge exposure studies,[142,143,147] but it is uncertain whether ADE occurs in a natural setting. In neither of 2 extensive placebo-controlled double-blind field trials[145,146] were there signs of induction of FIP or ADE.

Advisory Panel recommendations—The Advisory Panel continues to place this vaccine in the not generally recommended category. Numerous attempts to develop an effective FIP vaccine have not been successful, in part because of ADE following challenge. Presently, only 1 FIP vaccine is licensed. The MLV vaccine is a temperature-sensitive mutant of the FCoV strain DF2-FIPV administered IN to cats 16 weeks of age and older.

Most authors agree that the current FIP vaccine is safe and that ADE among cats seen in clinical practice is not a consideration. However, considerable controversy surrounds the vaccine's efficacy.[140-143] Among the limited studies available, only cats known to be seronegative for antibodies against FCoV at the time of vaccination are likely to develop some level of protection. Vaccination of cats living within households in which FIP is known to exist or cats that are known to be seropositive for antibodies against FCoV is not recommended.[144]

The vaccine is not licensed for kittens younger than 16 weeks of age. However, most kittens born and reared in environments in which FCoV infection is endemic are infected prior to reaching this age.[131,134] Current protocols for the prevention of FCoV infection among kittens do not include vaccination.[148]

Chlamydophila felis

Agent—*Chlamydophila felis* (formerly *Chlamydia psittaci* var *felis*) is a bacterial pathogen with worldwide distribution. The organism predominantly infects the conjunctiva and causes conjunctivitis. It is labile, and transmission is mainly through direct cat-to-cat contact. Serous conjunctivitis, which may initially affect only 1 eye, is the most common clinical sign, but bilateral disease with chemosis and mucopurulent discharges often develops. Mild sneezing or nasal discharges sometimes develop. Although primarily an ocular pathogen, *C felis* has also been isolated from other mucosal and epithelial sites, including the lower respiratory tract, the gastrointestinal tract, and the reproductive tract.[149-151] Clinical signs are usually evident 5 to 10 days after infection and resolve with appropriate antimicrobial treatment.[152] Isolation rates have been reported to range from approximately 1% to 5% for cats without clinical signs of respiratory tract disease to approximately 10% to 30% for cats with conjunctivitis or upper respiratory tract disease.[153-155]

There is limited evidence that the organism may occasionally be transmitted between cats and humans, causing conjunctivitis.[156,157] Therefore, direct contact with respiratory discharges and ocular secretions from infected cats should be avoided, especially by immunocompromised people.[158]

Diagnosis of infection—Diagnosis of chlamydophilosis is based on the presence of appropriate clinical signs and the detection of the organism (by use of culture techniques or PCR assay) in material obtained from conjunctival swab specimens. Cytologic evaluation of conjunctival scrapings for *Chlamydophila*-associated inclusion bodies is not a sensitive diagnostic technique.

Vaccination—Immunity to chlamydial organisms relies on a combination of cell-mediated and humoral mechanisms, but even after natural recovery from disease, infected cats typically continue to shed the organism for many months.[151] Both inactivated adjuvanted and modified-live *C felis* vaccines for administration via injection are available. Similar to FCV and FHV-1 vaccines, *C felis* vaccines afford some protection against the development of clinical disease, but they do not prevent infection or shedding of the organism.[151,159]

Adverse events associated with vaccination— Reactions following vaccination for *C felis* appear to be uncommon. One study[160] highlighted transient pyrexia, anorexia, lethargy, and limb soreness in some cats 1 to 3 weeks after vaccination with a combined FPV, FHV-1, FCV, and *C felis* vaccine; similar clinical signs were not detected after administration of a similar vaccine without the *C felis* component. Inadvertent ocular inoculation of modified-live *C felis* vaccines will cause typical clinical disease.[161]

Advisory Panel recommendations—Vaccination against *C felis* infection is considered noncore. Vaccination may potentially be considered as part of a control regimen for cats in multiple-cat environments in which infections associated with clinical disease have been confirmed. If vaccination is determined to be appropriate, annual revaccination is recommended.

Shelter considerations—Vaccination is considered noncore in shelters; however, vaccination may be considered as part of a control regimen in multiple-cat environments in which disease caused by *C felis* infection has been confirmed. If used, the need for this vaccine should be reassessed periodically.

Bordetella bronchiseptica

Agent—*Bordetella bronchiseptica* is an aerobic, gram-negative coccobacillus, which has long been recognized as a respiratory tract pathogen of several animal species.[162] It also causes occasional opportunistic infection in humans, particularly in immunosuppressed individuals. In the past, *B bronchiseptica* was thought to play only a secondary role in respiratory tract disease in cats, but it is now established as a primary pathogen. Upper respiratory tract disease with

sneezing, oculonasal discharges, submandibular lymphadenopathy, and some coughing has been reproduced experimentally in SPF cats.[163-165] A number of naturally occurring cases have also been reported with clinical signs varying from URD to severe coughing and bronchopneumonia, which in some cases results in death.[162,166-168] In general, coughing appears to be less marked in cats than it is in dogs infected with *B bronchiseptica.* All ages of cats are susceptible, but disease may be more severe in young kittens.[166,167] Although *B bronchiseptica* can be a primary pathogen in cats, other factors, such as combined infections with respiratory tract viruses and stress factors such as weaning, overcrowding, and poor hygiene and ventilation, may all play a role in inducing disease.[169]

Bordetella bronchiseptica appears to occur worldwide, and serosurveys have found that exposure to the organism is common. Seroprevalences from 24% to 79% and isolation rates of as much as 47% have been reported, depending on the type and clinical status of the population of cats tested.[85,162,170-173] A high prevalence of infection with *B bronchiseptica* tends to be found in multiple-cat households and rescue shelters, especially where there is a history of respiratory tract disease. Infection is less common in households with few cats and no history of URD.[85,170,172,174]

The organism is shed in oropharyngeal and nasal secretions, in some cases for at least 19 weeks after infection.[164] Transmission is mainly by direct cat-to-cat contact but may also be by contact with infectious discharges. *Bordetella bronchiseptica* does not survive for long periods outside the host.[162,175] Epidemiologic evidence suggests a carrier state exists for *B bronchiseptica* infection, with as many as 9% of clinically healthy cats shedding the organism.[171,172] There is also some evidence that the stress of parturition may initiate shedding in seropositive queens.[164]

Bordetella bronchiseptica may be transmitted between dogs and cats. Results of an epidemiologic study[172] indicate that contact with dogs with recent respiratory tract disease was found to be a risk factor for *B bronchiseptica* infection in cats. In addition, results of molecular typing studies[173,176] indicate that isolates from both species on the same premises are likely to be similar. In 1 such household, URD in 2 cats closely followed contact with 2 dogs with kennel cough and isolates from all 4 animals appeared identical by use of pulsed-field gel electrophoresis.[177] *Bordetella bronchiseptica* also occasionally infects humans, particularly if immunocompromised, and such individuals should be made aware.

Diagnosis of infection—Diagnosis determined by clinical signs alone may be difficult because clinical signs may be similar to those detected with viral infections of the respiratory tract. For confirmatory diagnosis, oropharyngeal or nasal swab specimens should be obtained, placed into charcoal Amies transport medium, and cultured in the laboratory on appropriate selective medium that prevents overgrowth by other respiratory tract flora.[162] Tracheal wash and bronchoalveolar lavage specimens have also been used for isolation of *B bronchiseptica* from clinical cases. Serologic testing is not widely available, and many healthy cats are, in any case, seropositive.

Vaccination—A commercially available modified-live *B bronchiseptica* vaccine for IN administration has been found to have an onset of immunity of 72 hours and a DOI of at least a year.[165] The vaccine may be used in cats 1 month old or older.

Adverse events associated with vaccination—The vaccine may cause mild clinical signs of URD after vaccination. Cats with severe clinical signs after vaccination should be treated with appropriate antimicrobials. Vaccinated cats can also shed *B bronchiseptica* for several weeks and, in some cases, for as long as a year after vaccination and may spread the organism to other cats and possibly other susceptible species.

Advisory Panel recommendations—*Bordetella bronchiseptica* vaccination should be considered noncore but may be considered in cases in which cats are likely to be at specific risk of acquiring *B bronchiseptica* infection (eg, prior to confinement in environments such as rescue shelters, boarding facilities, or catteries in which bordetellosis has been confirmed).

Shelter considerations—The association between *B bronchiseptica* infection and URD in shelter and rescue cats is not clear; results of 1 study[178] indicate that a significant association was found, whereas results of another study[60] indicate that there was no increased risk of URD associated with infection. Vaccination in shelters is considered noncore but may be warranted if *B bronchiseptica* infection is confirmed by culture from an unusually high percentage of cats with URD where dogs on the same premises have confirmed *B bronchiseptica*–induced kennel cough or when characteristic bronchopneumonia is diagnosed by necropsy. The cost-to-benefit ratio of using this vaccine in a particular shelter or rescue population should be periodically reassessed by laboratory testing of cats with URD.

Giardia lamblia

Agent—Cats are commonly exposed to *G lamblia* with infection rates > 5% in some parts of the United States.[179,180] *Giardia lamblia* are enteric organisms transmitted by the fecal-oral route; infection can be acquired from contaminated water, mutual grooming, shared litter boxes, or ingestion of infected prey species or transport hosts. On the basis of genotyping, some feline *Giardia* isolates have been classified as the zoonotic assemblage A and others as host-restricted assemblages like C and F.[181-183] There are no microscopic characteristics that can determine a zoonotic *Giardia* isolate from a host-restricted *Giardia* isolate; therefore, all isolates should be considered potentially zoonotic.[158] Some cats with *G lamblia* detected in feces are clinically normal and others develop clinical signs of disease.[184] Currently, there are no approved treatment protocols for cats; however, administration of metronidazole benzoate[185]; fenbendazole[186]; or a combination product containing febantel, praziquantel, and pyrantel[187] lessened cyst shedding in most cats and apparently eliminated infection in some cats.

Diagnosis of infection—Although the diagnosis can be problematic in some cases, most cats with giardiasis can be identified by use of wet mount examination and fecal flotation. Use of in-clinic, soluble fecal antigen test kits in addition to zinc sulfate centrifugation may increase the likelihood of a correct diagnosis[188]; IFA tests and PCR assays are also available and can be used to aid in the diagnosis.

Vaccination—A vaccine licensed in the United States as an aid in the prevention of disease associated with *G lamblia* infection and reduction in the severity of shedding of cysts has been commercially available for several years. This vaccine is composed of quantified, homogenated, and chemically inactivated *G lamblia* trophozoites and contains an adjuvant. The vaccine is approved for use in cats 8 weeks of age and older. In studies required by the USDA and conducted by the manufacturer to gain vaccine licensure, vaccinates challenged with a heterologous *Giardia* isolate 1 year after vaccination had a significant reduction in severity of clinical signs (diarrhea), duration of cyst shedding, and prevalence of infection (percentage of infected cats at the end of the trial), compared with control cats. In an independent controlled study[189] of the use of the vaccine as a treatment in cats with experimentally induced giardiasis, there was no difference in cyst shedding between vaccinated and control cats.[189]

Advisory Panel recommendations—An adjuvanted *G lamblia* vaccine composed of chemically inactivated trophozoites is currently available. However, considering that there are insufficient studies available to support the role of vaccination against *G lamblia* in preventing clinical disease in cats, the Advisory Panel continues to place this vaccine in the not generally recommended category.

Whereas the *G lamblia* vaccine is licensed as an aid in the prevention of disease associated with infection, the vaccine has also been used in an attempt to treat some infected dogs and cats. Although use of the canine *G lamblia* vaccine was reported to be successful in a study[190] of naturally infected dogs, administration of 3 doses of the feline *G lamblia* vaccine did not lessen cyst shedding in experimentally infected cats when compared with control cats. However, only 1 strain of *G lamblia* was used. Whether the *G lamblia* vaccine is an effective therapeutic agent in naturally infected cats is currently not known.

Legal Considerations

In the United States, biological products, including vaccines, are licensed and regulated by the USDA CVB under the authority of the Virus, Serum, and Toxin Act[191] and the implementing regulations promulgated by CVB.[192] The licensing process is different in other parts of the world and varies from country to country. The CVB has the legal authority to prohibit the preparation, sale, barter, exchange, shipment, or import of any "virus, serum, toxin, or analogous product" that is "worthless, contaminated, dangerous, or harmful."[191] However, the CVB does not regulate the professional practice of veterinary medicine. In most circumstances, veterinarians have the discretion to exercise professional judgment in the use of biological products and may use them either consistent or inconsistent with their labeling. The Animal Medicinal Drug Use Clarification Act[193] and its implementing regulations apply to the extralabel use by a veterinarian of New Animal Drugs and New Drugs as those terms are defined under the Federal Food, Drug, and Cosmetic Act. It does not apply to veterinary biologic products. Two notable exceptions to discretionary use involve state or local law that dictates the frequency of administration of rabies virus vaccine and vaccines used in federal or state disease eradication programs. Some products may carry very specific label restrictions, such as for use only in USDA or state disease eradication programs that may prevent discretionary use. Additionally, should particular discretionary uses present serious safety concerns, the CVB could initiate an enforcement action against a veterinarian. Unless there is a serious safety concern, this is not an area of regulatory priority for the CVB.

Medical malpractice litigation has developed in the context of negligence cases against physicians. When veterinarians are sued for professional negligence, courts will typically apply the principles developed in the context of litigation against physicians. There are other potential causes of action outside of negligence, but the law is less developed in these areas because most professional liability insurance policies for physicians exclude coverage when these other theories are invoked. Some of these other theories include breach of contract, breach of fiduciary duty, breach of warranty, guaranty, battery, product liability, and violation of consumer protection or deceptive trade practice acts. These other causes of action could be brought against veterinarians under appropriate circumstances.

As with any decision involving the management of patients, there is the potential for liability arising from the use of vaccines. This potential, although not frequently manifested, exists regardless of whether a biologic product is used according to its label and flows from the legal duty that comes with the veterinarian-client-patient relationship. This relationship creates, in terms of negligence law, the duty to exercise "reasonable care" or "ordinary care." In malpractice cases, this is often referred to as a duty to follow the "standard of care" and is also described as the responsibility to exercise the same level of care and competence as a reasonably prudent practitioner with the same or similar training under the same or similar circumstances. These are legal terms of art carrying specific legal significance that may differ from common usage and will not necessarily equate with professional standards or practices. With few exceptions, the establishment of the "standard of care" and whether or not a practitioner met it under the specific facts and circumstances at issue must be established by competent expert testimony.

Informed consent actions are typically brought as variations of negligence cases. At its core, informed consent requires a practitioner to obtain consent prior to providing care to a patient. There are 2 primary stan-

dards used by states in evaluating informed consent cases, with a fairly even split among states. One standard can be referred to as the "reasonable practitioner" standard, and the other can be referred to as the "reasonable person" standard. The "reasonable practitioner" standard views the situation from the perspective of the practitioner. The focus is on whether the practitioner disclosed the information that a reasonably prudent practitioner would under the same or similar circumstances. The information that a reasonably prudent practitioner would have disclosed is established by expert testimony. The "reasonable person" standard views the situation from the perspective of the patient or, in the case of veterinary medicine, the client. The focus is on whether the practitioner disclosed the information that a reasonable person would need to make intelligent decisions about the care to be provided. Expert testimony is not necessary to establish this standard.

Documentation of obtaining a client's consent for treatment is important and helpful when defending informed consent cases. Documentation can range from noting the discussion in the patient's chart to generic consent forms to detailed procedure-specific consent forms listing potential adverse outcomes. The best approach to developing good consent forms is to consult with an attorney familiar with informed consent law in the practitioner's state.

Veterinarians should be cautious in their statements regarding the safety or effectiveness of vaccines. No vaccine is 100% safe or 100% effective. The default position is that there are no guaranties or warranties provided in the delivery of medical care. However, these can be established by statements made by or materials provided by a veterinarian or their staff. If a veterinarian guarantees or warrants that a particular vaccine product is safe or effective, the veterinarian, not the manufacturer, may be held liable. This type of cause of action may not be covered by veterinary malpractice insurance. Many consent forms will address this issue by stating that the client understands that the veterinarian does not guarantee or warrant a cure or specific outcome.

Vaccine Licensing

The Virus, Serum, and Toxin Act grants authority to the CVB to license animal vaccines intended for use in treating domestic animals. To obtain licensure, a vaccine manufacturer must demonstrate that the product meets requirements for efficacy, purity, potency, and safety and that personnel with appropriate qualifications can manufacture it consistently in an approved facility. After licensure, each serial or batch must be tested and approved by the CVB prior to commercial release. Veterinary vaccine licensing requirements are listed in Title 9 of the Code of Federal Regulations.[194,195]

Efficacy—Efficacy is a measure of a vaccine's ability to stimulate a protective immune response. Vaccine efficacy is an in vivo measurement, and depending on CVB policy for the disease of interest, it is usually determined by direct challenge exposure of test animals. The manufacturer must follow codified procedures whenever they exist. The procedures are usually quite specific, regulating the number and species of animals involved in the test and the method of challenge exposure and evaluation of efficacy.

Animals are usually challenge exposed 3 to 4 weeks after vaccination. Duration of immunity data, meaning a demonstration of efficacy at a specified time after vaccination (eg, 1 or 3 years), is required for rabies virus vaccines and all newly licensed antigens. The number of animals required for USDA efficacy assessment is usually small (eg, at least 20 vaccinates and 5 controls for modified-live FPV vaccines). In the European Union, duration of immunity must be determined for each product on the basis of controlled experimental challenge and field trials. Because of the expense and welfare considerations of maintaining experimental animals in isolation for a prolonged duration, the use of in vitro correlates of protection is being encouraged.[15,196]

The use of codified procedures has the potential to simplify comparisons of the efficacy of vaccines. However, the CVB does not have codified standards for all of the currently available feline vaccines (eg, FeLV vaccines), and the small number of animals included in challenge studies renders comparisons problematic at best. Where no codified efficacy standards exist, the manufacturer must submit to the CVB a test procedure believed to adequately demonstrate effectiveness; if the test procedure is approved, the manufacturer may then use that procedure to determine vaccine efficacy. Although the flexibility of this method allows new vaccines to enter the marketplace more quickly than might otherwise be the case, it hampers even rudimentary comparisons of vaccine efficacy because various manufacturers may have gained approval with different test procedures.

For most diseases, experimental results compare favorably with what veterinarians experience in practice. As examples, efficacy tests of FPV vaccines indicate that vaccine-induced immunity is sufficient to completely protect most cats against challenge exposure. Similarly, tests of the efficacy of FHV-1 and FCV vaccines demonstrate protection from serious disease in most vaccinated cats. Both of these results parallel the experience of most practitioners. However, many variables influence an individual cat's response to vaccination; therefore, efficacy trials may not tell users how vaccination will affect a specific animal or population of animals.

Purity—Pure cultures of the basic starting materials are used to produce a vaccine. These starting materials include the master seed, which may be an attenuated strain, a virulent strain that will be later inactivated, or a biotechnology-derived organism, as well as any master cell culture lines, primary cells, or ingredients of animal origin. An extensive array of tests are conducted to be as certain as possible that the organism in these cultures is indeed the intended agent, that no adventitious agents are present, and that the cell lines and other animal origin ingredients have been correctly identified and are themselves free of contamination. Once a manufacturer has established a master cell or master seed stock, the USDA performs its own con-

firmatory testing; if results are acceptable, the USDA releases the master stock for use by the manufacturer. To produce a vaccine, the manufacturer then creates working cells and seeds from the master stocks, which subsequently are frozen and stored in liquid nitrogen.

Although purity testing is extensive, it is not without potential error. Contaminants that are closely related to the intended infectious agent are occasionally missed, and adventitious agents that are present at concentrations below the threshold of detection may not be identified. This is particularly important if an adventitious agent is pathogenic, a risk associated with manufacturing of modified-live agent vaccines. Improvements in test methodologies have made creation of master stocks more difficult but also more precise and have allowed detection of contaminants missed by previous testing methods.

Potency—Potency testing determines the quantity of antigen in a vaccine. Potency and efficacy are closely related, but there are important differences. Potency is usually an in vitro assessment made during the manufacturing process, whereas efficacy is an in vivo assessment of how a vaccine performs in animals. The USDA must approve all potency test procedures and requires that the manufacturer demonstrate a correlation between potency test results and vaccine efficacy. Each batch of vaccine manufactured is tested for potency, and once the potency exceeds a predetermined limit, the vaccine can be sold.

One factor that makes in vitro potency testing attractive is that prior to use of potency testing, each batch of vaccine had to be tested for efficacy, an expensive requirement that cost the lives of many thousands of animals. Unfortunately, the correlation between potency and efficacy is not always strong. First, potency tests are usually comparisons between production batches of vaccine and a reference vaccine. Because of the way reference vaccines are made and approved, subsequent reference vaccines may contain more antigen mass than previous batches, with a resulting upward shift in the potency of manufactured vaccines. Increased potency may raise safety concerns. Second, vaccines of unequal efficacy may receive equivalent potency tests results. For instance, although a heated or frozen vaccine may maintain potency, its efficacy may be compromised. Third, potency tests tend to ignore the role that an adjuvant plays in vaccine efficacy. As an example, a vaccine adjuvant may be adversely affected by storage, yet potency test results may remain unaffected. For these reasons, potency test results parallel efficacy only under the limited set of conditions under which they were originally approved.

Safety—Vaccine safety is determined by monitoring vaccinates for clinically significant problems. Both laboratory safety data (eg, reversion-to-virulence studies, evaluation for local or systemic reactions, and shedding of live vaccine organisms) and field safety data must be generated. A standard field safety test must include a number of animals vaccinated at various geographic locations, usually multiple veterinary practices. Most feline vaccine field safety studies involve approximately 600 cats. In most instances, test animals are vaccinated by a veterinarian and observed for a brief period, usually 30 minutes. Owners are then instructed to monitor the animals at home and report any unusual clinical signs to the veterinarian.

Safety testing of this nature is likely to detect problems that occur with considerable frequency during the immediate postvaccination period; a vaccine with significant safety issues identified during safety testing is not likely to be licensed. However, the absence of problems during safety testing does not exclude the possibility that such issues will arise when the vaccine is used in a large number of animals in a clinical setting (ie, rare or subtle reactions or those that develop a long time after vaccination). Safety is never absolute; rather, it is a subjective balance between frequency and severity of adverse events and the benefits of disease reduction or prevention.

Several characteristics of vaccines are important in determining safety. Examples include the nature of the antigen (infectious vs noninfectious), the dose of antigens, the adjuvants, the number of vaccinal components, and extraneous materials (eg, fetal bovine serum, cell or medium components, or preservatives). With live agent vaccines, the minimum infectious dose is critical, whereas with killed agent products, the minimal immunizing dose of antigen is critical for effective immunization. Increasing the amount of antigen and extraneous materials, as is often necessary with killed agent vaccines, will more likely lead to adverse reactions. Although increasing the number of vaccine components in a single product may be more convenient for the practitioner or owner, the likelihood of adverse events may increase as more antigens are added to combination products. Also, interference among vaccine components can and will occur with certain combination products, although the efficacy of each component in the combination must be demonstrated to gain licensure.

Vaccine Labels

The set of rules under which a vaccine was developed influences the amount and type of information included on the label. When comparing vaccines, it is important to understand how the information presented on the label was obtained.

The label contains information about the disease that the vaccine is intended to prevent. If the disease produces many clinical syndromes, usually efficacy of the vaccine for only a single syndrome has been tested. Precisely which syndrome for which the vaccine was tested may not be stated on the label of older products, but the USDA now requires that specific disease syndromes be stated on the label of novel vaccines (ie, vaccines with an antigen or antigens not licensed prior to 1994).

Vaccine labels contain 1 of 3 common wordings describing the level of protection afforded by vaccination. The wording "...prevents infection with (certain microorganism)" may be placed on the label if data indicate that the product is able to prevent all colonization or replication of the challenge microorganisms in vaccinated and challenged animals. The wording "...indicated for the prevention of disease" normally

applies to vaccines that provide complete or partial protection from severe clinical signs of disease in most animals. The wording "...indicated as an aid in the prevention of disease" is found on vaccines for which results of efficacy testing indicate a significant difference between vaccinates and controls but not of the level required for the stronger wording. There are several reasons why a reduced level of efficacy may be observed: the vaccine may be less effective, the challenge exposure may have been less severe, or the disease the vaccine attempts to attenuate may cause only mild or subtle clinical signs. At any efficacy level, the manufacturer does not need to demonstrate that protection induced by the vaccine is clinically apparent or relevant to an individual animal or, in the case of the latter 2 levels, that use of the vaccine will reduce the prevalence of disease in a population. There is also no requirement that the label state how the vaccine is best used in a preventive medicine program.

Label directions usually reflect the way the vaccine was used during the required safety and efficacy testing. For example, the label may contain the following directions: "Administer intramuscularly a one-milliliter dose of vaccine. Repeat in two to three weeks. Annual revaccination is recommended." There is no requirement to demonstrate that both doses are necessary or that 2 to 3 weeks is the optimal revaccination interval, nor is there a requirement to indicate how to proceed if the second dose is administered more than 3 weeks after the first. The route of administration and dose volume indicated on the label should be carefully heeded because they were probably the only ones tested for safety and efficacy during the licensing process.

During the middle part of the last century, the paucity of data regarding the duration of protection induced by canine vaccines led experts to recommend annual administration as an attempt to ensure maintenance of protection from disease throughout the life of an animal and to maintain long-term population immunity. However, for most animal vaccines currently available, the CVB does not require manufacturers to provide observational data on the label to support the recommendation for annual revaccination. The USDA does require manufacturers introducing vaccines containing novel antigens to provide data indicating DOI claims stated on the product label, but there is no requirement to determine the maximal or optimal revaccination interval.

Vaccine labels often indicate the ages of animals to which the product may be administered. Age restrictions may exist for safety reasons, as a consequence of regulatory policy, or both. Unfortunately, there is no way for the reader of the label to know under which set of rules the vaccine was approved or why an age restriction is or is not indicated on the label. When in doubt, practitioners should consult with the vaccine manufacturer's technical support staff. Other than warning of the possibility of anaphylactic reactions, vaccine labels have historically provided little safety information. As is currently standard in the European Union, the CVB is beginning to require that manufacturers list vaccine-mediated events (eg, fever, lethargy, or swelling at the injection site) observed during safety testing, but this requirement only applies to newly approved products or to older products for which the manufacturer is submitting changes to the CVB. Currently, it is not possible for a reader to know why the label for 1 vaccine contains safety information not included on the label of a competitor's product. Consequently, labels of products that are nearly identical may list markedly different safety information; the converse is also true. Vaccine users can attempt to clarify the confusion by contacting the manufacturer's technical support staff.

Because of the confusion surrounding vaccine labeling and the desire for additional information, the CVB has indicated it is considering a comprehensive update to the labeling of biologics. The veterinary biologics industry and the AVMA Council on Biologics and Therapeutic Agents have had extensive discussion on labeling policy, which has been shared with CVB. If these revisions go forward, they will move through the formal notice and comment federal rule-making procedure.

Adverse Events and Adverse Event Reporting

Despite the admirable safety record of animal vaccines, adverse events do occur. They may be local or systemic; mild, severe, or even fatal; or peracute, acute, subacute, or chronic, and they may include vaccine-induced disease or failure to confer immunity. However, even when vaccination immediately precedes an adverse event, it may be difficult to determine with certainty whether the vaccine was responsible. There are many confounding factors that make it difficult to establish a cause-and-effect relationship between vaccination and subsequent illness or death (eg, simultaneous administration of more than 1 vaccine from the same or different manufacturers, concurrent administration of nonvaccine products, preexisting disease, or prior exposure to the organism and incubation of disease at the time of vaccination).

Calculating the rate of adverse events associated with a vaccine requires knowing both the number of such events and the number of vaccines administered during the same period. Because many adverse events go unreported, the calculated rate should be considered a minimum value; the actual rate is probably higher. Additionally, because the total number of doses administered is not known, caution must be exercised when evaluating the number of adverse events associated with a particular product. If the numbers of adverse events reported for 2 products are the same but 1 vaccine has 50% of the sales of the other, the rate of adverse events for the less popular product is actually double that for the more popular one. A reasonable alternative to the current system in the United States would be to report adverse events per 10,000 doses sold, similar to that in the United Kingdom.[15]

Although the reporting by practitioners of adverse events associated with vaccination is not mandatory, it is helpful for all vaccine users to assist in development of databases of adverse events. Plus, receiving reports of known or suspected adverse events is the only way manufacturers can obtain data necessary to evaluate

the safety and efficacy of their products in clinical settings. Suspected or known adverse events should be reported to the CVB and the manufacturer of the product (The US Pharmacopoeia no longer accepts reports of adverse events). Adverse events may be reported to the CVB electronically at the center's Web site,[197] by mailing or faxing a completed report form available on the Web site,[198] or by calling (800) 752–6255. If more than 1 manufacturers' product was used concurrently, all manufacturers should be contacted.

The CVB is currently in a rule-making procedure to alter how manufacturers of biologic products handle adverse events. Currently, manufacturers are required to maintain records of adverse events reported to them and make them available to CVB either during inspections or on request. Additionally, manufacturers are required to immediately notify CVB if they have information causing them to suspect problems affecting safety, efficacy, purity, or potency. The proposed rule provides regulatory definitions and would require manufacturers to periodically provide adverse event reports to CVB.[199] The final text may be altered on the basis of comments that were submitted. It is uncertain when the proposed rule will be finalized, as it has been pending since 2002.

In the European Union, member states are required to have an adverse reaction reporting scheme, similar to SARSS, which collates reports from veterinarians and the general public and from Marketing Authorization Holders. However, the development of such schemes in individual member states varies considerably. The European Medicines Evaluation Agency also operates a centralized European Union–wide system, including a Rapid Alert System.[15] In Canada, adverse events should be reported to the Canada Food Inspection Agency.[200]

Vaccine-associated sarcomas—Although regarded as rare (estimated to be approx 1 to 2 cases/10,000 vaccinated cats[201,202]), vaccine-associated sarcomas are arguably the most serious vaccine adverse events reported in cats. The Vaccine-Associated Feline Sarcoma Task Force was formed in 1996 to address the issue[203]; although no longer seeking funding or financially supporting research, The Task Force continues to provide information to cat owners and veterinarians. For more information about vaccine-associated sarcomas, the reader is referred to extensive reviews published elsewhere.[204-206]

The precise cause of vaccine-associated sarcomas is not currently known. Vaccine-associated sarcomas were recognized in 1991 following the introduction of an aluminum adjuvanted FeLV vaccine and the transition from modified-live rabies virus vaccines to adjuvanted killed rabies virus vaccines in the mid 1980s. In 1993, epidemiologic evidence of a causal association between vaccination with aluminum adjuvanted rabies virus and FeLV vaccines was established,[201] and authors of several studies[207-209] have implicated vaccine adjuvant-induced inflammation at the injection site as the inciting cause. Chronic inflammation and wound healing can contribute to oncogenesis in many mammalian species, and by some unknown mechanism, inflammation induced by leakage of lens material after trauma can lead to development of ocular sarcomas in cats.[210]

However, results of a multicenter case-control study[211] of risk factors did not support the hypothesis that specific brands or types of vaccine within antigen class increase or decrease the risk of vaccine-associated sarcoma formation. In that study, investigators did not find a higher average risk of sarcomas among cats that received adjuvanted vaccine brands, compared with nonadjuvanted ones (conditional on antigen class) but cautioned that the purportedly less inflammatory vaccines (eg, recombinant products) were not used frequently enough in the study population to allow claims of relative safety. A direct association between the presence or severity of postvaccinal inflammation and tumor risk has not specifically been established, but after taking all currently available evidence into consideration, the Advisory Panel suggests that veterinarians use less inflammatory products whenever possible; nonetheless, the subsequent impact of this practice on sarcoma risk is currently not known. Adjuvanted rabies vaccines appear to induce greater inflammation than do nonadjuvanted rabies vaccines,[i] and the same appears true for FeLV vaccines[i,j]; it is not known, however, if this is true for other vaccines (Table 2). Administering injectable vaccines in specific recommended sites on the body facilitates monitoring vaccine site reactions and managing sarcomas, should they develop (**Appendix 2**).

Vaccination in Shelters and Multiple-Cat Environments

In the United States, an animal shelter is generally understood to be a holding facility for homeless animals awaiting adoption, rescue, or reclamation by owners and may be either permanent or makeshift (eg, as may be necessitated by a large-scale disaster). Random-source populations of animals in which the vaccination status is not known, high resident turnover, and high levels of infectious disease risk characterize most shelters. A wide range of variation exists, however. Some shelters comprise stable populations; resident cats in such facilities (sometimes called sanctuaries) have little more disease risk than do cats living in private multiple-cat homes. Some shelters admit dozens or even hundreds of cats daily and may euthanize a high proportion of those admitted. Rescue and foster homes, breeding catteries, and pet shops fall somewhere along this spectrum. For the purpose of discussion, high-risk shelters are defined as those in which the prevalence of URD is moderate to high or in which there are occasional to frequent cases of panleukopenia.

The high likelihood of exposure to infectious disease in most shelters and the potentially devastating consequences of infection mandate a well-conceived vaccination program. Not only is it necessary to decide what vaccines are appropriate, but also when they should be administered with respect to shelter entry, which cats should be vaccinated, and how and by whom vaccines will be administered. How each cat should be housed and whether quarantine is required until vaccine-induced immunity has developed should be considered. Detailed vaccination records, including documentation of adverse events, should be main-

tained. Differences in vaccine costs become considerable when multiplied by thousands of doses. Therefore, only those antigens in which a clear benefit against common and serious shelter diseases is indicated should be used. Adopters should be encouraged to discuss an individually tailored vaccination program with their own veterinarian following adoption.

Core vaccines in shelter environments

Feline parvovirus, FHV-1, and FCV should be considered as core vaccines. All other vaccines should be considered as noncore or not generally recommended vaccines (**Table 3**).

Modified-live vs killed agent vaccines in shelter environments

In most cases and when available, modified-live agent products should be used. The greatest benefit of modified-live agent vaccines in shelter environments is rapid onset of protection, an important factor when exposure is likely to occur soon after admission. In addition, live agent vaccines are better able to overcome MDA in young kittens than are inactivated agent vaccines, thus helping to protect the most vulnerable and most adoptable shelter subpopulation.[24]

Modified-live agent vaccines for respiratory tract pathogens may cause mild clinical signs of disease, leading to vaccine-induced disease resulting in euthanasia. Fortunately, most shelters do not euthanize all cats with clinical signs of URD. However, even in shelters that must euthanize cats with clinical signs of URD (caused by natural infection or, erroneously, by vaccination), the overall rate of euthanasia may not be affected, as these shelters generally have overwhelming numbers of healthy, adoptable cats. The population may still benefit from decreased disease in adopted cats and, consequently, improved public perception and increased numbers of adoptions.

Intranasal vs injectable vaccination in shelters and other multiple-cat environments

In addition to inducing local immunity, IN vaccination for FHV-1/FCV has the advantage of a rapid onset of protection.[24,55] Results of 1 study[74] indicate that cats receiving 1 dose of FHV-1/FCV/FPV vaccine administered IN had significantly less severe clinical disease than unvaccinated control cats when challenged with virulent FHV-1 4 or 6 days after vaccination. Because of the likelihood of early viral exposure, FHV-1/FCV vaccines for IN administration may be advantageous in shelters and other environments with endemic infections. Such vaccines may cause mild clinical signs of disease, creating the same concerns for vaccine-induced disease resulting in euthanasia as previously described. However, results of 1 shelter study[67] indicate that there was no difference in the incidence of sneezing within 7 days after vaccination when cats were given vaccines administered via injection and IN, compared with those given a vaccine via injection only.

Timing of vaccinations

When possible, vaccination prior to shelter admission is ideal (eg, for owner-surrendered cats or for those returning from foster care). In almost all other cases, cats entering a shelter should be vaccinated immediately on admission. A delay of even 1 or 2 days compromises a vaccine's ability to induce protection.

It is increasingly common for shelters to hold cats for months or even years. Cats entering a long-term care facility (or any cat for which a long-term shelter stay is anticipated) should be vaccinated for rabies, depending on local regulations, as well as core vaccines at the time of admission. Noncore vaccines should be considered as for pets, depending on risk profile. In the event a cat resides in the facility for a sufficiently long period to justify booster vaccination, it is recommended that the same schedule for revaccination be followed as is recommended for pets. There is no indication for more frequent vaccination in a long-term shelter facility with a stable population.

Patient considerations

General health—Most kittens and cats should be vaccinated regardless of physical condition. If the cat's immune system is so weakened that a modified-live agent vaccine will induce disease, exposure to the wide variety of infectious pathogens present in most shelters will likely result in death of the cat. In general, if a cat cannot be safely vaccinated, it cannot safely remain in an animal shelter. Injured or ill cats should then be revaccinated when healthy (no earlier than 2 weeks later).

Kittens—Remaining in foster care in clean homes is preferable for kittens younger than 8 weeks of age. Interference from MDA and immature immune systems negatively impacts the ability of vaccines to induce a protective immune response, and kittens placed in shelters are at high risk of disease. If kittens younger than 8 weeks of age must be kept in shelters, they should be kept quarantined in areas isolated from the general population. In rare and unusual circumstances (eg, when challenge dose is high and exposure is not avoidable), FHV-1 and FCV vaccines may be administered IN or via injection to kittens younger than 6 weeks old. Additionally, some facilities may administer 1 or 2 drops of vaccine IN rather than administering the entire dose to each kitten. However, unless specifically stated on the label, manufacturers have not evaluated the safety and efficacy of these vaccines when used in this manner and such practices have not been independently evaluated. Vaccine-induced URD and other adverse events may be encountered, especially in kittens with little or no MDA. Nonetheless, in environments with endemic URD in which the risk of serious disease is high, the benefits of vaccinating in this manner may outweigh the risks.

Injectable or IN vaccination with a modified-live FPV vaccine may potentially cause cerebellar hypoplasia if given to kittens prior to 4 weeks of age.[51] Kittens in high-risk shelters should therefore be vaccinated with a modified-live FPV vaccine via injection no sooner than 4 weeks of age. Vaccination should be repeated every 2 to 4 weeks until 16 weeks of age. The shorter end of the intervaccination interval and early age of first vaccination are appropriate when infectious

Table 3—Summary of vaccination of cats in shelter environments.

Vaccine	Kittens (≤ 16 weeks old)	Adult and adolescent (> 16 weeks old)	Comments
Panleukopenia virus (FPV)	Administer a single dose at the time of admission as early as 4 to 6 weeks of age, then every 2 to 4 weeks until 16 weeks of age if still in the facility. The earlier recommended age (4 weeks) and short end of the interval (2 weeks) should be used in high-risk environments or during outbreaks.	Administer a single dose at the time of admission; repeat in 3 to 4 weeks (or at an interval of no less than 2 weeks) if still in the facility.[a]	Core • MLV preparations are preferable. • Usually administered in combination with modified-live FHV-1 and FCV vaccine. • Use of FPV vaccines for IN administration is generally not recommended in shelter environments.
FHV-1 and FCV	Administer a single dose at the time of admission and as early as 4 to 6 weeks of age, then every 2 to 4 weeks until 16 weeks of age if still in the facility. The earlier recommended age (4 weeks) and short end of the interval (2 weeks) should be used in high-risk environments or during outbreaks.	Administer a single dose at the time of admission; repeat in 3 to 4 weeks (or at an interval of no less than 2 weeks) if still in the facility.[a]	Core • Usually administered in combination with modified-live FPV vaccine except when bivalent FHV-1 and FCV combined vaccines for IN administration are chosen. • Use of MLV vaccines for IN administration may be preferable when rapid onset (48 hours) of immunity is important. • NOTE: Postvaccinal sneezing, more commonly seen following IN administration of vaccine, may be impossible to distinguish from active infection.
Rabies virus	If the shelter administers rabies virus vaccine, a single dose should be administered to kittens > 12 weeks of age at the time of discharge from the facility, and the adopters should be advised that a booster vaccination in 1 year is indicated. Long-term shelters or sanctuaries may consider vaccination against rabies at the time of admission.	If the shelter administers rabies virus vaccine, a single dose should be administered at the time of discharge from the facility, and the adopters should be advised that a booster vaccination in 1 year is indicated. Long-term shelters or sanctuaries may consider vaccination against rabies at the time of admission.	Recommended at discharge • Cats maintained in most indoor shelters are at low risk of infection; therefore, rabies virus vaccination is not generally recommended at the time of admission. • If rabies virus vaccine is administered, a single dose of either the recombinant or a 1-year rabies virus vaccine is recommended at the time of discharge; a booster is recommended 1 year later. • State or local statutes apply.
C felis	If used, administer the initial dose at the time of admission and as early as 9 weeks of age; a second dose is administered 3 to 4 weeks later if still in the facility.	If used, administer the initial dose at the time of admission; a second dose is administered 3 to 4 weeks later if still in the facility.	Noncore • Vaccination may be considered as part of a control regime in facilities in which disease caused by *C felis* infection has been confirmed.
B bronchiseptica	If used, administer a single dose IN at the time of admission.	If used, administer a single dose IN at the time of admission.	Noncore • Vaccination may be considered when cats are likely to be at specific risk of acquiring infection.[b] • NOTE: Postvaccinal sneezing or coughing can be impossible to distinguish from active infection.[c]
FeLV			Not generally recommended[d]
FIV			Not generally recommended
G lamblia			Not generally recommended
FIP (FCoV)			Not generally recommended

[a]If adult cats were ill or otherwise compromised at the time of initial vaccination, consider repeating the vaccine a single time when the cat is in good health (no sooner than 2 weeks after the initial vaccine). [b]For example, prior to confinement in environments where *B bronchiseptica* infection is confirmed by culture from an unusually high percentage of cats with URD, where dogs on the same premises have confirmed *B bronchiseptica*–induced kennel cough, or when characteristic bronchopneumonia is diagnosed by necropsy. [c]Vaccinated animals can shed *B bronchiseptica* for several weeks and, in some cases, up to a year after vaccination and may spread the organism to other cats and possibly other susceptible species. [d]In facilities where cats are group-housed, such as in some shelters and foster homes, FeLV vaccination is recommended; the protocol recommended for the general cat population should then be followed.

See Table 2 for remainder of key.

risk is high, such as during an outbreak or in a known contaminated environment.

Pregnant queens—Vaccination of pregnant queens against FPV, FHV-1, and FCV upon shelter admission is recommended in high-risk shelters. Use of modified-live agent vaccines in naïve queens (ie, those that have never been naturally exposed or vaccinated) during pregnancy has generally been discouraged because of concerns regarding adverse effects on developing fetuses; panleukopenia infection during pregnancy can cause abortion and fetal damage, and modified-live FPV vaccines may perhaps have similar effects.[51] Nonetheless, the likelihood of exposure to panleukopenia is extremely high in many shelters, and infection may result in the death of the queen as well as her offspring. Therefore, the risks posed by vaccination with modified-live agent vaccines must be weighed against the risks of not vaccinating (ie, maternal, fetal, or neonatal infection and death). When pregnant queens are being placed into shelters in which panleukopenia exposure is likely, the Advisory Panel believes the benefits of vaccinating with modified-live FPV vaccines outweigh the risks; otherwise, use of inactivated agent products is preferable.

In some cases, vaccination with FHV-1 and FCV vaccines during pregnancy may actually be beneficial for both queens and kittens. Vaccines given early in pregnancy will not only protect the queen, but may provide kittens with high concentrations of MDA to protect them during the first few weeks of life. Reduced morbidity rates and mortality rates from URD was detected in kittens born to queens vaccinated against FHV-1 and FCV during early pregnancy, compared with offspring of queens not vaccinated during pregnancy.[72] There was no increase in abortions or stillbirths associated with this practice.[69]

Previously vaccinated cats—There is no reason to administer vaccines at the time of shelter admission if clear documentation of previous vaccination is provided (**Appendix 3**). If such documentation is not available at the time of admission, vaccination is indicated.

Economic considerations

If financially feasible, vaccination of all cats that can be safely handled is ideal, but to limit cost, shelters may be tempted to vaccinate only those cats that are likely to be adopted. Although better than not vaccinating at all, this approach has several disadvantages: a high number of nonvaccinated, susceptible cats in the population may lead to overwhelming concentrations of infectious agents in the environment, unvaccinated cats reclaimed by their owners will be at risk of acquiring infectious disease and carrying it back into the community, and cats that do not appear to be adoptable at first (but become so after a period of time) will be at risk.

Vaccination of Cats in TNR Programs

Unowned feral cat populations exist worldwide and may approximate or exceed the population of owned pet cats in some locations. Because feral cats usually do not receive veterinary care, they constitute both a reservoir for infectious diseases and a population of cats at risk for illness caused by preventable diseases. There is increasing enthusiasm for controlling feral cat populations by large-scale TNR programs in which cats are trapped, spayed or neutered, and returned to their colonies. For most cats, the single visit to the TNR clinic will be the only veterinary care they receive throughout their lives.

For TNR programs to be effective in controlling cat populations, they must maximize the number of cats that are spayed or neutered. Because resources are often limited, these programs often take a "herd health" approach and prioritize their procedures for the best cost-to-benefit outcome. Sterilization is the single universal procedure performed among TNR programs, whereas testing for infectious diseases, vaccination, and aftercare are variable. In addition to costs associated with vaccinating feral cats, other considerations include uncertainty about what proportion of free-roaming cats are naïve to infectious diseases and would benefit from vaccination; whether administration of a single vaccine is beneficial; and whether cats can mount an adequate immune response when they are stressed by capture, transportation, anesthesia, and surgery.

Although adult cats have a degree of natural resistance to many infections, death attributable to FPV appears to be increasing in animal shelters, which may indicate a reemergence of this disease. With the exception of Australia, Great Britain, Japan, and some other islands, rabies is present worldwide. Depending on the location, the natural reservoirs for rabies virus are wildlife or dogs. Cats are occasional incidental victims of rabies and may constitute a link between the natural reservoirs and humans. These findings suggest that feral cats and public health could benefit from protection against these infectious diseases if feral cats are capable of responding to immunization.

In 1 study,[e] 61 feral cats admitted to a large-scale TNR clinic were administered a 3-year rabies virus vaccine and a modified-live or inactivated FPV/FHV-1/FCV vaccine by SC injection during anesthesia following spaying or neutering. Blood for serum was collected prior to vaccination and then again 2 to 3 months later. Before vaccination, the proportion of cats with protective titers against FPV, FCV, FHV-1, and rabies virus was 33%, 64%, 21%, and 3%, respectively, whereas after vaccination, the proportion of cats with protective titers against FPV, FCV, FHV-1, and rabies virus was 90%, 93%, 56%, and 98%, respectively. There was no difference in proportions of cats with protective titers relative to vaccine type; however, median titers were significantly higher for FPV in cats receiving the MLV vaccine and for FHV-1 in cats receiving the inactivated virus vaccine.[J] In that study, feral cats had a robust serologic response to immunization, indicating that they were capable of responding to a single set of vaccines administered during the stressful conditions of a TNR clinic. Because serologic response to FeLV vaccination is not predictive of immunity, it is not known whether administration of a single dose of FeLV vaccine is of sufficient benefit to warrant its use.

Rabies virus vaccines labeled for 3-year duration of immunity should be administered to all feral cats undergoing sterilization in areas endemic for rabies. Vaccination of all feral cats against FPV, FHV-1, and FCV with MLV vaccines at the time of sterilization is also highly recommended. An ear should be tipped in compliance with the universally accepted method of identifying sterilized feral cats. An attempt should be made to retrap cats for administration of booster rabies virus vaccines at 1 year and every 3 years thereafter. Booster vaccines for FPV, FHV-1, and FCV may also be administered at that time, but the need to boost these antigens in adult free-roaming cats is less clear.

Vaccination for Kitten Socialization Classes

Socialization and training classes for kittens give clients realistic expectations of living with a cat, teach them how to train their cat and make their home cat-friendly, and thus help prevent medical and behavior problems. Behavior problems may lead to destruction of the human-animal bond, mistreatment, relinquishment, and euthanasia.

Classes are open only to kittens 7 to 14 weeks old, the sensitive period of socialization, and usually consist of 2 to 3 sessions.[212] Class size should be limited to 3 to 8 kittens. Because most kittens are not old enough to have received their complete set of kitten vaccinations, kittens should receive at least 1 FPV, FHV-1, and FCV vaccine a minimum of 10 days prior to the first class.

If these vaccination recommendations are followed and all kittens are healthy, the Advisory Panel believes it is unlikely that infection will be acquired during socialization classes. However, infectious agents of kittens can be shed prior to the development of clinical signs of disease, and not all infections are preventable by vaccination. Thus, owners should be warned of the potential for their kitten to acquire an infectious disease, regardless of the kitten's vaccination status. Owners should be encouraged to attend classes alone if their kittens harbor infectious disease.

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Appendix 1

Certificate of Exemption from Rabies Vaccination

Owner Name _____ Tel. No.: _____
First Last

Address: _____
Street City State Zip

Animal Name: _____ Species: _____ Breed: _____ Sex: ☐M ☐F

Age: _____ Weight: _____ Colors: _____ Neutered: Yes ☐ No ☐

The animal described above has been examined by me and determined to be exempt from the New York State law requiring rabies vaccination because to do so would endanger the life of the animal.

Describe nature and duration of health risk:

Veterinarian's Signature: _____ License #: _____

Printed Name: _____

Address: _____
Street City State Zip

By signing below, I acknowledge that I am the owner of the animal described above. I have been informed that this animal is exempt from rabies vaccination for a period of up to one year, and also that I have been informed of the following important information:

- This animal must be re-examined by the expiration date listed above. At that time the animal must either be vaccinated against rabies or, if exemption status still applies, a new certificate must be issued.
- This animal is not protected against rabies, and as a result is at increased risk of becoming infected if exposed to a rabid animal.
- Under State law, unvaccinated dogs, cats or domesticated ferrets cannot be at large. At large means anywhere other than on the premises of the owner or of another person with that person's knowledge and consent.
- Unvaccinated horses, cattle, sheep and goats are not permitted at fairs or other animal exhibitions in New York State.
- Exemption from rabies vaccination does not exempt the animal from other NYS laws related to rabies. If this animal potentially exposes a person to rabies (by bite or other means), it must be confined for 10 days in a facility approved by the county health department where the exposure occurred. If this animal is potentially exposed to rabies (e.g., due to a bite from an unknown animal), the county health department may require it to be quarantined for six months.

Owner's Signature: _____ Date signed: _____

A copy of this certificate must be provided to the owner of the animal listed above and kept as proof of exemption. For dogs, this certificate must be presented with an application for a dog license.

Appendices continued on next page.

Appendix 2

Injectable vaccination site recommendations

Vaccines designed to be given by injection should be administered by the SC route. Intramuscular administration does not mitigate the risk of vaccine-associated sarcoma formation and may delay detection, should a mass develop.

To facilitate management of vaccine-associated sarcomas, to avoid multiple injectable vaccinations at single sites (a putative risk factor for sarcoma formation[201]), and to aid in documenting vaccine placement, the following injection sites are recommended:

- Injectable vaccines containing antigens limited to FPV, FHV-1, and FCV (with or without *Chlamydophila felis*) should be administered SC on the lateral side of the right forelimb below the elbow joint.
- Injectable vaccines containing *Giardia lamblia* antigen should be administered SC on the lateral side of the left forelimb below the elbow joint.
- Injectable vaccines containing rabies virus antigen (plus any other antigen) should be administered SC on the lateral side of the right hind limb below the stifle joint (vaccine-associated sarcomas arising in the proximal femoral area are difficult to completely excise; thus, placement of vaccines in this area is strongly discouraged).
- Injectable vaccines containing FeLV or FIV antigen (plus any other antigen except rabies) should be administered SC on the lateral side of the left hind limb below the stifle joint (vaccine-associated sarcomas arising in the proximal femoral area are difficult to completely excise; placement of vaccines in this area is strongly discouraged).
- Injection sites of other medications should be recorded.

Monitoring of postvaccination masses

Encourage clients to monitor vaccination sites and to contact their veterinarian if a mass is detected. Biopsy the mass (incisional or wedge biopsy or multiple cores with a Tru-Cut–type device) if any of the following criteria are met (the 3-2-1 rule):

- the mass is present 3 months after vaccination.
- the mass is $\geq$ 2 cm in diameter.
- the mass is increasing in size after 1 month.

Appendix 3

Vaccination documentation

Good documentation is required for health certificates and facilitates investigation of suspected adverse reactions or vaccine failure. If people other than the veterinarian writing the record administer vaccines (such as in some shelters), documentation is important in case training and compliance issues lead to vaccine failure. The cat's cage card or computer record may serve the purpose of a medical record in an animal shelter, depending on state and local regulations. Document the following clearly in the medical record:

- Proprietary name of product
- Manufacturer
- Serial/lot No. and expiration date
- Date administered
- Vaccine type
- Location on the cat's body
- Person administering the vaccination

Appendix 4

Vaccine handling and storage

- Lyophilized vaccine, once reconstituted, should be administered within 30 minutes. Reconstituted vaccine must never be frozen prior to administration, nor stored for use at a later time.
- Heat, excessive cold, and exposure to light can render vaccines ineffective.
- Vaccines should arrive cold from the manufacturer and be refrigerated immediately.
- Vaccines should be stored in a middle compartment of the refrigerator. Avoid storing in the door and near the freezer compartment. Avoid the use of refrigerators with open freezer compartments.
- Excessive cold can alter the vaccine by uncoupling antigen-adjuvant complexes.
  - Uncoupled adjuvant may collect at the bottom of a multidose vial, causing pain and local injection reaction.
  - Uncoupling of the antigen-adjuvant complex may reduce the efficacy of the vaccine.
- Keep a thermometer in the refrigerator to ensure the temperature is between 2° to 7°C (35° to 45°F) at all times.
  - Make sure refrigerator doors close and latch securely.
  - Place a sign by the refrigerator plug stating, "Do not unplug."
  - In case of a power failure, keep refrigerator door closed and note temperature when power is restored.

Appendix 5

Vaccine preparation

- Always follow manufacturer's guidelines for preparing vaccines.
- Use appropriately sized syringes and needles to prepare and administer the vaccine.
- Use only 1 vaccine per single-use syringe and needle.
- Use only the diluent provided by the manufacturer.
- Completely dissolve reconstituted vaccines before drawing into syringe.
- Mix the vaccine with the diluent immediately prior to administration.
- Vaccines may be warmed to room temperature (approx 18.3° to 23.9°C [65° to 75°F]) before injection, but use is recommended within 30 minutes following reconstitution.
- If an injectable vaccine is spilled, clean vaccine off animal's fur with alcohol swabs. Use standard 5% chlorine bleach diluted at 1:32 in water (or another disinfectant proven effective against FPV and FCV) for contaminated surfaces.

Appendix 6

Vaccine administration tips

- All vaccines should be administered by the route designated by the manufacturer. If a vaccine is accidentally given by an inappropriate route, the vaccine manufacturer should be contacted for specific recommendations.
- Modified-live respiratory virus vaccines intended for SC administration may cause serious URD if administered IN or if a cat makes oral contact with the vaccine.[100]
- Do not split vaccine doses (ie, 1 dose divided among several cats) unless such use is specifically permissible by the manufacturer.
- Cats can usually be vaccinated single-handedly by use of little or no restraint; at most, 1 other person may be needed to help hold and distract the cat.
- Administering a vaccine over a limb can often be done while someone calmly distracts the cat. If the cat is tense, place it on its side and lay the palm of the hand not administering the vaccine medial to the stifle or elbow joint. This painlessly prevents the cat from jerking the limb away.
- Minimizing the number of people handling the cat minimizes stressing the cat; even fearful cats can be vaccinated with minimal stress when handled gently in a calm and quiet environment.
- Unusual noises, smells, visual cues, and handling can be stressful to cats; a quiet environment with people talking in soft and calm voices decreases auditory stimuli.
- To decrease visual stimuli and prevent what an anxious cat may perceive as threatening, never approach from the front or make direct eye contact.
- Most cats can be safely handled when approached from behind. Using a towel as protection if necessary, gently move the cat's body toward you, with its hind quarters against the crook of the arm. Most cats respond favorably to slow and gentle massage around the chin and neck. For extremely anxious cats, restrict massage to the top of the head and neck.
- Some cats, especially young cats, can be distracted completely with treats while vaccines are administered. Ask the client to bring favorite treats and withhold food for 6 hours prior to the visit to increase appetite.
- When vaccines are administered, consider distracting the cat with toys. Ask the client to bring some of the pet's favorite toys, combs, or brushes to the hospital to help the cat feel more comfortable.
- Always reward good behavior with treats and praise immediately following vaccination. Never punish or heavily restrain a cat; ignore negative behavior while calmly proceeding with your procedure.
- For IN administration of vaccines, it's best to approach from behind or attempt to distract an anxious cat. Administer the vaccine by gently tipping the muzzle upward and placing a drop in each nostril. Allow the cat's mouth to remain open so breathing is not impeded. If the cat is alarmed to see hands moving towards its face, gently cover the eyes with the same hand tipping the muzzle upward.
- The sound of the currently available transdermal administration device can alarm some cats. Speak calmly and consider distracting the cat with toys or treats to reduce anxiety related to the noise. Make clients aware of the pop sound prior to administration of the vaccine so they, too, don't startle and alarm the cat. Use of this administration system requires careful adherence to manufacturer instructions.
- More information on patient handling can be found in the Feline Behavior Guidelines from the AAFP.[213]