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2024 guidelines for the vaccination of dogs and cats – compiled by the Vaccination Guidelines Group (VGG) of the World Small Animal Veterinary Association (WSAVA)

AUTHORS:

R. A. Squires *[,1], C. Crawford[†], M. Marcondes[‡] and N. Whitley[§]

*Formerly, Discipline of Veterinary Science, James Cook University, Townsville, QLD 4814, Australia
[†]College of Veterinary Medicine, University of Florida, 2015 SW 16th Avenue, Gainesville, FL 32608, USA
[‡]Department of Clinical Medicine, Surgery and Animal Reproduction, São Paulo State University, Rua Sergipe 575, ap. 32, São Paulo, 01243-001, SP, Brazil
[§]Internal Medicine, Davies Veterinary Specialists, Manor Farm Business Park, Higham Gobion, Hertfordshire, SG5 3HR, UK
[1]Corresponding author email: r.a.squires@hotmail.com

[Correction added on 23 August 2024, after first online publication: The copyright line was changed.]

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EXECUTIVE SUMMARY

The World Small Animal Veterinary Association (WSAVA) Vaccination Guidelines Group (VGG) was convened to develop guidelines for the vaccination of dogs and cats intended to be helpful to veterinarians globally. Previous guidelines, published in 2007, 2010 and 2016, have been cited in the peer-reviewed scientific literature several hundred times and downloaded tens of thousands of times. The present document is an updated version of these guidelines. The VGG recognises that its recommendations must be broad and based on fundamental immunological principles because detailed recommendations about vaccines and vaccination of dogs and cats that might be suitable for some countries or regions may be much less applicable elsewhere.

Guidelines are intended to provide broad guidance for veterinarians in decision-making. They do not describe mandatory or minimum standards of care. These guidelines can be used by national and regional veterinary associations and individual veterinarians or veterinary practices to develop their own vaccination schedules suitable to their own local conditions. Notwithstanding this, the VGG strongly recommends that ALL dogs and cats should receive the benefit of vaccination. This will not only protect individual animals but will improve "herd immunity" to help minimise the risk of contagious disease outbreaks.

With this background in mind, the VGG has defined *core vaccines* as those that ALL dogs and cats should receive, after considering their lifestyle and the geographical areas in which they live or to which they travel. Some core vaccines protect animals from potentially life-threatening diseases that have global distribution while others protect against life-threatening diseases that are prevalent only in particular countries or regions. Core vaccines for dogs *in all parts of the world* are those that protect against canine distemper virus (CDV), canine adenovirus type 1 (CAV) and canine parvovirus type 2 (CPV). Core vaccines for cats in all parts of the world are those that protect against feline parvovirus (FPV), feline calicivirus (FCV) and feline herpesvirus-1 (FHV). In areas of the world where rabies is endemic, vaccination against rabies virus should be considered essential for both dogs and cats (*i.e.* rabies vaccines are *core* in those places), even if there is no legal requirement for this. Leptospirosis in dogs is another life-threatening, zoonotic disease that is widely distributed around the world. In countries or regions where canine leptospirosis is endemic, where implicated serogroups are known and where suitable vaccines are available, vaccination of all dogs against leptospirosis is highly recommended and the vaccines should be considered *core* in those places. In many parts of the world, feline leukaemia virus (FeLV)-related diseases are endemic. In these places, FeLV vaccines should be considered *core* for young cats (<1 year of age) and for adult cats with outdoor access or that live with other cats that have outdoor access.

The VGG recognises that maternally derived antibodies (MDAs) interfere substantially with the efficacy of most currently available core vaccines that are administered to puppies and kittens early in life (protecting against CDV, CAV and CPV in puppies, FPV, FCV and FHV in kittens). As the level of MDA varies substantially within and between litters, VGG recommends the administration of multiple core vaccine doses to puppies and kittens, every 2 to 4 weeks, with the final dose being delivered at 16 weeks of age or older. In situations where a puppy or kitten can only receive a single vaccination (*e.g.* in the case of cost constraints), vaccination should be with the core vaccines at 16+ weeks of age. Revaccination at or after 26 weeks of age (rather than waiting until 12 to 16 months of age) is advised to immunise without unnecessary delay the minority of animals that may still have had interfering MDA present at the time of their 16+ week vaccination.

The VGG supports the use of serological testing from 20 weeks of age onwards to detect seroconversion (to CDV, CAV and CPV in dogs and FPV in cats) following vaccination. This can help confirm active immune protection in young and young adult animals, help optimise revaccination intervals in mature adult animals, and in some situations, can help in the management of contagious disease outbreaks in shelters.

Vaccines should not be given needlessly. Core vaccines should not be given any more frequently than necessary in adult animals. There is an abundance of peer-reviewed, published evidence showing that the duration of immunity (DOI) provided by most, modern, modified live virus (MLV) core vaccines is many years.

The VGG has defined *non-core vaccines* as those that should be highly recommended in animals whose geographical location and/or lifestyle (*e.g.* indoor-outdoor access, multi-pet household) places them at risk of contracting particular infections not designated as core. A careful conversation between veterinarian and owner is needed to inform the decision about which non-core vaccines to recommend for each patient. The VGG has classified some vaccines as *not recommended* where there is insufficient scientific evidence to justify recommending their use anywhere. The VGG has not considered a few "minor" vaccine products that have very restricted geographical availability or applicability.

The VGG strongly encourages veterinarians to educate their clients about the value of regular health checks (usually annual, sometimes more often) as opposed to speaking of "vaccination consultations." The annual health check is much more than just a vaccination consultation, although it will often include administration of selected vaccines that need to be administered annually. The DOI provided by most non-core vaccines is about 1 year.

Veterinarians are also encouraged to undergo training intended to improve the experience of pets, owners and veterinary staff before and during pet health check visits. The Free Fear training programme (https://fearfreepets.com/fear-free-certification-overview/) and the Cat Friendly Certificate programme (https://catvets.com/cfp/cat-friendly-certificate-program/) are examples.

The VGG has considered the use of vaccines in shelters and sanctuaries, again recognising the financial constraints under which some of these facilities operate. The VGG minimum shelter guidelines state that all dogs and cats entering such establishments should be vaccinated before, or at the time of their entry, with the core MLV vaccines. Where finances permit, these

vaccines should be administered every 2 to 3 weeks starting at 4 weeks of age and continuing until 5 months of age. Vaccines against respiratory disease are considered non-core for pet dogs living in typical homes but should be considered core for shelter-housed dogs.

The VGG recognises the importance of adverse reaction reporting schemes but understands that these are variably developed in different countries. Veterinarians are strongly encouraged to report all possible adverse events to the manufacturer and to the regulatory authority to expand the knowledge base that drives development of improved, safer vaccines.

The most fundamental concepts proposed by VGG are captured in the following brief statement:

> We should aim to vaccinate every dog and cat with the core vaccines.
> Selected non-core vaccines may be recommended after careful consideration of each pet's lifestyle and local prevalence of vaccine-manageable diseases.
> Core and non-core vaccines should be stored and administered correctly, and used only as frequently as necessary to provide lifelong protection against the diseases that threaten our dogs and cats, wherever they live or travel.

INTRODUCTION

The WSAVA VGG was convened in 2006 to develop guidelines for the vaccination of dogs and cats intended to be helpful to veterinarians globally. Previous guidelines were published in 2007 (Day, Horzinek & Schultz 2007a), 2010 (Day et al., 2010) and 2016 (Day et al., 2016). Previous versions of the guidelines have been cited in the peer-reviewed scientific literature several hundred times and downloaded from publishers' websites tens of thousands of times. The present document is an updated version of the guidelines. The VGG recognises that, given its ambition to produce guidelines with global applicability, its recommendations must be broad and based on fundamental immunological principles. Detailed recommendations about vaccines and vaccination of dogs and cats that might be suitable for some regions may be much less applicable elsewhere. In some countries where excellent national or regional vaccination guidelines have already been published these WSAVA guidelines may be less pertinent than what is already available. For example, guidelines have been authored for Israeli veterinarians that deal with vaccination of both dogs (Harrus, 2020) and cats (Baneth, 2020) in that country. Guidelines for the vaccination of dogs are available for Sri Lankan veterinary practitioners (Silva, 2016). The American Animal Hospital Association (AAHA) and the American Association of Feline Practitioners (AAFP) have produced feline vaccination guidelines particularly relevant to North America (Stone et al., 2020). AAHA has also produced canine vaccination guidelines particularly relevant to North America (Ellis et al., 2022). The Advisory Board on Cat Diseases (ABCD) has produced feline vaccination guidelines most pertinent to Europe (ABCD, 2020a, 2020b, 2022; Hosie et al., 2015).

A key feature of these and other guidelines is the categorisation of vaccines as core, non-core or not recommended. In this latest version of the guidelines, the definition of core vaccines has been adjusted slightly to avoid self-contradictions and to improve clarity. This has also resulted in recategorisation of some vaccines. *Core vaccines* are those that ALL dogs and cats should receive, after considering their lifestyle and the geographical locations where they live or to which they travel. Core vaccines for dogs *in all countries of the world* are those that protect against CDV, CAV and CPV variants. Core vaccines for cats in all countries of the world are those that protect against FPV, FCV and FHV. For both cats and dogs, rabies virus vaccines should be considered core in all countries or regions where the disease is endemic.

Leptospirosis in dogs is another life-threatening, zoonotic disease that is widely distributed around the world. Vaccines to protect dogs against leptospirosis were categorised as non-core in previous versions of these guidelines. In countries or regions where canine leptospirosis occurs, where implicated serogroups are known and where suitable vaccines are available, vaccination of all dogs against leptospirosis is highly recommended and the vaccines should be considered core in those places. Feline leukaemia virus (FeLV) remains an important cause of morbidity and mortality in cats in many but not all parts of the world. In places where FeLV is prevalent or remains of concern, FeLV vaccines should be considered core in cats less than 1 year of age and in adult cats that have outdoor access or live with other cats that have outdoor access.

Non-core vaccines are highly recommended only for those animals whose geographical location and/or lifestyle (*e.g.* indoor-outdoor access, multi-pet household) place them at risk of contracting specific infections not designated as core. *Not recommended vaccines* are those for which there is insufficient scientific evidence to justify recommending their use anywhere.

The basic structure of this latest revision of the guidelines is similar to that in the most recent previous version (Day et al., 2016). However, this document has been extensively updated and includes numerous new reference citations.

Specific changes in the current document include:

1. A revised definition of "core" vaccines with an explanation as to why this change was considered helpful.
2. A new section dealing specifically with MDA.
3. A renewed section on current and emerging topics in canine and feline clinical vaccinology.
4. An updated section on "types of vaccine."
5. A rewritten section on "vaccines in shelters and sanctuaries."

6. Deletion of the previously included section on "passive immunisation" so as to sharpen focus on prophylactic vaccines.
7. Inclusion of many new references and removal of some older references.
8. Discontinuation of the use of evidence base (EB) notations EB1 to EB4 throughout the guidelines (Day et al., 2016). EB2 evidence previously referred to unpublished, commercially sensitive studies submitted as part of regulatory packages for licensing veterinary vaccines. EB3 evidence referred to similar studies not submitted as part of regulatory packages. Very few EB2 and EB3 reference sources have ever been cited in previous iterations of these WSAVA guidelines.
9. Further discussion of the recommendation to vaccinate puppies and kittens with selected core vaccines at 26+ weeks of age rather than waiting until 12 to 16 months of age.
10. Inclusion of some information about vaccines released since the last version of these guidelines was written.
11. Further consideration of anatomical sites for vaccination of cats.
12. A new list of frequently asked questions (FAQs).

THE PURPOSE OF WSAVA VACCINATION GUIDELINES

These guidelines are intended to provide national small animal veterinary associations, veterinary practices and individual veterinarians with broad, up-to-date, scientifically supported advice about vaccination of dogs and cats. They offer strong advice in some areas but are not a set of rules. It would be impossible to produce a useful set of guiding rules that could apply to the more than 100 member associations in as many countries, and to the more than 200,000 individual veterinarians who comprise WSAVA. Across the WSAVA member associations, there are vast differences between countries and geographical regions in terms of infectious disease prevalence, how much is known about disease prevalence, vaccine products available, size of owned *versus* free-roaming dog and cat populations, practice and client economics and societal attitudes towards pets. A vaccine known by veterinarians to be crucially important in one country or region might justifiably be considered unhelpful and unnecessary elsewhere. Alternatively, it might simply be unavailable. It is up to national associations, local academic leaders and individual veterinarians to read, discuss and adapt these broad guidelines, in the context of local infectious disease prevalence and other factors, for their own member veterinarians and practices. In some countries and regions, this has already been done in recent years.

Practitioners are sometimes concerned that some guidelines recommendations run contrary to information in the product leaflet or datasheet (termed the "Summary of Product Characteristics" [SPC] in Europe). Some therefore worry that if they adopt guidelines recommendations, for example if they revaccinate adult animals less frequently than suggested in the product leaflet, or if they give additional doses of vaccine to animals between 12 and 20 weeks of age, they may leave themselves open to serious criticism. This is not generally the case (Thiry & Horzinek, 2007); however, practitioners should ensure they remain up to date about any local or national regulations that may impede them from following guidelines. If such regulations run contrary to guidelines based on current scientific evidence and understanding, local or national veterinary organisations could consider lobbying authorities with the aim of having the regulations amended.

The product leaflet/data sheet/SPC is a legal document that forms part of the registration package for a vaccine. This document provides details about the safety and efficacy of the product and states the *minimum* DOI that can be expected after proper vaccination. Guidelines are based on all available evidence about DOI induced by vaccines for dogs and cats, not just on the minimum DOI data generated by manufacturers. Guidelines may therefore recommend triennial or less frequent revaccination with core vaccine products that may still carry a 1-year DOI claim in some countries. Although guidelines advice sometimes differs from information in the product leaflet, veterinarians can generally use a vaccine according to guidelines (and therefore current scientific thinking) by obtaining informed owner consent for this deviation from product leaflet recommendations ("off-label use"). Documentation of the informed consent in the medical record is advisable. A possible, rare exception would be countries where veterinarians might be compelled by government regulations to comply with label recommendations. Knowledge of any local regulations limiting veterinarians' freedom to deviate from product leaflet instructions is therefore important. Veterinarians should also bear in mind that company representatives will generally continue to advise that the veterinarian adheres to the instructions provided in their leaflets. They are required to do this, sometimes by law, even if they would prefer to support guidelines' recommendations.

These guidelines are based on published, peer-reviewed evidence wherever possible, but also, unavoidably, on unpublished or non-peer-reviewed scientific evidence and on expert opinions. Given the remarkable breadth of material to be covered in a single document, a narrative review format has once again been adopted as the only one suitable to the task (Baethge et al., 2019). The same format has been chosen by all other international companion animal vaccination guidelines authoring teams (Ellis et al., 2022; Hosie et al., 2015; Stone et al., 2020). Use of a systematic review format or a formal, structured approach to reach consensus recommendations based on the Delphi process, was considered by the VGG when planning this update (Gattrell et al., 2022). These approaches were quickly deemed inapplicable given the breadth of material intended to be covered in a single document and the size of the authoring team. Nevertheless, these recommendations are based on the strongest scientific evidence that was found.

This document aims to address current issues in canine and feline vaccinology and to suggest practical steps that will help veterinarians and veterinary organisations to enhance their rational use of vaccines in these species. The most important messages of the VGG are captured in the following, brief statement:

> We should aim to vaccinate every dog and cat with the core vaccines.
> Selected non-core vaccines may be recommended after careful consideration of each pet's lifestyle and local prevalence of vaccine-manageable diseases.
> Core and non-core vaccines should be stored and administered correctly, and used only as frequently as necessary to provide lifelong protection against the diseases that threaten dogs and cats, wherever they live or travel.

VACCINES AS PART OF COMPREHENSIVE PREVENTATIVE HEALTH CARE

Regular assessment of vaccination needs is just one component of a comprehensive lifetime health care plan. Individualised patient care requires regular (usually annual) health checks, with the preventative health care plan designed around the age, breed, lifestyle, environment and travel activities of the pet and owner. Discussion of vaccination is one important part of such a visit, alongside consideration of ecto- and endoparasite detection, treatment and prevention, vector-borne and zoonotic disease prevention, dental care, nutritional advice, behavioural assessment and advice, and the necessity for any more frequent, tailored examinations of the pet.

In adult animals, decisions about revaccination with some of the core products (protecting against CDV, CAV and CPV in dogs and FPV in cats) can be informed by serological testing (Burr, 2006). Some practitioners who offer this alternative to vaccination report that it is greatly appreciated by some owners (Killey et al., 2018). This will be discussed in more detail in a later section.

There is little evidence that aged dogs and cats that have been vaccinated according to these guidelines throughout life require a specialised or enhanced programme of core revaccination late in life (Day, 2010; Horzinek, 2010; Schultz et al., 2010). There is evidence that most aged dogs and cats have persisting immunological memory to core MLV vaccines (Dall'Ara et al., 2023; Day, 2010; HogenEsch et al., 2004; Schultz et al., 2010), with defence rapidly regained after administration of a single vaccine dose (Mouzin et al., 2004a, 2004b). By contrast, aged animals may not be so effective at mounting *primary* immune responses to novel agents or antigens that they have not previously encountered (Day, 2010). In one recent study (Dall'Ara et al., 2023) geriatric dogs vaccinated >3 years earlier were less likely to have protective antibody titres against CDV and CAV than geriatric dogs vaccinated 1 to 3 years earlier. Serological responses of these geriatric dogs to revaccination were not studied. Nevertheless, on the basis of these findings, revaccination of aged pets triennially or perhaps more frequently can be recommended.

Studies of UK dogs and cats vaccinated for the first time against rabies for pet travel have shown clearly that many aged animals fail to achieve the legally required antibody titre (Kennedy et al., 2007; Mansfield et al., 2004). Younger animals were more likely to be successfully immunised.

Medical records documentation

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

- Date of vaccine administration;
- Identity (name, initials or code) of the person administering the vaccine;
- Vaccine name, lot or serial number, expiry date and manufacturer;
- Anatomical site and route of vaccine administration.

The use of peel-off vaccine labels and stamps that imprint the medical record with the outline of a pet facilitate this type of record-keeping, which is mandatory in some countries.

Any adverse events should be recorded in a manner that will alert all staff members during future visits. Informed consent should be documented in the medical record in order to demonstrate that relevant information was provided to the client and that the client authorised the procedure (*e.g.* for "off-label" use of vaccines as discussed above). At the very least, this notation should indicate that a discussion of risks and benefits took place before vaccination.

The VGG recommends that vaccination certificates be designed to include not just the dates on which vaccines were administered, but also a field for the veterinarian to state how long into the future the animal is expected to be protected by vaccination. This will help diminish confusion in the minds of pet owners and kennel/cattery proprietors.

DIFFERENT TYPES OF VACCINE

New kinds of vaccine have been developed and marketed since the last WSAVA vaccination guidelines were published (Day et al., 2016). However, globally, the well-established vaccine types remain predominant and important, especially modified live and inactivated kinds.

Modified live or live attenuated vaccines contain live but attenuated (*i.e.* weakened) whole viruses or bacterial organisms that can attach to cells, infect them and replicate within them, establishing a low-level and transient infection that engenders a strong immune response, without causing overt disease. Modified live vaccines are generally more immunogenic than most other kinds. Many MLV vaccines are particularly potent. They typically require fewer doses to achieve a strong immune response. Some modified live vaccines generate a consistent and long-lasting immune response (for many years) after a single dose, when administered to an animal in the absence of MDA interference. MLV vaccines have the advantage of more effectively inducing immunity at relevant anatomical sites when administered parenterally (usually subcutaneously) and are more likely than most other kinds to induce robust cellular as well as humoral (antibody-mediated) immunity. Some modified live vaccines are administered directly to mucosal sites (*e.g.* intranasal or oral vaccines) where they induce local, protective mucosal immunity.

Inactivated (or killed) vaccines contain entire, inactivated, antigenically complete microorganisms that are not able to infect or replicate, but are able to stimulate an immune response. As they do not mimic a natural infection, they usually produce less potent immune responses, may not produce adequate mucosal or cellular immunity, and generally require multiple doses and an adjuvant to stimulate an adequate immune response. However, some inactivated vaccines are unusually potent, for example killed rabies virus vaccines. Some of these are highly immunogenic and can induce long-lasting protection after a single dose. Seroconversion of kittens after a single dose of inactivated vaccine has also been shown for FHV and FPV vaccines in kittens (Lappin, 2012). In a subsequent FHV challenge study (Summers et al., 2017), an inactivated vaccine provided similar protection to a MLV vaccine after challenge on day 7 after vaccination.

However, most inactivated vaccines are thought to require at least two initial doses to immunise, regardless of the animal's age. The first dose generally primes the immune response and the second (and sometimes a third) dose, usually administered 2 to 4 weeks apart, provides the protective immune response. A full protective immune response may not develop until 2 weeks after the second or final dose is given. Inactivated vaccines usually engender a shorter DOI when compared to MLV vaccines, and more frequent revaccination (*i.e.* boosting) is needed to maintain protection.

Subunit vaccines consist of antigenic sub-components of pathogenic microorganisms that have been extracted and purified from cultures or have been synthesised using recombinant DNA technology (*i.e.* gene splicing and protein expression). These vaccines tend to be less immunogenic than MLV vaccines, so usually contain an adjuvant and engender a shorter DOI, like most inactivated vaccines. There are subunit vaccines for Lyme disease (Eschner & Mugnai, 2015; Grosenbaugh et al., 2018) and more recently for *Bordetella bronchiseptica* (containing fimbrial antigens), marketed for use in dogs (HPRA, 2024; MSD Animal Health, 2024).

Recombinant DNA technology has recently been used to produce a *novel live recombinant vaccine* against CPV (Pearce et al., 2023). The novel CPV component is combined with a more conventional MLV CDV component (European Medicines Agency, 2021). This vaccine is intended to protect puppies against CPV infection at a very young age (4 weeks) by breaking through MDA interference more effectively than previous generation vaccines. This vaccine contains a recombinant, chimaeric parvoviral genome, part CPV-2c and part CPV-2. During manufacture, the recombinant genome is used to produce live parvovirus that can infect cells and multiply in vaccinated puppies, just like a conventionally manufactured live attenuated vaccine.

Vectored vaccines are another kind of recombinant vaccine, in which one or more genes that encode immunogenic proteins of one or more pathogens are cloned directly into the genome of a vector virus or organism (*e.g.* an attenuated canarypoxvirus vector with the rabies virus surface glycoprotein gene spliced into place). This avian recombinant, chimaeric virus can replicate only to a very limited extent in the mammalian host but does express the introduced gene(s) on host cell surfaces, mimicking a natural infection. Vectored vaccines cannot revert to virulence and the vector is chosen to be non-pathogenic and sometimes immunostimulatory. These vaccines can induce both humoral and cellular immune responses, usually without the need for an adjuvant. Attenuated canarypoxvirus has been used in vectored vaccines against rabies, canine distemper and FeLV infection.

Nucleic acid-based vaccines (DNA and RNA vaccines) are relatively new forms of vaccine created by manipulating nucleic acids to produce copies of viral antigenic target proteins upon immunisation. Messenger RNA (mRNA) vaccines have become familiar to many people during the current COVID-19 pandemic. They generally require very cold transportation and storage. Messenger RNA vaccines employ delivery systems, such as lipid nanoparticles, that protect the nucleic acid from degradation and that allow cellular uptake and mRNA release. DNA is much less fragile than mRNA, so naked DNA vaccines are more robust. There are currently no mRNA vaccines, nor naked DNA vaccines, available for use in dogs and cats.

EFFECTS OF MATERNALLY DERIVED ANTIBODIES ON IMMUNISATION

MDA are mostly acquired by neonatal puppies and kittens by consuming colostrum in the first hours after they are born (Chastant & Mila, 2019; Rossi et al., 2021). MDA provides passive immunity. Although important to protect puppies and kittens in the first weeks of life, MDA can also interfere with the ability of the young animal to mount its own, active immune response to most vaccines (DiGangi, Levy, et al., 2011b; Friedrich & Truyen, 2000). Serum MDA inhibits immunoglobulin G (IgG) production within the young animal and prevents vaccine antigens from stimulating an active immune response. In most puppies and kittens, MDA declines to levels that allow an active immune response to vaccination by about 8 to 12 weeks of age. Puppies with low amounts of MDA may be vulnerable (and capable of responding to vaccination) at an earlier age, while others

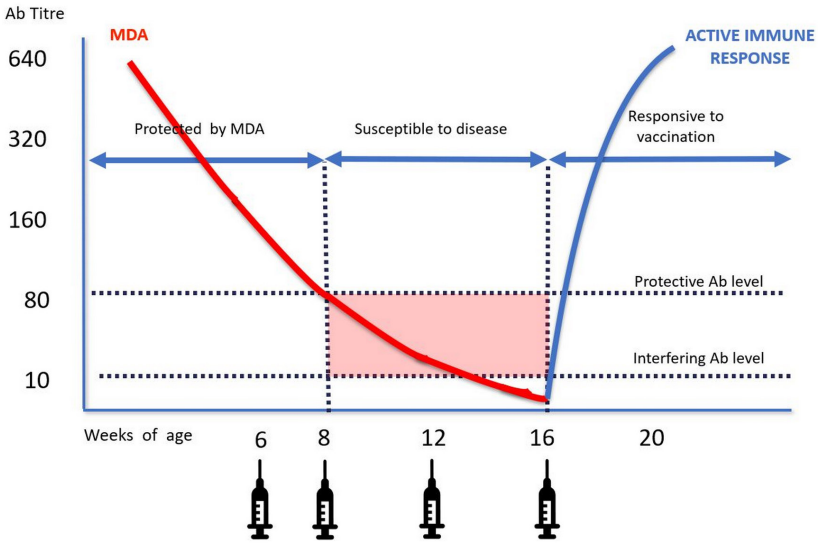

FIG 1. How maternally derived antibody (MDA) interferes with a veterinarian's ability to immunise puppies or kittens through early vaccination. This graph shows a puppy's serum antibody (Ab) concentration or "titre" on the vertical axis and age in weeks on the horizontal axis. The antibody shown happens to be against canine parvovirus, but the same principles apply in both puppies and kittens to a variety of pathogenic agents. Shortly after birth, this puppy acquired a substantial amount of anti-parvoviral antibody from its mother, via colostrum. This is the so-called "maternally derived antibody" or MDA (the red line). MDA declines exponentially with a half-life of approximately 9 to 10 days. The syringe icons represent repeated vaccinations, the first of which was given at 6 weeks of age. This first vaccination did not immunise the puppy because of interfering MDA, which neutralised the vaccine. The same is true of the next two vaccinations. At 8 weeks of age, this puppy became susceptible to parvoviral enteritis, because its MDA concentration fell below the level required to protect from a moderate challenge with canine parvovirus. Yet it could not be immunised at that age, because the level of MDA was still sufficient to interfere with the vaccine and to prevent active immunisation. By approximately 13.5 weeks of age, the level of MDA in this puppy fell low enough to permit immunisation. At 16 weeks of age, the puppy was revaccinated and promptly made its own active immune response (the blue curved line). The pink-shaded rectangle between dotted lines represents the "window (or period) of susceptibility" for this puppy, during which it was susceptible to parvoviral disease. It is not recommended to routinely measure MDA in very young puppies. Some puppies might receive more or much less than did this puppy. So this is why repeated vaccinations are given every 2 to 4 weeks, to narrow the "window of susceptibility" for puppies and kittens as much as practicable. Ab Antibody, MDA Maternally derived antibody; syringe icon, vaccination.

may possess MDA at such high levels that they are incapable of responding to vaccination until ≥12 weeks of age (Friedrich & Truyen, 2000; Thibault et al., 2016). The period when MDA is insufficient to provide complete immunologic protection, but still enough to interfere with an active immune response, is known as the "window of susceptibility" for the puppy or kitten. During this "window," a puppy or kitten cannot be immunised by conventional vaccines but is susceptible to disease if it comes into contact with "street" or virulent pathogen. It is not possible, without serological testing, to predict when this "window" will open or close (*i.e.* begin or end) because the amount of MDA transferred to individual puppies or kittens varies between litters and within litters. As it is impossible to predict, without blood testing, when sufficient waning of MDA will occur, the initial core vaccination series usually involves the administration of multiple, sequential doses. The repeated doses are not booster doses. They are applied with the aim of triggering an active immune response as soon as possible after MDA has dropped sufficiently (see Fig 1). MDA can interfere with immune responses to both modified live and inactivated vaccines. If, when administering the first dose of an inactivated vaccine, there is enough MDA to block an active immune response, immune priming will not occur. A second dose of inactivated vaccine would then fail to immunise the animal. Conversely, a single dose of MLV vaccine given after MDA has waned sufficiently is usually sufficient to immunise.

SEROLOGICAL TESTING OF DOGS AND CATS TO ASSIST IN VACCINATION-RELATED DECISION-MAKING

An advance in companion animal practice is the commercial availability of in-practice diagnostic test kits that can detect antibodies against CDV, CPV and CAV in dogs and FPV in cats. Some of these test kits have been validated for use in practice and shelter settings and are simple to use (Egerer et al., 2022; Gray et al., 2012; Litster et al., 2012; Meazzi et al., 2022). They provide a rapid result (positive or negative) within 20 to 30 minutes. Some of these test kits may usefully complement traditional laboratory-based methods (*e.g.* virus neutralisation and haemagglutination inhibition testing), which remain the "gold standards" for serological testing (Jenkins et al., 2020).

For CDV, CPV and CAV in adult dogs and FPV in adult cats, the presence of serum antibody provides evidence of an active humoral immune response, which is very likely to indicate protection from disease. In some pets, these antibodies persist for

well over 3 years. Vaccinated dogs may maintain protective immunity against CDV, CPV and CAV for many years (Bohm et al., 2004; Jensen et al., 2015; Mitchell et al., 2012; Mouzin et al., 2004a, 2004b; Schultz, 2006; Schultz et al., 2010). The same is true of FPV in cats.

Conversely, the presence of antibody against FHV or FCV is currently not considered to be a reliable predictor of immune protection against either of these viruses (Egberink et al., 2022; Stone et al., 2020) although an earlier study did provide supportive results in shelter cats (DiGangi et al., 2011a). Vaccines intended to protect against FHV and FCV cause seroconversion but may only provide partial protection against disease and do not protect effectively against infection or development of the carrier state. In cats, tests for anti-FPV antibodies are considered more reliable indicators of protection than tests that detect anti-FHV and anti-FCV antibodies (Mende et al., 2014).

As opposed to the presence of antibody, the *absence* of detectable antibody does not reliably predict susceptibility to infection and disease. This is because cellular and innate immunity are not evaluated in antibody detection testing and many animals are thought to be robustly protected by immunological memory in the absence of detectable serum antibody (Killey et al., 2018). In support of this, prompt, strong anamnestic antibody responses have been demonstrated in previously vaccinated, seronegative pet animals shortly after revaccination, indicating that they would likely have been robustly protected from challenge (Mitchell et al., 2012; Mouzin et al., 2004a, 2004b). Despite these findings, absence of antibodies has generally been taken as a clinical indication for revaccination. This is based on a precautionary principle because proof of memory (other than retrospectively by revaccination and retesting) cannot readily be achieved in most clinical settings.

An owner may wish to confirm that a puppy or kitten has mounted an active immune response after the course of primary vaccinations has finished. If so, a serum sample taken at or after 20 weeks of age and at least 4 weeks after the last vaccine dose can be tested. Animals discovered to be seronegative (probably only a small percentage) should be revaccinated and retested several weeks later. If the animal again tests negative, it should tentatively be considered a non-responder that may be incapable of developing protective immunity against the pathogen(s) for which it tests seronegative. Performing a gold standard serological test at this stage may refute the earlier in-practice results or show a low or undetectable antibody titre typical of a non-responder dog (see Fig 2).

In-practice serological test kits have gained favour with some veterinarians who wish to offer their clients a convenient alternative to routine revaccination at (for example) 3-yearly intervals. However, in-practice serological test kits have been shown to vary in sensitivity, specificity, positive and negative predictive value (PPV and NPV), and overall accuracy (OA) when compared to reference, gold standard tests (Bergmann et al., 2020; Bergmann, Halzheu, et al., 2021a; Bergmann, Zablotski, et al., 2021b; Dall'Ara et al., 2021; DiGangi, Gray, et al., 2011a; Egerer et al., 2022; Meazzi et al., 2022; Mende et al., 2014).

The specificity of in-practice serological test kits needs to be high if they are to be relied upon (Bergmann et al., 2020; Bergmann, Halzheu, et al., 2021a; Bergmann, Zablotski, et al., 2021b). A false positive result would suggest that an animal has antibodies and is protected. In fact, because the result is a *false* positive, current guidelines recommend that the animal should be revaccinated. Recently, several different in-practice diagnostic test kits were compared with gold standard testing in Germany (Bergmann et al., 2020; Bergmann, Halzheu, et al., 2021a; Bergmann, Zablotski, et al., 2021b). The kits varied in ease-of-use and in performance relative to the gold standard tests. Some of the tested kits performed very well for detection of CPV-2 antibody in canine serum (Bergmann et al., 2020) but kits for detection of CDV antibody, and a kit for detection of CAV antibody, performed much less well (Bergmann, Halzheu, et al., 2021a; Bergmann, Zablotski, et al., 2021b). Four different in-practice kits for detection of CDV antibody were compared to a gold standard. Against the gold standard, they were not reliable when used to test dogs with acute illness or healthy-looking dogs with chronic disease (Bergmann, Zablotski, et al., 2021b). The reliability of the gold standard virus neutralisation test for CDV, when used in acutely ill or chronically diseased dogs, was also questioned in this paper. Overall, the usefulness of in-practice serological testing for detection of anti-CDV antibody using these test kits, certainly in acutely ill dogs or in dogs with chronic disease, was not supported by this work (Bergmann, Zablotski, et al., 2021b). A single test kit for detection of anti-CAV antibodies had poor specificity (Bergmann, Holzheu, et al., 2021a). Further research is needed to boost progress in this important area.

Understanding the utility and limitations of serological testing as an aid to vaccination-related decision-making is demanding. Veterinarians should not feel obliged to start using serological or "titre" testing in their practices, if they are not inclined to do so. Several FAQs dealing with serological testing have been included in this latest version of the guidelines. These are for those veterinarians who may be interested in exploring this topic further.

CURRENT AND EMERGING TOPICS IN CANINE AND FELINE CLINICAL VACCINOLOGY

Most of the contemporary issues discussed in the 2016 version of these guidelines (Day et al., 2016) remain of current interest although many further topics and issues have emerged since then. Since 2016, concerns about a low proportion of all pets receiving the benefit of vaccination have grown in some countries (Malter et al., 2022; Taylor et al., 2022). A low proportion of vaccinated pet animals adversely impacts "herd immunity" (Datta & Roy, 2022). The concept of herd immunity needs to be understood and acted

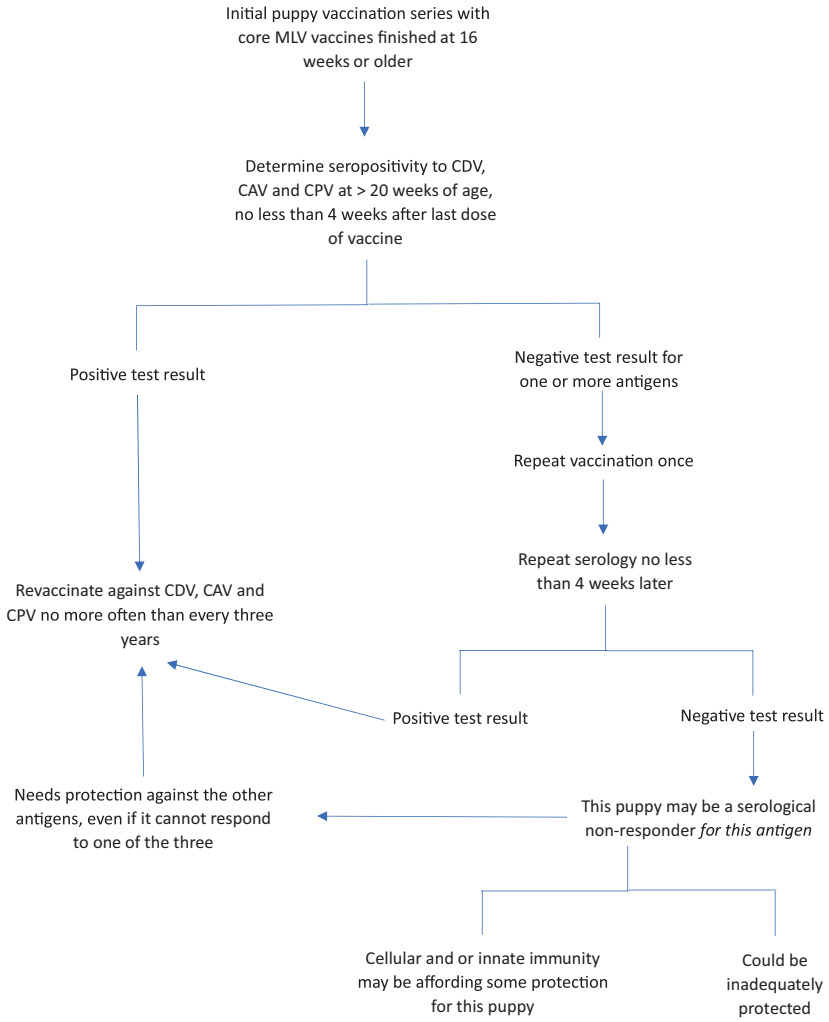

FIG 2. Algorithm showing the recommended approach to interpreting and acting upon serological test results obtained >4 weeks after the last puppy or kitten vaccination at 16 weeks of age or older. Ideally, serological testing, especially testing for anti-CDV antibodies, should be done in a reference laboratory, not using point-of-care testing. CAV Canine adenovirus, CDV Canine distemper virus, CPV Canine parvovirus, MLV Modified live virus

upon by companion animal veterinarians. Frequent revaccination of a small proportion of pets within a population will do little to improve herd immunity. Conversely, increasing the proportion of vaccinated pets within the population, even if each of those pets receives only a single, well-timed core vaccine, will achieve far more.

Excessive, unwarranted "vaccine load" remains of concern and, indeed, the situation has deteriorated in some countries. Multi-component vaccines that contain a mixture of core and non-core components remain common. In at least one country, monovalent vaccine choices have diminished rather than expanding, as would be preferable.

The concept of "One Health" has never been more pertinent to companion animal practice than it is today. The suffering of humans and the suffering of their companion cats and dogs have been interwoven during the COVID-19 pandemic (Baptista et al., 2020). Just as the pandemic delayed elective surgical and medical procedures in countless humans, it prevented pet owners from obtaining timely veterinary care, especially vaccinations, for their pets (Owczarczak-Garstecka et al., 2022). Thankfully, that situation has improved in many countries since the beginning of the pandemic. There have been many other One Health implications of COVID-19. A renewed global focus on pandemic preparedness is an opportunity for the One Health initiative, since many potential human pathogens either have animal reservoirs or equivalent animal pathogens. Further, new vaccine platform technologies used for human pathogens may catalyse innovative veterinary vaccine development.

"Vaccination hesitancy" is another issue of considerable contemporary importance. Concerns about worsening vaccine hesitancy have been expressed by members of both veterinary and medical organisations (Lee et al., 2022; Mattson, 2020). Vaccine or vaccination hesitancy has been described as a "…*delay in acceptance or refusal of vaccination despite availability of vaccination services*." (MacDonald, 2015). Vaccine hesitancy is of enormous and growing concern to public health authorities around the world, including the World Health Organization (WHO). Indeed, in 2019, vaccine hesitancy was listed as one of the top 10 threats to global human

health (WHO, 2019). The phrase "vaccine hesitancy" first appeared in the Web of Science Core Collection in 2010. Since then, use of the phrase has increased substantially with more than 350 papers on this topic published in 2020 alone (Squires, 2021a). The description provided above is not sufficiently inclusive for small companion animal practitioners. This is because many people who choose not to vaccinate their pets do so without ever consulting a veterinarian. They do not delay acceptance, nor refuse, they simply avoid any discussion (Squires, 2021b).

There are scant data on vaccine hesitancy in small companion animal practice, but over 2500 veterinary practitioners in numerous countries responded in an informal survey and the results indicated that it is perceived by many veterinarians as a growing problem (Squires, 2021b). In support of this, data about many aspects of companion animal welfare collected in the United Kingdom from 2011 to 2022 (PDSA, 2022) began to reveal an alarming decline (first noticed in 2017) in the proportion of UK pets reported by owners as being vaccinated. In the PDSA's 2019 PAW Report only 72% of owners reported that their puppy had received a primary course of vaccines (down from about 88% in 2016). The figure was lower for kittens: 61%, down from about 82% in 2016. The proportion of adult dogs and cats receiving regular booster revaccinations was even lower. In 2020 to 2022 (PDSA, 2022), the situation seemed to stabilise or improve, with slightly larger proportions of animals receiving vaccines, but the confounding effects of the COVID-19 pandemic make it difficult to interpret these more recently reported figures.

In the 2019 PAW report, *"It's too expensive"* was a top reason for not having vaccination done (17% of all pet owners). For owners of adult cats, not wanting to stress the cat by taking it to the veterinary clinic was a powerful inhibitor to seeking revaccination, slightly more powerful than cost (influencing 22% of owners *versus* 21% influenced by cost). Thus, Fear Free Pets® and other similar organisations may be able to play important roles in improving compliance with vaccination recommendations. Interestingly, concern about vaccine safety was not mentioned as a reason for failure to vaccinate pet dogs or cats in the 2019 PAW report.

In a recent study of almost 1 million UK dogs, Taylor et al. (2022) showed that only 49% had received at least one vaccine against leptospirosis in the 12-month study period. In this study, Dogs over 8 years of age were 12.5 times less likely to have received the benefit of vaccination against leptospirosis than were dogs under 1 year of age.

Another recent study looked at variability in non-core vaccination rates of dogs and cats in veterinary clinics across the USA (Malter et al., 2022). These animals were all up to date for their core vaccines. Nationally, in this study, median clinic vaccination rates for dogs were 70.5% for leptospirosis and 68.7% for *Bordetella bronchiseptica*. In cats, for FeLV, median clinic vaccination rates were reportedly low for adult cats (34.6%) and only slightly higher for kittens and 1-year-old cats (36.8%).

Clearly, there remains considerable scope for veterinarians and veterinary associations to work to improve small companion animal vaccination rates, including in some rather wealthy countries.

Regarding excessive "vaccine load" it is disappointing that, for example in Australia, it is no longer possible to purchase a monovalent FeLV vaccine. The situation has deteriorated since the last iteration of these guidelines. The only option now is to inject a pentavalent, inactivated vaccine that includes FeLV. Previously there were several monovalent choices. Presumably, commercial imperatives in a relatively small market have led to this situation.

CANINE VACCINATION GUIDELINES

Core vaccines for pet dogs

Summary information about core vaccines for dogs not living in shelters is provided in Table 1. Information about the different kinds of vaccine (*e.g.* MLV, inactivated, recombinant) is provided in an earlier section of these guidelines.

Core vaccines for dogs that are relevant throughout the world protect against disease caused by *CDV*, *CAV* and *CPV*. In addition, veterinarians working in certain places designate other vaccines as core, for example those that protect against rabies and leptospirosis. Wherever rabies is endemic, all dogs and cats should be vaccinated for the protection of both pets and humans even if legislation does not require this. Mass canine vaccination has been shown to greatly reduce or eliminate rabies cases (Zimmer et al., 2018). Leptospirosis is another life-threatening, zoonotic disease that is widely distributed around the world. In countries or regions where canine leptospirosis is endemic, implicated serogroups are known, and where suitable vaccines are available for use, vaccination of all dogs against leptospirosis is highly recommended and these vaccines should be considered *core* in those places.

The VGG recommends initial vaccination of puppies against CDV, CAV and CPV at 6 to 8 weeks of age, then every 2 to 4 weeks until 16 weeks of age or older. The more frequently these vaccinations are given, the narrower (or shorter) will be the "window of susceptibility" for the puppy. Vaccinating more frequently than every 2 weeks is not advised. It follows that the number of these primary core vaccinations will vary somewhat and will depend on the age at which vaccination is started and the chosen intervals between vaccinations. The most important of these early vaccine doses is the one administered at 16 weeks of age or older. MDA can be expected to have waned substantially by that age in a large majority of puppies, so almost all puppies should be able to respond to vaccination then, if not before.

Table 1. Vaccines for pet dogs (non-shelter)

Vaccine	Puppies ≤16 weeks	Dogs >16 weeks	Revaccination	Comments and recommendations
Core vaccines for pet dogs, all parenteral				
Canine parvovirus-2 (modified live virus, MLV)+canine distemper virus (MLV or recombinant)+canine adenovirus-2 (CAV-2, MLV)	Start no earlier than 6 weeks of age. Revaccinate every 3 to 4 weeks until 16 weeks of age In especially high-risk situations continue until 20 weeks of age and consider vaccinating every 2 to 3 weeks	Two doses 2 to 4 weeks apart are recommended by some manufacturers However, a single dose of MLV or recombinant vaccine will likely protect most dogs	Consider revaccinating at about 6 months of age, rather than waiting until the dog is 12 to 16 months of age. This will narrow the window of susceptibility for any puppies that failed to mount an active immune response earlier Thereafter, revaccinate at 3 years of age and thereafter no more frequently than every 3 years	These core vaccines are among the most important received by puppies and dogs. The aim should be to vaccinate as large as possible a proportion of the entire population Careful socialisation of puppies (during their sensitive period for socialisation) can begin before the completion of this vaccination series
Canine parvovirus-2 (recombinant)+canine distemper virus (MLV)	Administer a single dose from 4 weeks of age before commencing routine primary vaccinations			This recently introduced product is aimed specifically at young puppies, likely to have interfering MDA, rather than for revaccination of older dogs
Rabies (inactivated)	Follow any local laws or regulations as a priority. Follow the product leaflets of locally manufactured vaccines. In some countries, the first dose is generally not given before 12 weeks of age	Follow any local laws or regulations as a priority. Follow the product leaflets of locally manufactured vaccines	Follow any local laws or regulations as a priority. Follow the product leaflets of locally manufactured vaccines. Revaccination at 1 year of age (or in some countries 1 year after the primary vaccination) is required. Canine rabies vaccines with either a 1- or 3-year DOI are available. Timing of boosters is determined by the licensed DOI, but in some areas may be dictated by law	Core wherever the disease is endemic or wherever local laws or regulations require
Leptospira spp. (killed bacterin). The serogroups included in vaccines depend on the geographical region. Most vaccines include at least two serogroups, but some are monovalent, some trivalent and some quadrivalent	Initial dose is usually from 8 weeks of age. Follow the advice in the product leaflet about when to start. A second dose is given 2 to 4 weeks later	Two doses 2 to 4 weeks apart	Annually	Core for dogs in regions where canine leptospirosis is endemic, implicated serogroups are known and suitable vaccines that include implicated serovars are commercially available
Non-core vaccines for pet dogs				
Canine Parainfluenza Virus (CPiV, MLV, parenteral)	Administer from 6 weeks of age onwards, then every 2 to 4 weeks until 16 weeks of age or older	Two doses 2 to 4 weeks apart are generally recommended by manufacturers	Annually	Non-core The duration of immunity provided in pet dogs is uncertain. Use of CPiV (MLV-mucosal) in combination with *Bordetella bronchiseptica* may be preferable as CPiV is not broadly available as a single antigen product

Table 1. (Continued)

Vaccine	Puppies ≤16 weeks	Dogs >16 weeks	Revaccination	Comments and recommendations
Bordetella bronchiseptica (live avirulent bacteria, intranasal) *B. bronchiseptica*+CPiV (MLV) intranasal *B. bronchiseptica*+CPiV (MLV)+CAV-2 (MLV) intranasal *B. bronchiseptica* (live avirulent bacteria, oral) *B. bronchiseptica*+CPiV (MLV) oral	Each of these mucosally applied vaccines provides protection after a single dose Some can be applied as early as 3 weeks of age, others at 7 or 8 weeks of age. Follow the product leaflet advice	A single dose	Annually	Non-core These live vaccines intended for intranasal or oral administration MUST NOT be inadvertently injected parenterally as this may lead to a severe adverse reaction
Bordetella bronchiseptica (killed bacterin, parenteral) *Bordetella bronchiseptica* (cell wall antigen extract, parenteral) *Bordetella bronchiseptica* (fimbrial antigen, parenteral)	These parenteral bacterin or subunit vaccines require two doses to immunise, generally given 2 to 4 weeks apart. Review and follow product leaflet intervals	Two doses Review and follow the specific product leaflet intervals as there are differences between products	Annually for most. Review and follow the specific product leaflet intervals There are special revaccination instructions for the fimbrial antigen vaccine	Non-core These vaccines intended for parenteral use should not inadvertently be given intranasally or orally. This would not be effective and might cause unnecessary discomfort
Borrelia burgdorferi (Lyme borreliosis; killed whole bacterin, parenteral) *Borrelia burgdorferi* [subunit-Outer surface protein A (OspA), parenteral] *Borrelia burgdorferi* (subunit OspA and chimaeric OspC proteins)	These parenteral bacterin or subunit vaccines require two doses to immunise, generally starting at about 8 weeks of age. Review and follow the specific product leaflet intervals	Two doses 2 to 4 weeks apart. Review and follow the specific product leaflet intervals	Annually. Revaccinate just before the start of the tick season, as determined regionally	Non-core. Generally recommended only for use in dogs with a known high risk of exposure, living in or visiting regions where the risk of vector tick exposure is considered to be high, or where disease is known to be endemic. The mainstay of *Borrelia* prevention is diligent ectoparasite control. Direct dog to dog transmission does not occur
Canine influenza virus (H3N8; killed adjuvanted, parenteral) Canine influenza virus (H3N2; killed adjuvanted, parenteral) Canine influenza virus (Bivalent H3N8+H3N2; killed, adjuvanted, parenteral)	These parenteral, inactivated viral vaccines require two doses to immunise. The initial dose can be given from 6 weeks of age. Review and follow the specific product leaflet intervals	Two doses. Review and follow the specific product leaflet intervals, generally 2 to 4 weeks apart	Annually	Non-core. Licensed only in USA. Consider for use in at-risk groups of co-housed dogs such as those in kennels, dog shows or day care
Canine leishmaniosis (CanL; recombinant protein A2, parenteral)	Three doses, 3 weeks apart with the initial dose at >4 months of age	Three doses, 3 weeks apart	Annually	Non-Core. Prevention of canine leishmaniosis depends crucially on diligent ectoparasite control so as to minimise contact with the vectors. Vaccination can be regarded as a supplementary control measure, not a substitute for diligent ectoparasite control
CanL [excreted-secreted proteins (LiESP) of *L. infantum*, parenteral]	Three doses, 3 weeks apart with the initial dose at >6 months of age	Three doses, 3 weeks apart	Annually	
CanL (recombinant Protein Q, parenteral)	A single dose at >6 months of age	A single dose	Annually	
Canine herpesvirus-1 (CHV-1; subunit, parenteral)	Not applicable. This vaccine is intended for pregnant bitches	Two doses during pregnancy First dose – During oestrus or 7 to 10 days after the presumed date of mating Second dose – 1 to 2 weeks before the expected date of whelping Follow the product leaflet	Manufacturer recommends repeating the two injection protocol during each subsequent pregnancy	This vaccine is intended to protect newborn puppies. Infection (usually from the dam) can be fatal in young puppies, <3 weeks old, that are not kept warm

Table 1. (Continued)

Vaccine	Puppies ≤16 weeks	Dogs >16 weeks	Revaccination	Comments and recommendations
Vaccines not recommended for pet dogs				
Canine parvovirus-2 (CPV; killed, parenteral)	Not recommended for general use in pet dogs where MLV vaccines are available			MLV vaccines against canine parvovirus-2 are more potent and induce longer duration of immunity. Some MLV vaccines have been proven to be safe for use in pregnant bitches. Check the product leaflet to be sure. If safe MLV vaccines are unavailable in particular areas, use of inactivated vaccine is justified
Canine coronavirus (CCoV; killed and MLV, parenteral)	Not recommended			The evidence that CCoV is an important primary pathogen in adult dogs is weak. The diarrhoea associated with CCoV infection in puppies is usually mild, and the infection usually occurs in young puppies, sometimes before they are first vaccinated. Co-infection with canine parvovirus-2 can be managed by protecting robustly against parvoviral infection. There is no evidence that the CCoV vaccines currently available would protect against mutant pathogenic forms of the virus (pantropic or more highly pathogenic strains) that emerge and are identified infrequently
Giardia spp. vaccines	Not recommended. There is insufficient scientific evidence to justify their use			*Giardia duodenalis* infection is non-life threatening, responds to therapy, and is rarely transmitted from puppies or dogs to humans. There is insufficient evidence that *Giardia* vaccines can prevent the shedding of *Giardia* oocysts. Vaccines do not prevent infection and vaccinated dogs can develop clinical signs of infection
Microsporum canis vaccines	Not recommended. There is insufficient scientific evidence to justify their use			

Even when the last puppy vaccine dose is administered at 16 weeks of age or slightly later, a small percentage of puppies may not respond adequately to vaccination because of persisting MDA (Friedrich & Truyen, 2000; Thibault et al., 2016). For this reason, the VGG recommends either serological testing at least 4 weeks after the last puppy vaccination (*i.e.* at or after 20 weeks of age if these guidelines are followed) or, alternatively, an additional vaccination at or shortly after 26 weeks of age. This recommendation, first made and explained in a previous iteration of these guidelines (Day et al., 2016), replaces an earlier recommendation for a "first annual booster" with core vaccines at 12 to 16 months of age. Vaccinating puppies at 26+ weeks of age rather than waiting until 52 weeks of age or later does not increase the number of core vaccine doses administered to the animal but will substantially reduce the period of susceptibility for those few that have not yet mounted an active immune response. The VGG's previous recommendation (Day et al., 2016) was for this vaccination to be given at 26 to 52 weeks of age. In these latest guidelines, the revised recommendation is for this vaccination to be given at or shortly after 26 weeks of age. Puppies in which serological testing at 20+ weeks of age reveals protection against CPV, CDV and CAV do not need the 26+ week vaccination.

This recommendation for earlier revaccination is certainly not mutually exclusive to, nor should it preclude, a first annual health check at approximately 1 year of age with administration of rabies vaccine (where needed) plus any non-core vaccines deemed necessary. Understandably, many veterinarians are keen to re-examine the dogs under their care as they reach or approach skeletal and behavioural maturity.

Some licensed vaccines have datasheet recommendations for a 10- or 12-week finish to the puppy vaccination series. Small experimental studies (*e.g.* Bergman et al., 2006), have supported this recommendation. However, other experimental studies and field studies have produced contrary results and some of the supportive experimental evidence was compromised by the so-called "pen effect" (Ellis, 2015). The "pen effect" describes a situation in which experimental puppies are group-housed and have the opportunity to share mucosally shed vaccinal virus within each group. This would substantially and artificially increase their opportunities to become immunised, leading to potential over-estimation of the benefits afforded by vaccination. The VGG therefore continues to recommend finishing no earlier than 16 weeks and preferably following that with serological testing or a 26+ week revaccination.

Part of the rationale for "early finish" protocols was to permit early socialisation of puppies. The VGG strongly supports early socialisation as essential to healthy behavioural development and future well-being of dogs (Korbelik et al., 2011). Early socialisation can be achieved while following these WSAVA vaccination guidelines. Research has shown that the risk to puppies partway through their initial vaccination series of developing CPV-related disease by attending early socialisation classes is low (Stepita et al., 2013). The same is likely to be true for CDV and CAV.

Dogs that have responded optimally to vaccination with MLV core vaccines maintain solid immunity for many years in the absence of repeated vaccinations (Bohm et al., 2004; Jensen et al., 2015; Mitchell et al., 2012; Mouzin et al., 2004a; Schultz, 2006; Schultz et al., 2010). Once puppies have mounted an active immune response, subsequent revaccination need be given no more often than triennially. If a core vaccine is given at 26+ weeks of age, then to synchronise core vaccinations with annual health checks, simply for client convenience, the next dose might be given at 3 years of age (rather than waiting until 3.5 years of age).

It should be emphasised that *inactivated* core viral vaccines for dogs do not provide such long-lasting protection as do MLV vaccines. Recombinant core canine vaccines provide protection similar to MLV vaccines. A detailed comparison is beyond the scope of this document.

Adult dogs with an unknown or incomplete vaccination history are frequently presented for vaccination. A single dose of MLV core vaccine will very likely be sufficient to induce immunity in pet dogs over 26 weeks of age and will provide long-lasting protection. In high-risk situations (*e.g.* outbreaks), it would be prudent to consider providing a second dose, 2 to 4 weeks later.

In rabies endemic areas, *rabies vaccines* should also be administered. Most rabies vaccines are inactivated but are remarkably immunogenic. A single dose can immunise, in contrast to many other inactivated vaccines. A recommendation in some parts of the world is to give a first rabies vaccine dose at 12 weeks of age with a second dose one year later, although recommended dosing schedules for locally manufactured vaccines in some countries may differ from this and should be followed (Pimburage et al., 2017). Revaccination intervals for canine rabies vaccines are often mandated by law. Rabies vaccines usually carry a 1- or 3-year licensed DOI. Revaccination intervals should be based primarily on local regulations and, in the absence of these, on datasheet DOI claims. In countries where the legal requirement is at odds with the vaccine datasheet, the law must be followed. Locally manufactured rabies vaccines with a 1-year DOI should not be assumed to be safe and effective for triennial use. Veterinarians should be mindful of the law, but where they have access to a product that has been shown to provide a minimum of 3 years of immunity, national veterinary associations might consider lobbying to have local regulations changed to match the current scientific evidence.

Vaccines to protect against canine *leptospirosis* are now considered *core* in these guidelines if, in the regions where the dog lives or to which it travels, leptospirosis in dogs is prevalent, implicated serogroups are known and suitable vaccines are commercially available. This means that, according to these guidelines, vaccines to protect against canine leptospirosis will be designated as core in many but not all parts of the world. In a few parts of the world that have been studied carefully, for example South Australia, there is little to no evidence that canine leptospirosis occurs (Zwijnenberg et al., 2008). Alas, in many parts of the world, it remains undetermined which serogroups would need to be included in vaccines for local use to protect dogs against leptospirosis. A vaccine cannot be designated as "core" if it is uncertain which vaccine should be given. Currently, this remains true despite some interesting, paradigm-challenging French work that suggests there may be a degree of cross protection among members of different serogroups (André-Fontaine & Triger, 2018). The commercial development of "pan-protective" vaccines (Chaurasia et al., 2022), which may be able to protect dogs against leptospirosis caused by a large majority of the known pathogenic variants, should be eagerly awaited and, if such vaccines are successfully developed, will substantially extend the regions of the world in which leptospirosis vaccines can be considered "core."

Globally, there are currently monovalent, bivalent, trivalent and quadrivalent vaccines to protect dogs against canine leptospirosis. These variously contain serovars belonging to serogroups Icterohaemorrhagiae, Canicola, Grippotyphosa, Pomona and Australis (Francey et al., 2020; Klaasen et al., 2012, 2014; Schuller et al., 2015; Sykes et al., 2023; Wilson et al., 2013). Quadrivalent vaccines provide broader protection. In general, these vaccines provoke strong but transient seroconversion (Martin et al., 2014). Immunity (protection against virulent challenge) lasts much longer than the period of seropositivity (up to 15 months; Grosenbaugh & Pardo, 2018). Two doses of inactivated vaccines, such as those that protect against leptospirosis, are required to immunise.

Non-core vaccines for pet dogs

Summary information about non-core vaccines for dogs is provided in Table 1.

The most widely used non-core vaccines for dogs are those against *Bordetella bronchiseptica* and canine parainfluenza virus (CPiV). Other non-core vaccines with more restricted geographical availability include those against *Borrelia burgdorferi*, canine influenza virus (CIV) and *Leishmania infantum*.

There is also a subunit vaccine against Canine Herpesvirus-1, specifically for use in bitches during pregnancy. This vaccine has been shown to induce an increase in maternal serum neutralising antibodies in seronegative bitches. This antibody is passively transferred in colostrum and was shown to protect puppies during early life (<3 weeks), when infection may be fatal (Poulet et al., 2001; Rota et al., 2020). Puppies that suckle poorly shortly after birth will not be well protected (Larsen et al., 2015).

Non-core vaccines generally need to be given annually to provide reliable protection. Therefore, an adult dog may, according to these guidelines, be vaccinated annually, but the components received will differ from year to year. Vaccines that provide particularly long-lasting protection, such as those that protect against CPV, CDV and CAV can be given much less often than the others. In many dogs, vaccines that protect against CPV, CDV and CAV are administered no more often than triennially, with other needed products being given annually. For non-core and leptospirosis vaccines, if protection is allowed to "lapse" (*i.e.* a dog was previously immunised properly but there has been a long interval since it last received that vaccine) then it is recommended, as a precaution, to "start again" and provide two doses, 2 to 4 weeks apart.

Non-core vaccines against respiratory tract pathogens cannot prevent infection but may reduce disease severity. Vaccines to protect against CPiV, *B. bronchiseptica* and canine adenovirus type 2 (CAV-2) are available in different combinations of these three antigens, either as parenteral (subunit *B. bronchiseptica*; inactivated *B. bronchiseptica*; MLV CPiV), intranasal (attenuated *B. bronchiseptica* with or without CPiV and CAV-2) or oral (attenuated *Bordetella bronchiseptica* with or without CPiV) formulations. Parenterally administered CPiV and *B. bronchiseptica* vaccines may provide a level of protection that differs from that provided by mucosal vaccines (Ellis, 2015), and there is some evidence that the intranasal route provides superior clinical outcomes when compared to the oral route

(Ellis et al., 2016). Transient coughing, sneezing and ocular or nasal discharge may occur in a small percentage of dogs vaccinated with intranasal or oral vaccines (Ellis et al., 2016; Scott-Garrard et al., 2018).

Canine influenza A virus (CIV) subtypes H3N8 and H3N2 have been documented as causes of disease in dogs in North America and southeast Asian countries (Crawford et al., 2005; Klivleyeva et al., 2022; Payungporn et al., 2008; Song et al., 2008; Voorhees et al., 2017). These influenza viruses cause respiratory illness similar to other respiratory viral pathogens and most dogs are susceptible to infection due to a lack of pre-existing immunity. CIV causes sporadic outbreaks in communities, especially in facilities where dogs are co-housed, such as shelters, boarding kennels, dog day care centres, dog shows and dog farms (Anderson et al., 2013; Lee et al., 2009; Parrish & Voorhees, 2019). Therefore, inactivated H3N8 and H3N2 CIV vaccines are recommended for dogs that are more likely to be exposed based on co-mingling with other dogs. Similar to vaccines for other respiratory pathogens, the CIV vaccines do not prevent infection but may reduce the severity and duration of clinical signs (Deshpande et al., 2009). The CIV vaccines are currently available only in USA.

In some countries of Europe and Latin America, vaccines against canine leishmaniosis (CanL) are available. CanL vaccines cannot reliably prevent infection and therefore even vaccinated dogs can act as a reservoir for *L. infantum* and continue to transmit the disease to other dogs and to people (Fernandez Cotrina et al., 2018; Regina-Silva et al., 2016; Velez et al., 2020). Vaccination can prevent clinical signs of disease in some dogs (Fernandez Cotrina et al., 2018; Regina-Silva et al., 2016; Velez et al., 2020). Vaccines against CanL are an additional tool that can help to protect dogs that are exposed and are already being treated with crucially important topical repellents and insecticides (such as collars).

The use of *Borrelia burgdorferi* vaccines is controversial (Littman et al., 2018). Tick control is considered much more important. In Lyme disease endemic regions, the prevention of other tick-borne diseases is essential and relies on the use of rapid-acting ectoparasiticides and routine inspection of dogs for ticks. This also helps to prevent Lyme disease. No vaccine against Lyme disease provides complete protection. The efficacy of these vaccines is uncertain, and it is unclear whether these vaccines protect against Lyme nephritis, the most severe form of the disease (O'Bier et al., 2021; Vogt et al., 2019; Vogt & Stevens, 2021). Depending on the region, several bacterins (monovalent, bivalent and trivalent) and subunit vaccines (a recombinant, monovalent, non-adjuvanted, lipidated, OspA vaccine and another chimaeric recombinant vaccine consisting of OspA and seven types of OspC) are available for the prevention of Lyme disease in dogs (Grosenbaugh et al., 2018; Izac & Marconi, 2019; Littman et al., 2018; Marconi, Garcia-Tapia, et al., 2020a; Marconi, Honsberger, et al., 2020b; Vogt et al., 2019; Vogt & Stevens, 2021). A systematic review on the efficacy of *B. burgdorferi* vaccines in dogs in North America suggests that vaccinated dogs have a lower chance of developing clinical signs than do unvaccinated dogs (Vogt et al., 2019). Authors of the ACVIM consensus update on Lyme borreliosis in dogs and cats (Littman et al., 2018) did not reach consensus on whether or not to recommend vaccine use in dogs in *B. burgdorferi* endemic areas. They did agree that sick or proteinuric dogs should not be vaccinated.

Not recommended vaccines for dogs

Summary information about vaccines commercially available in some countries but not recommended for use in dogs is provided in Table 1.

Vaccines against canine enteric coronavirus (CCoV) and *Giardia duodenalis* are not recommended. The evidence that CCoV is a primary pathogen that leads to intestinal disease in adult dogs is weak, the diarrhoea associated with the infection in puppies is generally mild, and the infection usually occurs in young puppies. Therefore, vaccination from 6 to 12 weeks of age would be too late to prevent many infections. Moreover, protection against CCoV is dependent on the presence of secretory IgA in the intestine and dogs vaccinated parenterally do not develop a protective intestinal IgA antibody response (Decaro et al., 2004) There is no evidence that the vaccines currently available would protect against mutant pathogenic forms of the virus (pantropic strains) that occasionally emerge.

Canine *Giardia* vaccines have been removed from most global markets but persist in some countries. *Giardia duodenalis* infection is non-life threatening, responds to therapy, and is rarely transmitted from puppies or dogs to humans (de Lucio et al., 2017; McDowall et al., 2011). There is insufficient evidence that *Giardia* vaccines can prevent the shedding of oocysts. Vaccines do not prevent infection and vaccinated dogs can develop clinical signs.

FELINE VACCINATION GUIDELINES

Core vaccines for pet cats

Summary information about core vaccines for cats not living in shelters is provided in Table 2.

The core vaccines for cats relevant in all parts of the world are those that protect against feline panleukopenia virus (FPV), FHV and FCV. The VGG recommends an initial trivalent kitten core vaccine at 6 to 8 weeks of age, then every 2 to 4 weeks until 16 weeks of age or older, with a subsequent dose given at 26 weeks of age or older, by which time MDA is likely to have waned sufficiently so that all kittens can respond to vaccination. These recommendations are based on evidence that MDA interference is important and long-lasting in some kittens (DiGangi, Levy, et al., 2011b; Jakel et al., 2012). The number of primary core vaccinations will depend on the age at which vaccination is started and the selected interval between vaccinations. The recommendation for vaccination at 26 weeks of age or older, as an alternative to vaccination at about 1 year of age, is certainly not mutually exclusive to, nor does it preclude, a first annual health check at approximately 1 year of age.

Table 2. Vaccines for pet cats (non-shelter)

Vaccine	Kittens ≤16 weeks	Cats >16 weeks	Revaccination	Comments and recommendations
Core vaccines for pet cats				
FPV+FCV+FHV: parenteral, live attenuated				
Feline panleukopenia virus (FPV)+feline herpesvirus-1 (FHV)+feline calicivirus (FCV)	Start no earlier than 6 weeks of age and revaccinate every 3 to 4 weeks until 16 weeks of age In especially high-risk situations continue until 20 weeks of age and consider vaccinating every 2 to 3 weeks	Two doses 2 to 4 weeks apart are generally recommended although a single dose can be expected to protect many cats	Consider revaccinating at about 6 months of age, rather than waiting until the cat is 12 to 16 months of age. This will narrow the window of susceptibility for any kittens that failed to mount an active immune response earlier Thereafter, revaccinate "low risk" cats at 3 years of age and then no more frequently than every 3 years	Core worldwide The live attenuated FPV component provides rapid, potent, long-lasting protection More frequent revaccination (up to annually) should be considered for cats at higher risk. For example, cats that go into boarding catteries or visit other high-stress, high-risk environments should be revaccinated 1 to 2 weeks before exposure Pregnant queens and kittens <4 weeks of age should not be vaccinated with live attenuated vaccines Signs of upper respiratory tract disease may be seen following inadvertent aerosolisation of this vaccine or if there is excessive leakage from the injection site
FPV+FCV+FHV: parenteral, inactivated				
Feline panleukopenia virus (FPV)+feline herpesvirus-1 (FHV)+feline calicivirus (FCV)	Start no earlier than 6 weeks of age and revaccinate every 3 to 4 weeks until 16 weeks of age In especially high-risk situations continue until 20 weeks of age and consider vaccinating every 2 to 3 weeks	Two doses 2 to 4 weeks apart	Consider revaccinating at about 6 months of age, rather than waiting until the cat is 12 to 16 months of age. This will narrow the window of susceptibility for any kittens that failed to mount an active immune response earlier Thereafter, revaccinate "low risk" cats at 3 years of age and then every 3 years Annual revaccination is advised for cats at higher risk	Core worldwide Inactivated, parenteral FPV vaccines do not generally provide such rapid-onset, potent, long-lasting protection as do MLV FPV vaccines Non-adjuvanted options are available Considered safer than MLV vaccines for use in pregnant queens Vaccination should not be avoided in retrovirus-infected cats. Inactivated vaccines may be preferable to MLV vaccines in some retrovirus-infected cats Dual-strain (bivalent) inactivated FCV vaccines are intended to provide broader protection More frequent revaccination (up to annually) should be considered for cats at higher risk. For example, cats that go into boarding catteries or visit other high-stress, high-risk environments can be revaccinated 1 to 2 weeks before exposure
FHV+FCV ±FPV: intranasal, live attenuated				
FPV+FHV+FCV *or* FHV+FCV	Follow product leaflet	A single dose	Annually	Intranasal FPV vaccination is not as effective as parenteral vaccination. Even if a trivalent intranasal vaccine is used, vaccinate concurrently with a parenteral (subcutaneous) FPV vaccine Signs of upper respiratory tract disease may be seen following use Rapid onset of protection against FHV and FCV Concurrent use of intranasal and parenteral FHV/FCV vaccine may provide enhanced protection Cats that go into boarding catteries or visit other high-stress, high-risk environments can be revaccinated 1 to 2 weeks before exposure

Table 2. (Continued)

Vaccine	Kittens ≤16 weeks	Cats >16 weeks	Revaccination	Comments and recommendations
Rabies: recombinant and inactivated				
Rabies (canarypoxvirus-vectored recombinant, non-adjuvanted, parenteral)	Follow local regulations as a priority. If there are no regulations, follow the product leaflet	Follow local regulations as a priority. If there are no regulations, follow the product leaflet	Revaccination as required by local regulations or as per licensed duration of immunity (DOI)/product leaflet	Core in areas where the disease is endemic
Rabies (1- and 3-year DOI inactivated, adjuvanted products, parenteral)	Follow local regulations as a priority. If there are no regulations, follow the product leaflet	Follow local regulations as a priority. If there are no regulations, follow the product leaflet	Revaccination as required by local regulations or as per licensed duration of immunity (DOI)/product leaflet	Core in areas where the disease is endemic
FeLV: recombinant and inactivated				
FeLV (recombinant, adjuvanted, parenteral)	Start as early as 8 weeks of age A second dose to be administered 3 to 4 weeks later	Two doses, 3 to 4 weeks apart	Revaccinate 1 year following the last dose of the initial series Thereafter, annually revaccinate cats at continuing high risk of exposure to other, FeLV infected cats (indoors or outdoors)	FeLV vaccines are core for young cats <1 year old that live in regions where FeLV infection is prevalent and in older cats that have continuing risk of exposure, *e.g.* adult cats that have regular, unsupervised outdoor access in areas where FeLV is endemic Avoiding exposure is the best way to prevent FeLV infection Only FeLV-negative cats should be vaccinated. FeLV testing should be performed prior to vaccine administration Further research is warranted to determine how frequently adult cats at continuing high risk of being bitten by potentially FeLV-infected cats should be revaccinated against FeLV
FeLV (inactivated, adjuvanted, parenteral)	Start as early as 8 weeks of age A second dose to be administered 3 to 4 weeks later	Two doses, 3 to 4 weeks apart	Revaccinate 1 year following the last dose of the initial series Thereafter, annually revaccinate cats at continuing high risk of exposure to FeLV infected cats (indoors or outdoors) Revaccinate according to product leaflet (*e.g.* every 2 or 3 years) those cats at low risk of exposure to potentially FeLV-infected cats	
Non-core vaccines for pet cats				
Feline immunodeficiency virus (FIV; killed, adjuvanted, parenteral)	Three doses are required to immunise The initial dose is administered as early as 8 weeks of age; two subsequent doses should be administered at intervals of 2 to 3 weeks	Three doses are required Each dose is administered 2 to 3 weeks apart	A single dose 1 year following the last dose of the initial series, then annually in cats determined to be at sustained risk of exposure	Avoiding exposure is the best way to prevent FIV infection This vaccine is currently only available in Japan, Australia and New Zealand. Reports of its efficacy vary widely. Vaccination will induce production of antibodies used for diagnosis of infection. However, some in-practice diagnostic test kits can reliably discriminate between vaccinated, uninfected cats and infected cats. Validated, reliable PCR diagnostic tests are also becoming more widely available

Table 2. (Continued)

Vaccine	Kittens ≤16 weeks	Cats >16 weeks	Revaccination	Comments and recommendations
Chlamydia felis (avirulent live, non-adjuvanted, parenteral) *Chlamydia felis* (killed, adjuvanted, parenteral)	Administer the initial dose as early as 9 weeks of age; a second dose is administered 2 to 4 weeks later	Administer two doses, 2 to 4 weeks apart	Annual boosters are indicated for cats at sustained risk of exposure	Vaccination is most appropriately used as part of a control regime for animals in multi-cat environments where infections associated with clinical disease have been confirmed. Inadvertent conjunctival inoculation of live vaccine has been reported to cause clinical illness
Bordetella bronchiseptica (avirulent live, non-adjuvanted, intranasal)	Administer a single dose intranasally as early as 4 weeks of age	Administer a single dose intranasally	Annual boosters are indicated for cats at sustained risk of exposure	Not routinely used in pet cats Consider use in pet cats that are kept in unusually large colonies
Vaccines not recommended for pet cats				
Feline infectious peritonitis (FIP; live attenuated, non-adjuvanted, intranasal)	There is insufficient scientific evidence to justify a broad recommendation for the use of this vaccine. This vaccine is labelled for use in kittens from 16 weeks of age. It contains a live, temperature-sensitive virus that can replicate in the nose, but not at higher core body temperatures. This is important for the safety of the vaccine. According to the limited studies available, only cats known to be feline coronavirus antibody-negative at the time of vaccination are likely to develop some level of protection. It is uncommon for cats to be coronavirus antibody negative at 16 weeks of age or older In addition, this vaccine contains a virus strain that differs from clinically important strains found in some well-studied parts of the world			
Giardia spp. vaccines	There is insufficient scientific evidence to justify use			
Microsporum canis vaccines	There is insufficient scientific evidence to justify use			

In regions where rabies is endemic, the VGG recommends that all cats should be vaccinated against rabies for the protection of both pets and humans, even if legislation does not require this for cats. Licensed rabies vaccines for cats generally have a 1- or 3-year DOI claim. Revaccination frequency should be based primarily on local regulations and, if these are absent, on datasheet DOI claims.

Whereas all three globally relevant canine core vaccine components (CPV, CDV and CAV) provide strong and long-lasting protection when used properly (Schultz et al., 2010), the protection afforded by the core FCV and FHV vaccine components will not match that provided by FPV vaccines. FCV vaccines produce a degree of cross-protective immunity against multiple strains of FCV. However, it is still possible for infection and disease to occur in fully vaccinated adult animals (Pedersen et al., 2000; Schorr-Evans et al., 2003). There is no FHV vaccine that can prevent infection. Infection often leads to the virus becoming latent in neural tissue with the possibility of reactivation during periods of stress (Maes, 2012; Richter et al., 2009). Reactivated virus may cause clinical signs in vaccinated animals, or the virus may be shed to susceptible animals and cause disease in them.

Cats that have responded to vaccination with MLV core vaccines maintain solid immunity against FPV for many years in the absence of repeated vaccination. Immunity against FCV and FHV is only partial (Jas et al., 2015) and may be weakened by the stress of boarding (Gourkow et al., 2014; Gourkow & Phillips, 2015). The VGG recommendation for adult "low risk" cats (solitary, indoor animals that do not visit boarding catteries) is for revaccination with MLV core vaccines at intervals of 3 years or longer. For "higher-risk" cats more frequent revaccination to protect against FCV and FHV (up to annually) may be warranted. This includes cats that regularly visit boarding catteries or have other contact with potentially infected cats. In cats that board, a FCV/FHV vaccine can be given 1 to 2 weeks before the main annual visit to the boarding cattery (Gaskell et al., 2007; Stone et al., 2020). In some countries, bivalent FCV/FHV vaccines are commercially available, alongside the more typical trivalent FPV/FCV/FHV vaccines. These bivalent vaccines enable veterinarians to vaccinate higher risk cats against FCV/FHV annually and against FPV triennially, or less frequently. Intranasal MLV FPV/FHV/FCV and FHV/FCV vaccines are available in some countries (Lappin, Sebring, et al., 2006b; Reagan et al., 2014).

These recommendations about revaccination frequency apply to MLV vaccines. Inactivated FPV vaccines typically do not provide such long-lasting protection as do MLV FPV vaccines. Inactivated FCV and FHV vaccines have been shown experimentally to provide long-lasting, partial protection (Scott & Geissinger, 1997, 1999). However, the environment used in this study was extremely stable and most likely experienced as "low stress" by the cats. It was unlike a typical boarding cattery situation.

In this latest iteration of these guidelines, the VGG has decided to designate FeLV vaccines as core in parts of the world where FeLV-related diseases are known to occur. In these parts of the world, this designation applies to young cats (<1 year) and to older cats with outdoor access or that live with other cats that have outdoor access. There are some regions of the world where FeLV infections are known to be rare and where FeLV-related diseases are diagnosed only very rarely in imported cats (Westman, Paul, et al., 2016b). Exposure to FeLV and FeLV infections are now markedly reduced in many parts of the world due to successful control programmes (Studer et al., 2019). This should not be a reason for complacency, as the rate of improvement may have plateaued. The VGG fully supports the use of FeLV vaccines based on lifestyle and perceived exposure risk of individual cats. In the many regions where FeLV infections remain prevalent, any cat less than 1 year old should receive the benefit of protection through routine vaccination. In these places, FeLV vaccines should be viewed as core in young cats and also in older cats with exposure to

the outdoors. Older cats need protection if they are allowed to go outdoors unsupervised: bites are an increasingly recognised mode of FeLV transmission in adult cats (Little et al., 2020). Further research is needed to determine how frequently adult cats at risk of being bitten outdoors should be revaccinated against FeLV. Challenge studies supporting biennial or triennial revaccination of adult cats against FeLV were not designed to provide direct proof of long-lasting protection against FeLV transmitted through *biting*.

The cost, risks and potential benefits of FeLV vaccination should be considered in every annual health check, except in regions where FeLV infections are known to be exceedingly rare. Only FeLV-negative cats should be vaccinated. A range of FeLV vaccines is available, including inactivated whole virus and subunit vaccines, both of which are adjuvanted, and a recombinant, virus-vectored (attenuated canarypoxvirus), non-adjuvanted product. These vaccines provide protection against progressive FeLV infection and associated diseases but may not protect against all outcomes of FeLV infection (Little et al., 2020).

Adult cats with an unknown or incomplete vaccination history are frequently presented for vaccination. A single dose of MLV FPV vaccine would be sufficient to induce long-lasting immunity in a large majority of pet cats over 26 weeks of age. However, most manufacturers of MLV vaccines that contain FPV, FHV and FCV recommend two doses, 2 to 4 weeks apart. Given that MLV FHV and FCV vaccines are less potent than MLV FPV vaccines, the VGG supports this recommendation. Importantly, if *inactivated* core vaccines are used (FPV, FHV, FCV, FeLV), it is recommended that two doses be provided to immunise.

Non-core vaccines for pet cats

Summary information about non-core vaccines for cats is provided in Table 2.

Non-core vaccines for cats include those that protect against *Chlamydia felis*, *Bordetella bronchiseptica* and Feline Immunodeficiency Virus (FIV).

Vaccines against *C. felis* provide incomplete protection against infection and disease. They can be recommended for use in cats that live in multi-cat households where this pathogen is known to have previously caused disease. Live attenuated and inactivated adjuvanted parenteral vaccines are available. These may be used in kittens from 8 to 9 weeks of age with a second dose 2 to 4 weeks later, and an annual booster for adult cats at continuing risk of exposure.

The feline *B. bronchiseptica* vaccine available in some countries can be considered for use in cats living in high-risk situations, for example, cats kept in large colonies. The vaccine is an attenuated intranasal product that may be used as a single dose in kittens over 4 weeks of age, with annual boosters.

Only one FIV vaccine has ever been licensed. It has never been licensed in Europe and, in 2017, it was taken off the market in the USA and Canada. This vaccine remains available in Japan, Australia and New Zealand. Although efficacy of this vaccine against experimental, heterologous FIV challenge has been shown, there has long been debate about whether it can effectively cross-protect against the many different subtypes of FIV found in different geographical areas (Beczkowski et al., 2015; Coleman et al., 2014; Dunham et al., 2006; Hosie et al., 1995; Stickney et al., 2020; Westman et al., 2022; Yamamoto et al., 2007). Experimental studies have shown conflicting results, some showing strong protection afforded by this vaccine and others showing absence of protection. An excellently designed retrospective field study was carried out in Australia (Westman, Malik, et al., 2016a). The resulting research paper reported a protective rate of 56% in vaccinated cats. However, the study lacked statistical power. The confidence interval in the study was very large (20 to 84%) and the difference in infection rates between vaccinated and unvaccinated cats was not statistically significant. A more recent field study showed a lack of vaccine-induced protection in a New Zealand context (Stickney et al., 2020). Neither of these studies provided compelling evidence of efficacy or lack of efficacy of this vaccine in two distinct field contexts. Further research is needed.

In the meantime, the VGG has decided to continue to categorise the sole commercially available FIV vaccine as "non-core." By far the most effective way to protect cats from FIV infection is to restrict their unsupervised access to the outdoors, where they may be at risk of being bitten by FIV-infected cats. However, some owners cannot be persuaded to protect their cats by restricting them to the indoors or within protected outdoor enclosures.

Until recently, use of this FIV vaccine complicated diagnosis of FIV infection. Vaccination leads to the production of antibodies, presence of which is typically used to make a diagnosis of FIV infection (Westman et al., 2022). Fortunately, there are commercially available, in-practice antibody detection test kits that can discriminate between FIV infected and uninfected cats, so long as testing is not done soon after vaccination (Westman et al., 2017). Polymerase chain reaction (PCR) testing for the diagnosis of FIV infection has also become more reliable and more widely available (Nichols et al., 2017).

The FIV vaccine is an inactivated, adjuvanted product that may be given to kittens from 8 weeks of age with two further injections 2 to 3 weeks apart, followed by a 12-month injection. Annual revaccination is recommended thereafter for cats at continued risk of exposure. Given the strong likelihood of incomplete protection afforded by the vaccine, annual retesting is warranted. Only uninfected cats should be vaccinated.

The VGG is aware that, in some countries, only multi-component products containing core and non-core vaccine combinations are available for cats and would encourage manufacturers to make a full range of vaccines available wherever possible or, at the very least, make a core-only combination available for use in situations where use of non-core vaccines is unjustified.

Recommendations for vaccination of immunocompromised cats have recently been provided in an excellent review (Hartmann et al., 2022).

Not recommended vaccines for cats

Summary information about vaccines commercially available but not recommended for use in cats is provided in Table 2.

The vaccine against feline infectious peritonitis (FIP) is not recommended for cats. There is insufficient evidence that this FIP vaccine induces clinically relevant protection. Only cats known to be feline coronavirus antibody-negative at the time of vaccination are likely to develop some level of protection. This vaccine is labelled for administration from 16 weeks of age, but many kittens become infected with coronaviruses before this age. Moreover, this vaccine contains a serotype II strain of FIP virus that does not induce cross-reactive protection to serotype I, the strain that predominates in America and Europe.

Feline vaccines intended to protect against *Giardia* spp. and *Microsporum canis*, available in some parts of the world, are also not recommended because there is insufficient scientific evidence that they provide benefit.

VACCINATION OF DOGS AND CATS IN SHELTERS AND SANCTUARIES

There are two basic types of shelter for housing homeless animals: *traditional shelters* that provide temporary housing pending placement into homes and *sanctuaries* where animals remain for life. The traditional shelter population has a higher turnover rate and short periods of residence with constant arrival and departure of animals. Sanctuaries have more stable populations based on long-term residence and low turnover. The average population in either type of shelter can range from a few dozen to hundreds of animals. Both types admit animals from random sources in the community, most of which have no prior veterinary care, substantially increasing the risk for introduction and spread of contagious diseases and establishment of endemic disease.

The high risk for disease exposure in shelters requires a robust vaccination programme that not only protects each animal but the population as a whole. What best serves individual animals in lower exposure risk home environments is not ideal for the high-risk shelter environment. According to the Association of Shelter Veterinarians' Guidelines for Standards of Care in Animal Shelters, 2nd Edition (The Association of Shelter Veterinarians, 2022) "*Shelter vaccine protocols differ from protocols used in private practice because shelter animals are subject to an increased risk of infectious disease… Key differences in [shelter vaccine] protocols compared to those recommended in private practice include an earlier and longer age range for juveniles, a shorter time span between vaccines, and different core and noncore products.*"

For shelters, the risk assessment for determining which vaccines to administer, which animals receive them, and when they are received is conducted for the entire population, not just for each individual animal. There are three components of a best practice shelter vaccination programme critical to protection of both individuals and the entire population:

1. Vaccinate all animals at admission with core vaccines;
2. Use vaccines that induce rapid protection; and
3. Start primary vaccination of juvenile animals at 1 month of age and repeat every 2 to 3 weeks while in the shelter until 5 months of age.

CDV, CPV and FPV commonly cause life-threatening illness in dogs and cats in shelters. Every shelter is a high-risk environment for exposure to these pathogens and most have been affected by costly outbreaks in terms of animal suffering and death. While CDV, CPV and FPV infections cause highest mortality, contagious respiratory infections are the most frequently occurring form of illness in shelters. *B. bronchiseptica*, CAV-2, CPiV and CDV are prevalent respiratory pathogens in shelter dogs (Day et al., 2020; Lavan & Knesl, 2015; Monteiro et al., 2016; Schulz et al., 2014; Sowman et al., 2018). FHV and FCV are the most prevalent respiratory pathogens detected in shelter cats (Bannasch & Foley, 2005; McManus et al., 2014).

Most puppies and kittens less than 6 months old, and 30% to 50% of adult dogs and cats, have little or no detectable antibody to CDV, CPV, FPV, FHV and FCV on admission into shelters in the USA (DiGangi et al., 2012; Fischer et al., 2007; Lechner et al., 2010; Litster et al., 2012). This indicates that many animals enter shelters with inadequate protection against the most common diseases. For this reason, early immunisation of as many individuals as possible is paramount to disease control in shelters. The cornerstone is vaccination of *all dogs and cats immediately upon admission*. A delay of even 1 day can significantly increase the risk for infection and spread of disease within the population (Bannasch & Foley, 2005). Delays in vaccination have greater consequences for animals in shelters than in typical homes.

Core vaccines for shelter dogs and cats

Summary information about core vaccines for use in dogs and cats living in shelters is provided in Table 3 and Table 4, respectively.

Modified-live vaccines are considered the vaccines of choice for shelters because they are thought generally to provide faster onset of immunity and break through MDA interference sooner than do inactivated vaccines, important factors when exposure is likely to occur soon after admission (DiGangi et al., 2012; Fischer et al., 2007; Jas et al., 2009; Lappin, 2012; Lappin et al., 2009; Patterson et al., 2007). Core vaccines for dogs in shelters include modified-live CDV, CPV, CAV-2, CPiV and *Bordetella bronchiseptica*. The core vaccines for shelter cats are modified-live FPV, FHV and FCV.

Table 3. Core vaccines for dogs in shelters

Vaccines	<5 months old	≥5 months old	Comments
CDV+CAV+CPV+CPiV (MLV, parenteral) Recombinant CDV with MLV CAV+CPV+CPiV (parenteral)	Administer immediately at admission starting at 1 month of age Repeat every 2 to 3 weeks until 5 months old	Administer immediately at admission Repeat in 2 to 3 weeks	Use combination vaccines containing modified-live viruses or the recombinant CDV for more rapid onset of immunity
Bordetella bronchiseptica+CPiV (modified-live, intranasal) *B. bronchiseptica*+CPiV+CAV (modified-live, intranasal)	Administer immediately at admission starting at 3 weeks of age	Administer immediately at admission	Intranasal vaccines containing modified-live *B. bronchiseptica* and at least CPiV are preferred for rapid onset of optimum immunity. They can be given as early as 3 weeks of age
B. bronchiseptica (modified-live, oral) *B. bronchiseptica*+CPiV (modified-live, oral)	Administer immediately at admission starting at 7 or 8 weeks of age, depending on the vaccine chosen	Administer immediately at admission	The oral vaccines can be used in dogs 7 or 8 weeks of age and older, but the intranasal vaccine must be used for dogs that are younger
Rabies Virus (inactivated, parenteral)	Follow local laws for minimum age for vaccination. Administer at discharge for short-term stay shelters or at admission for long-term stay shelters		Rabies-endemic countries only. Administer according to local law

CDV Canine distemper virus, CAV Canine adenovirus type 2, CPV Canine parvovirus type 2, CPiV Canine parainfluenza virus, MLV Modified live virus

Table 4. Core vaccines for cats in shelters

Vaccines	<5 months old	≥5 months old	Comments
FPV+FHV+FCV (MLV, parenteral)	Administer immediately upon admission starting as early as 1 month of age	Administer immediately upon admission Repeat in 2 to 3 weeks	Use combination vaccines containing modified-live viruses for rapid onset of immunity
FPV (MLV, intranasal)	Repeat every 2 to 3 weeks until 5 months of age		Intranasal FPV vaccines are *not recommended* for use in shelters as they do not provide reliable protection against FPV
FHV+FCV (MLV, intranasal)			Intranasal vaccines containing modified-live FHV+FCV can be used for more rapid onset of immunity
Rabies Virus (inactivated, parenteral)	Follow local laws for minimum age for vaccination. Administer at discharge for short-term stay shelters or at admission for long-term stay shelters		Rabies-endemic countries only. Administer according to local laws or regulations

FPV Feline panleukopenia virus, FHV Feline herpesvirus-1, FCV Feline calicivirus, MLV Modified live virus

Vaccination of all dogs and cats on intake with the modified-live core vaccines should be comprehensive. This includes stray animals, owner-surrendered pets, animals impounded for rabies quarantine, cruelty cases, pregnant or lactating animals, animals with a mild illness or injury, and community dogs and cats admitted for trap-neuter-release (TNR) or return-to-field (RTF) programmes. While vaccination of pregnant, sick, or injured pets that live in typical homes with certain modified-live vaccines is not advised, the rapid protection afforded by these vaccines in the shelter environment outweighs the risk for harm to foetuses or the animal itself. In short, if a dog or cat cannot be safely vaccinated on admission with the modified-live core vaccines, the risk for infection is too great for that animal to stay in the shelter. For financial reasons, shelters may be tempted to vaccinate only those dogs and cats likely to be adopted and not vaccinate those at risk for euthanasia. Restricting vaccination to adoptable animals creates a large pool of susceptible animals with subsequent development of endemic disease and disease outbreaks that are costlier than vaccines.

Vaccination of puppies and kittens in home settings typically starts at 6 to 8 weeks of age with repeat vaccinations at 3- to 4-week intervals until at least 4 months of age. In contrast, vaccination of puppies and kittens entering shelters starts at 1 month of age with re-vaccination every 2 to 3 weeks to break through maternal antibody interference with as little delay as possible. Up to 37% of kittens and a less certain proportion of puppies have been shown to have persistent maternal antibody interference with response to one or more core vaccines beyond 4 months of age (Carmichael, 1983; Dawson et al., 2001; DiGangi et al., 2012; Jakel et al., 2012; Johnson & Povey, 1985; Kruse et al., 2010; Pollock & Carmichael, 1982; Reese et al., 2008). Therefore, based on a precautionary principle, shelter veterinarians recommend that vaccination of shelter puppies and kittens, with core vaccines, should be continued until 5 months of age. The precautionary principle is also the basis for the recommendation to give shelter-housed dogs that are over 5 months of age *two* doses of modified live core vaccine, 2 to 3 weeks apart.

While the *B. bronchiseptica* ±CPiV vaccine is a non-core vaccine for dogs in home environments, this is a core vaccine for dogs in shelters due to the high risk for exposure and transmission with consequent widespread morbidity. All adult dogs and puppies at least 3 weeks old should be vaccinated on admission with an intranasal, modified-live *B. bronchiseptica* vaccine that also contains modified-

live CPiV. These vaccines induce a rapid mucosal immune response against both pathogens within 3 to 7 days and significantly reduce clinical disease and pathogen shedding (Ellis et al., 2016, 2017; Jacobs et al., 2007; Kontor et al., 1981; Larson et al., 2013). When administration of the intranasal vaccine is not feasible, the oral *B. bronchiseptica* vaccine can be given to adults and puppies at least 7 or 8 weeks old (depending on which vaccine is chosen). This oral vaccine also includes CPiV in some countries. Studies have shown the oral vaccine to be almost as effective as the intranasal vaccine and both are superior to parenteral inactivated *B. bronchiseptica* vaccines containing cellular antigen extracts (Ellis et al., 2016, 2017; Jacobs et al., 2007; Kontor et al., 1981; Larson et al., 2013; Scott-Garrard et al., 2018). The intranasal and oral vaccines only need to be administered once at intake as they are not inactivated by maternal antibody and confer a 13-month DOI (Jacobs et al., 2005; Scott-Garrard et al., 2020). Vaccination of all shelter dogs on admission with a parenteral vaccine containing modified-live CDV, CAV-2 and CPiV coupled with the intranasal modified-live *B. bronchiseptica* and CPiV vaccine is associated with reduced occurrence of respiratory disease (Andrukonis et al., 2021).

Parenteral vaccines containing modified-live FPV must be used for shelter cats to induce rapid and robust immunity to this pathogen. Intranasal modified-live vaccines containing FHV and FCV are available in some countries. These induce rapid protection within 4 to 6 days, which is advantageous for cats in shelters (Edinboro et al., 1999; Lappin, Sebring, et al., 2006b).

Rabies virus is a core vaccine for dogs and cats in shelters in rabies-endemic regions. For shelters where animals stay for a short period of time, vaccination at the time of adoption is advisable to help ensure compliance with local rabies vaccination requirements. All dogs and cats that live in sanctuaries or are anticipated to stay in a shelter for many months, should be vaccinated against rabies at the time of admission according to local laws. Revaccination of dogs and cats in long-term shelters and sanctuaries should follow local laws.

Non-core vaccines for shelter dogs and cats

The *Borrelia burgdorferi* (Lyme disease) vaccine, leptospirosis vaccines and H3N8/H3N2 canine influenza vaccines are non-core vaccines with restricted use for dogs in shelters. If the exposure risk is high based on documented cases in the local community or even within the shelter population, the primary vaccination series should be started for every dog in the shelter and every new dog on admission according to manufacturer instructions. In short-term-stay shelters, many dogs leave the shelter before finishing the primary vaccination series and adopters should be encouraged to pursue follow-up vaccination with their veterinarian. Where indicated by substantial risk for exposure, the *Borrelia*, leptospirosis or CIV vaccines should be included in the vaccination programme for dogs in a long-term care shelter such as a sanctuary where they remain for life, or when a long-term shelter stay of many months is anticipated.

The FeLV vaccine is a non-core vaccine for cats in shelters. According to the 2020 AAFP Feline Retrovirus Testing and Management Guidelines (Little et al., 2020), all cats should be tested for FeLV infection before FeLV vaccination: "*If a vaccinated cat's status is unknown and the cat is later determined to have a FeLV infection, vaccine efficacy would be questioned, and vaccine failure suspected. Cats should be tested for FeLV infection before initial vaccination*." Well-resourced shelters may elect to test and vaccinate every uninfected cat, but FeLV testing and vaccination is not necessary for individually housed cats in less well-resourced shelters due to the low risk of viral transmission (Little et al., 2020). For these shelters, adopters should be advised to discuss testing and vaccination with their veterinarian. In shelters that group-house cats, FeLV testing is essential for identifying uninfected cats to place in the group. FeLV vaccination of group-housed cats is based on length of stay. This vaccine is recommended for group-housed cats in long-term stay shelters or sanctuaries, but is not recommended for group-housed cats in short-term stay shelters (Little et al., 2020). Adopters of unvaccinated cats from these shelters can discuss with their veterinarian whether to vaccinate based on the cat's lifestyle in the new home (Little et al., 2020).

Bordetella bronchiseptica and C. felis vaccines are non-core vaccines for cats in shelters because these bacterial infections are less prevalent causes of respiratory infections. The intranasal modified-live *B. bronchiseptica* vaccine for cats is warranted when shelters have coughing cats with pneumonia due to confirmed *B. bronchiseptica* infection (Williams et al., 2002). In this circumstance, the intranasal modified-live vaccine should be given to all cats at least 1 month old on admission for a period of several months to build up population immunity and stop transmission of the pathogen. Similarly, the *C. felis* vaccine may be part of an infection control programme in shelters where disease caused by *C. felis* infection has been confirmed. Interspecies transmission between dogs and cats can occur with *B. bronchiseptica*. Shelters having problems with *B. bronchiseptica* in cats should consider the possibility of interspecies transmission if the shelter also houses dogs, or if staff handle both dogs and cats.

The practice of simultaneously vaccinating and neutering dogs and cats in shelters and in TNR or RTF programmes is widespread. While vaccination ideally should be separated from procedures such as neutering, several studies have demonstrated that anaesthesia and surgery do not significantly impair antibody responses to vaccination (Fischer et al., 2007; Kelly, 1980; Miyamoto et al., 1995; Reese et al., 2008).

ADVERSE EVENTS FOLLOWING VACCINATION (AEFVs)

Adverse events are detrimental, unintended consequences that follow vaccine administration (including lack of protection). They include any hypersensitivity reaction, illness, injury, or apparent toxic effect. Local reactions such as pain and swelling at the injec-

tion site and systemic reactions such as lethargy, anorexia, fever and vomiting are commonly observed (Miyaji et al., 2012; Moore et al., 2005, 2007; Yoshida et al., 2021, 2022). Urticaria and anaphylaxis are less common (Tizard, 2021). AEFVs should be reported *even when their association with vaccination is only suspected*. Each vaccine adverse event report should identify the implicated vaccine product (including batch number), details of the animal involved, details of the adverse event and contact details of the veterinarian submitting the report.

Veterinarian-reported field observations of suspected AEFVs are the most important way that manufacturers and regulatory authorities can be alerted to potential vaccine safety or efficacy problems. Pre-licensure safety studies will only detect relatively common adverse events. Rarer adverse events are detected through post-marketing surveillance and analysis of reported adverse events. Reports should be sent to the manufacturer and to the local regulatory authority. In some countries government surveillance schemes do not yet exist and therefore AEFVs can only be reported to the manufacturer. The VGG recognises that there is gross under-reporting of AEFVs. This impedes growth of knowledge about the safety and efficacy of vaccine products. The VGG actively encourages all veterinarians to participate vigorously in reporting suspected vaccine-associated adverse events.

Lack of expected efficacy of a vaccine is an adverse event. As explained previously, a very common cause in young animals is interference caused by maternally transferred colostral antibodies. However, there are other important causes. Poor vaccine husbandry, a surprisingly common problem, may be responsible. Practices should consider nominating specific staff members to be responsible for overseeing, monitoring and reporting upon vaccine husbandry. Vaccines that are batch-reconstituted and left to stand for hours before being drawn up and injected may lose potency. This particularly affects the more fragile vaccine components, such as CDV. Vaccines placed in the refrigerator too close to the freezer compartment may freeze, losing potency. Old refrigerators are especially prone to this and may also have defective seals, so that vaccines are not stored at a sufficiently low temperature (generally 2 to 8°C). Use of multidose vials (*e.g.* 10 rabies vaccine doses in a single vial) may be associated with lack of efficacy if a vaccine suspension is not adequately mixed before each and every dose is drawn up. This may also cause overdosing of some recipients, increasing the probability of other kinds of adverse event, such as hypersensitivity reactions or pain at the time of injection and post-vaccinal swellings.

Given the unique, enormous, almost 100-fold, variation in size and bodyweight of adult domestic dogs, it is interesting that vaccine manufacturers continue to recommend that adult dogs of all sizes receive the same dose of vaccine (Tizard, 2021). In addition, for most vaccines, the dose supplied for young puppies is identical to what is supplied for much larger and more mature adults. Conversely, for humans, it was recently decided that smaller doses of COVID-19 vaccine should be supplied for young children as compared with adults. Geriatric adults receive higher doses of influenza vaccines.

Provision of identical doses to dogs of all sizes and ages remains current, standard practice, and the VGG is *not* encouraging veterinarians to deviate from manufacturers' advice in this regard. However, it is noteworthy that small dogs are the ones more prone to experience post-vaccinal adverse events (Moore et al., 2005; Yao et al., 2015). The adverse reaction rate also increased as more, separate vaccines were given at the same visit. Large and giant dogs are less likely to mount a sufficient immune response to rabies vaccination than are small dogs (Jakel et al., 2008; Tizard, 2021). In one study, bodyweight was inversely correlated with the magnitude of anti-CPV and anti-CDV antibody responses; that is, small dogs mounted stronger antibody responses than did large and giant ones, although adequate, protective responses were produced by dogs of all sizes (Taguchi et al., 2012). Recent work done in the USA on a very large population of dogs (nearly 5 million) has shown that breed appears to be a determinant of the likelihood of AEFVs, independent of bodyweight (Moore et al., 2023). Some breeds of dog have a much higher risk of experiencing acute AEFVs than does the general population. French Bulldogs, Dachshunds and Boston terriers, were at highest risk. Small dogs (<5 kg bodyweight) that received multiple vaccines per visit were at particular risk. More research is needed into appropriate vaccine doses for individual dogs, given the enormous size and breed variations among domestic dogs.

In future, the definition of AEFVs may be broadened to include more explicitly some rare, potential or actual adverse health consequences of pet vaccination for immunocompromised *owners*. For example, mucosally administered modified live bacterial vaccines (such as some of the *B. bronchiseptica* vaccines) have recently been suggested to represent a health hazard for some humans, including those with cystic fibrosis (Moore, Rendall & Millar, 2022). Although the risk appears small, it has been suggested that it might be prudent to ask immunocompromised client pet owners to leave the consulting room while modified live *B. bronchiseptica* mucosal vaccines are being administered (Weese, 2021). This begs the question: how would the veterinarian know which clients to ask to leave the room? Questioning clients about their immunological health is not yet common practice in companion animal medicine (although occasionally clients volunteer this sort of information). Use of subunit or inactivated *B. bronchiseptica* vaccines would presumably be safer for immunocompromised pet owners, assuming equivalent protection is provided by these vaccines (Ellis, 2015).

Feline injection-site sarcomas

Vaccines and other injected products have been implicated in the pathogenesis of feline injection-site sarcomas (FISS; Carminato et al., 2011; Srivastav et al., 2012). FISS has been the subject of much research with multiple reviews on the subject (Hartmann et al., 2015; Kass, 2018; Stone et al., 2020; Zabielska-Koczywas et al., 2017). Particular attention was initially focused on the at-the-time novel adjuvanted FeLV and rabies vaccines. Seminal work showed that these vaccines were associated with FISS development

(Kass et al., 1993). Although the aetiopathogenesis of FISS remains uncertain, there is some evidence that adjuvanted vaccines may be more implicated than are non-adjuvanted ones (Hartmann, 2021; Srivastav et al., 2012; Stone et al., 2020), although some experts contend that this evidence is not compelling (Kass, 2018; Stone et al., 2020). Some vaccine adjuvants cause inflammation. It has therefore been conjectured that mesenchymal cells within a localised, chronic, inflammatory reaction undergo malignant neoplastic transformation (Day, Schoon, et al., 2007b; Stone et al., 2020). Feline ocular post-traumatic sarcomas, which usually develop after head trauma, often many years afterwards, may have a comparable aetiopathogenesis (Wood & Scott, 2019). Cats are especially predisposed to these forms of neoplasia (as compared with dogs and humans).

Most subcutaneous injections (including of vaccines) have traditionally been given into the interscapular furrow of the cat. This remains a challenging anatomical location for FISS development. The infiltrative nature of these tumours means that radical surgical resection is often attempted. When the tumour originates in the interscapular space, this is often unsuccessful (Muller & Kessler, 2018). To improve the chances of cure, adjunctive treatment modalities are often used together with surgery (immunotherapy, antineoplastic chemotherapy, radiation therapy; Zabielska-Koczywas et al., 2017). This is expensive and often unsuccessful. Masses growing in the interscapular furrow may not be detected until they become quite large. It is recommended not to make subcutaneous injections in this anatomical location in cats.

In North America, in response to the recognition of FISS, and a view that certain vaccines were more implicated than others, a recommendation of "left leg leukaemia" (*i.e.* FeLV vaccines) and "right leg rabies" (*i.e.* rabies vaccines) was made and was widely adopted. The hind legs were initially chosen and injection as far distal as possible, preferably at or below the stifle, was recommended. Many American veterinarians have become proficient at vaccinating cats subcutaneously in these anatomical locations over the last three decades. This remains a recommended anatomical location for vaccine injection in the current AAHA/AAFP feline vaccination guidelines (Stone et al., 2020). The VGG strongly endorses this approach. Subcutaneous injection of vaccines is preferable to the intramuscular route because an intramuscular FISS is generally more difficult to detect than a subcutaneous FISS.

However, in some countries where FISS is perceived or known to be much less prevalent than in North America, there is reluctance among veterinarians to carry out distal limb injections of feline vaccines. In one country, a recommendation to vaccinate 4 cm lateral to the dorsal midline, over the convexity of the shoulder musculature, was recently made by a local guidelines group, with practitioner input (Westman et al., 2022). This suggestion was not based on an incorrect belief that surgical resection of advanced FISS from that anatomical location would likely be curative. The logic was to ensure that any growing post-vaccinal masses would be more prominent and thus likely to be detected far earlier than they would be in the interscapular furrow, enabling much earlier investigation and therapy with, presumably, greater likelihood of therapeutic success. Distal limb injection of vaccines remains a gold standard approach and its adoption should be strongly encouraged.

The VGG strongly endorses and recommends the "3-2-1" rule or approach presented in the 2020 AAHA/AAFP Feline Vaccination Guidelines (Stone et al., 2020). Any post-vaccinal mass that (1) remains present 3 months after vaccination; or (2) is larger than 2 cm in diameter at any time point; or (3) is still increasing in size 1 month after vaccination should undergo incisional biopsy. Incisional rather than excisional biopsy is recommended, because if the diagnosis is FISS, surgical excision of that tumour will need to be radical and will likely involve extensive surgery, which is much less appropriate for a diagnostic biopsy.

In 2014, a study showed the efficacy of administering FPV and rabies vaccines into the tail of cats (Hendricks et al., 2014). Adult cats from a community TNR programme were given trivalent MLV core vaccine (FPV, FHV, FCV) into the distal third of the dorsal tail with inactivated rabies vaccine administered 2 cm distal to the site of the trivalent vaccination. Seroconversion occurred in all cats to FPV and all but one cat for rabies virus. Tail vaccination was reported to be well tolerated by the cats in this small study. Tail injection may in future prove to be an alternative to distal limb injections but further study of tail vaccination will be required.

The VGG makes the following comments and recommendations about FISS and anatomical locations for injection of cats:

- Subcutaneous injections should *not* be made into the interscapular furrow of cats.
- Vaccines should not be injected intramuscularly if subcutaneous injection is a legal alternative.
- Vaccines should be administered into different anatomical sites on each occasion of use.
- It is not clear that any kinds of vaccine are completely safe.
- Any risk of FISS is far outweighed by the benefits of protective immunity conferred by vaccines.
- FISS develops rarely and may be much less prevalent in some countries and regions than in others (Dean et al., 2013).
- Although the role of adjuvants and chronic inflammation in the aetiopathogenesis of FISS is unclear, there is some evidence to implicate adjuvanted vaccines over non-adjuvanted ones (Hartmann, 2021; Srivastav et al., 2012). Experts disagree about how to interpret this evidence. Some experts consider this evidence so weak that they do not favour one kind of feline vaccine over another (Stone et al., 2020). However, the VGG concurs with other experts (Hartmann, 2021) and recommends that use of non-adjuvanted feline vaccines should be favoured over adjuvanted vaccines in countries where FISS is known to occur and where alternative vaccine choices are available. If no acceptable alternatives are available, it is much preferable to vaccinate with an adjuvanted product than not at all.
- The anatomical site of injections should be recorded in the patient's medical record or on the vaccination card, including by use of a diagram, indicating which products were administered on any one occasion. The sites should be "rotated" on each occasion. Alter-

natively, a practice might develop a group policy that all feline vaccinations are administered to a specific site during one calendar year and this site is then changed for the following year.
- The VGG encourages all cases of suspected FISS to be notified via the appropriate national reporting route(s) for suspected adverse reactions or to the vaccine manufacturer.

FREQUENTLY ASKED QUESTIONS (FAQS)

Questions about vaccines and their use

Q. For how long can I expect a dog to be protected against disease, if I use the MLV core vaccines to protect against CDV, CAV and CPV, as recommended in these guidelines?
A. There is strong evidence that quality-assured canine core MLV vaccines that have been properly transported and stored will protect robustly for at least 3 to 4 years. In addition, challenge studies that were not described in detail were reported to indicate that immunity persists for at least 7 years (Schultz, 2006; Schultz et al., 2010).

Q. For how long can I expect a cat to be protected against disease, if I use the MLV core vaccines to protect against FPV, FCV and FHV as recommended in these guidelines?
A. There is strong evidence that quality-assured feline core MLV vaccines that have been properly transported and stored will protect robustly against FPV for at least 3 to 4 years. Partial, but clinically significant protection against challenge was provided for FCV and FHV by an inactivated vaccine for up to 7.5 years (Scott & Geissinger, 1999). However, these cats were in a stress-free housing situation when they were challenged. In general, MLV FCV and FHV vaccines are thought not to provide such potent, long-lasting protection as can MLV FPV vaccines.

Q. Do currently available *Leptospira* vaccines provide long lasting immunity, like the canine core MLV vaccines?
A. Not to the same extent. Currently available *Leptospira* vaccines (bacterins) provide relatively short-term immunity, thought to be less than 18 months. Several challenge studies have demonstrated protection lasting at least 12 to 14 months (Klaasen et al., 2003, 2014; Minke et al., 2009).

Q. Can I give all of the needed vaccinations at once to an adult dog or cat presented with no previous history of vaccination?
A. Yes, a healthy dog or cat should be able to respond to multiple vaccine antigens delivered concurrently. Indeed, government authorities in some regions have required manufacturers to prove that concurrent use of two or more vaccine products is safe and efficacious. This proof may be mentioned in the product leaflet. Importantly, you should never mix different vaccines in the same syringe unless this is supported in the product leaflets. It is recommended to inject different vaccines in different anatomical sites.

Q. Can some vaccines successfully immunise puppies at a younger age than others? I am concerned about puppies that probably still have some MDA against CDV, CAV or CPV, which might interfere with vaccination.
A. Yes, vaccines do differ in this respect. Some MLV and recombinant vaccines are more immunogenic than others and therefore able to break through maternal interfering immunity earlier. This may be because an especially immunogenic viral strain is included in the vaccine and/or because a larger than usual mass of virus is included in each vaccine ampoule.

Q. I have been told that certain canine core MLV vaccine products need only be given twice, with the second dose given as early as 10 weeks of age. Is that what your guidelines recommend?
A. No, it is not. Although some vaccines can indeed break through MDA at an earlier age than do others, a routine 10-week finish is not advised. The VGG is aware that certain vaccines for puppies in some countries are licensed for such an "early finish," supposedly to facilitate early socialisation. Puppy socialisation is of great importance and can generally be begun prior to completion of the puppy vaccination series. This has been shown to be safe for CPV when done properly (Stepita et al., 2013). The VGG advises that, whenever possible, the last dose in the puppy vaccination series be given at 16 weeks of age or older, regardless of the number of doses given earlier. Owners of puppies that have not completed a full puppy vaccination series should socialise them under controlled conditions (Stepita et al., 2013) but carefully prevent exposure of their puppies to potentially contaminated environments outside of the home and only permit contact with healthy puppies and fully vaccinated adult dogs.

Q. At what age should the last kitten/puppy MLV core vaccination be given?
A. The VGG recommends no earlier than 16 weeks of age; 18 to 20 weeks may be more appropriate in regions where there is a particularly high risk of exposure. After that, the VGG recommends revaccination with a core MLV vaccine at 26+ weeks of age.

Q. Do currently available CPV vaccines provide protection from disease caused by CPV-2c in dogs?

A. Yes, currently available MLV and recombinant CPV vaccines can stimulate an active immune response that provides long term protection against the currently circulating CPV variants (2a, 2b and 2c). This is assuming the vaccine has been used in accordance with these guidelines.

Q. The refrigerator in which I store my vaccines is getting rather old. Should I be concerned?
A. Not necessarily, but you should check regularly that your old refrigerator is still controlling its internal temperature reliably. In some parts of the world such checks are a veterinary hospital accreditation requirement: daily temperatures must be measured and recorded in a logbook. It is important that vaccines be stored between 2 and 8°C. They must not be frozen. In some refrigerators, items stored on the shelves immediately below or beside the freezer compartment may become too cold and may even freeze. If this old refrigerator is no longer reliable and is unable to hold its internal temperature between 2 and 8°C, it should be repaired or replaced.

Q. In the practice where I just started to work, the nurses routinely reconstitute multiple doses of vaccine prior to the beginning of each consultation period. Is this a good idea? How long can a reconstituted MLV vaccine sit at room temperature without losing some activity?
A. It is not a good idea. At room temperature, some of the more sensitive vaccine components (*e.g.* CDV, FHV) may lose their ability to immunise after several hours, whereas other components are more likely to remain immunogenic for several days (*e.g.* CPV, FPV). The VGG advises that MLV vaccines be reconstituted immediately or shortly before use.

Q. Should I give a *Leptospira* vaccine to each dog every 6 months? I work in a high-risk area and I see cases from time to time.
A. Considering licensed, quality-assured *Leptospira* vaccines, there is no clear evidence that 6-monthly revaccination confers greater protection that does annual revaccination, even in high-risk areas. Conversely, there is evidence of robust protection for 12 to 14 months and perhaps longer.

Q. How do I decide which *Leptospira* vaccine to use in the region where I live and work?
A. If you work in one of the many parts of the world where canine leptospirosis is endemic, the VGG recommends that you view *Leptospira* vaccines as "core". Hopefully, in the region where you work, implicated *Leptospira* serogroups will have been studied and suitable vaccines, able to protect against members of those serogroups, will have become commercially available. There may be some cross-protection between serogroups but this has not been studied in detail. A licensed vaccine that contains a member of as many as possible of the most frequently implicated serogroups, relevant in your particular region, would be preferred. Unfortunately, in too many countries and regions, there is insufficient knowledge about which serovars and serogroups are locally important and cause disease in dogs in those locations. The VGG would encourage collection of such data because it should help in development of optimised vaccines.

Q. For an adult dog with an unknown *Leptospira* vaccination history, what is the recommended vaccination protocol? Is it still two doses 2 to 4 weeks apart as in puppies?
A. Yes, this dog would require two doses of vaccine given 2 to 4 weeks apart and then annual revaccination thereafter.

Q. If a dog received its last *Leptospira* vaccine 18 or more months ago, do I need to recommend starting the series of vaccinations again (*i.e.* two doses 2 to 4 weeks apart)?
A. Although evidence supporting this recommendation is sparse, the answer is "yes" based on a precautionary principle.

Q. Would it not be better to use core vaccines that contain locally important strains rather than vaccines optimised for pet animals in other countries?
A. This is certainly true for *Leptospira* vaccines, but it is not true for vaccines to protect against CDV, CAV, CPV, FPV, FHV, FeLV and rabies virus. For these viruses, it seems that vaccines manufactured in one part of the world can protect pets satisfactorily around the world. In the case of FCV, there is enormous genetic variability, even within one country. There is no FCV vaccine available that can protect against all FCV strains. If FCV-related disease develops in a fully vaccinated cat, switching to a different vaccine brand, which contains different strain(s), has been suggested (Hofmann-Lehmann et al., 2022) and may be helpful.

Q. Will the number of different antigens in a multivalent vaccine adversely affect the efficacy of that vaccine?
A. No. The immune system of a typical, healthy dog or cat is assailed by a large number of different antigens every day and copes well. For a multivalent vaccine to be licensed, the manufacturer must prove that each component of the vaccine can induce protective immunity, generally in challenge studies.

Q. Why are canine coronavirus (CCoV) vaccines designated as "not recommended" in these guidelines?
A. The VGG does not recommend the use of CCoV vaccines as there is insufficient evidence that these vaccines provide useful protection (Pratelli et al., 2003). CCoV infection of puppies often occurs early in life, sometimes before routine vaccination is started. The diarrhoea associated with CCoV infection in puppies is usually mild. Dogs vaccinated parenterally do not seem to

develop a protective intestinal IgA antibody response. There is insufficient evidence that CCoV is a prevalent cause of severe intestinal disease in adult dogs. CCoV/CPV co-infections do occur, but can be prevented by properly vaccinating against CPV. Variant strains of CCoV have occasionally been reported to cause severe vomiting or systemic disease in adult dogs and puppies (Decaro & Buonavoglia, 2011; Radford et al., 2021), but there is scant evidence that the available CCoV vaccines would protect against such variant strains.

Q. Does glucocorticoid treatment in the cat or dog interfere substantially with development of vaccine induced immunity?
A. Studies in both species have indicated that anti-inflammatory and even immunosuppressive glucocorticoid treatment before or concurrently with vaccination does not have a substantial suppressive effect on antibody production in response to vaccines (even first vaccines in puppies; Nara et al., 1979). However, revaccination is recommended after glucocorticoid therapy has ended, especially if glucocorticoid was administered during the initial series of core vaccines. Recommendations concerning glucocorticoid dosing, tapering and duration of treatment vary, depending on indication and clinical judgement. For short courses of glucocorticoid, revaccination should be performed at least 2 weeks after cessation. For longer courses, this interval should be extended up to 3 months. If glucocorticoids are being used to treat a substantial illness, vaccination should be delayed until the animal has been returned to normal health. If discontinuation of therapy is not feasible, vaccination should only be performed when the disease has been well controlled by a stable dose of glucocorticoids over a period of several weeks. The unwell animal should be managed so as to avoid risk of exposure while it is unprotected. Serological testing using gold standard techniques (for CPV, CDV, CAV and FPV as appropriate) can be employed in glucocorticoid recipients and will often provide reassurance that animals are not left unprotected against core diseases during glucocorticoid therapy, or that revaccination is not required after cessation of therapy.

Q. Should I vaccinate a pet that is receiving potent immunosuppressive or antineoplastic therapy (other than or in addition to glucocorticoids)? The underlying disease for which this pet is being treated is under good control (perhaps in complete remission) and the animal appears healthy.
A. This is a situation where the advice of a clinical specialist should be sought. A clinical oncologist or immunologist could be helpful. In the past, a blanket recommendation not to vaccinate such an animal may have been provided, even though reports of vaccine-related adverse events in this subset of patients are sparse. The EB underlying these suggestions is slim but the topic has also been comprehensively reviewed, including comparative data from murine and human models, to supplement canine and feline data (Hartmann et al., 2022). According to these guidelines, a more nuanced, individualised approach is offered for consideration to accommodate the multiple drugs involved in such regimes, targeting different components of the immune response. For example, some traditionally "myelosuppressive" (cytotoxic) drugs can even be immunostimulatory rather than immunosuppressive in specific contexts.

Regarding the core MLV vaccines, and assuming the pet was thoroughly vaccinated as a puppy/kitten, it would be best to wait. MLV vaccines are generally avoided in human patients receiving potent immunosuppressive drugs. This pet is likely to be already protected by its previous core MLV vaccinations. In one study, significant changes were not detected in CDV, CPV and rabies virus titres following chemotherapy in tumour-bearing dogs (Henry et al., 2001). Use of serological testing using gold standard techniques is encouraged in this context and will often provide reassurance that immunity to some or all of the core vaccine antigens remains intact, reducing the number of diseases being considered for revaccination. If needed, revaccination with core MLV vaccine could be done no earlier than 3 months after the end of potent immunosuppressive or antineoplastic therapy.
A study of cats treated with high-dose ciclosporin demonstrated normal serological responses to FPV and FCV vaccines given during treatment, but delayed responses to FHV, FeLV and rabies. In contrast, treated cats failed to develop antibody after a primary course of FIV vaccine, suggesting that ciclosporin treatment may impair primary, but not memory, vaccinal immune responses (Roberts et al., 2015).

Regarding vaccination against leptospirosis in dogs, the owner may wish to maximise the dog's quality of life by continuing to enjoy some water-related activities. Canine leptospirosis is endemic in many parts of the world. Immunosuppressive therapy may reduce the efficacy of a leptospirosis vaccine, but not necessarily, especially if the dog was vaccinated against leptospirosis a year earlier. The dog may retain immunological memory. A bacterin vaccine is less likely to cause harm than a MLV vaccine. Inactivated vaccines are used in severely immunocompromised human patients (Ljungman, 2012).

Q. Should I vaccinate a cat persistently infected with FeLV or FIV (or both) that appears clinically well?
A. FeLV-infected cats should not be vaccinated against FeLV and FIV-infected cats should not be vaccinated against FIV because vaccination does not benefit cats that are already infected. In healthy-appearing retrovirus-infected cats, all other vaccination decisions (*i.e.* which vaccines and how often) should be based on an individualised risk–benefit assessment. Vaccination should not be avoided in retrovirus-infected cats. It may be prudent to choose to use inactivated or recombinant vaccines rather than MLV vaccines (Hartmann et al., 2022) although evidence of harm caused by MLV vaccines in retrovirus-infected cats is very sparse. Ideally, retrovirus-infected cats should be kept indoors, or in protected outdoor enclosures, to minimise the risk they pose to other outdoor cats and to minimise their exposure to other infectious agents. Retrovirus-infected cats can develop especially

severe disease if they become co-infected by FPV, FCV and or FHV, so protection against these viruses is important. In general, FeLV is more pathogenic than FIV. It has been suggested that even 100% indoor FeLV-infected cats need annual revaccination against FHV, FCV and FPV (Hartmann et al., 2022). FIV-infected cats that are allowed outdoors also need annual revaccination against these core agents. FIV-infected cats that live 100% indoors can be vaccinated less frequently against these core agents (*e.g.* triennially). In regions where rabies is endemic, vaccination against rabies should follow local regulations, as normal. Vaccination against the "other" retrovirus, in indoor-outdoor cats infected by FIV or FeLV alone, may also be considered. Management of other cats that live in multi-cat households with one or more retrovirus-infected cats has been reviewed elsewhere (Little et al., 2020).

Q. Should I vaccinate every week if an animal is at very high risk of disease (for example, in a shelter setting)?
A. This is not recommended in these guidelines, nor in others, although a published EB is lacking. Concerns expressed are that too-frequent revaccination of puppies may not allow sufficient time for immunological responses to develop properly and that vaccine antigen may bind to MDA, diminishing protection in young puppies and kittens. Although evidence is lacking, concerns have also been expressed about the potential development of immunological tolerance (*i.e.* hyposensitization) which would be the opposite of what is desired.

Q. Should I vaccinate puppies that are less than 4 weeks of age?
A. In general, no. Most puppies of this age will have MDA that can block the ability of vaccines to immunise. Moreover, vaccine product leaflets do not support this practice and parenteral MLV vaccines may cause harm in such young animals. One exception is the use of intranasal vaccines against CIRDC. These can be given safely from 3 weeks of age.

Q. In aggressive dogs, can I inject the modified live intranasal *Bordetella* vaccine subcutaneously and expect a good result?
A. Absolutely not. The modified live intranasal *Bordetella* vaccine can cause a severe local reaction if injected subcutaneously. It may even cause severe systemic disease (*e.g.* a hepatopathy) and lead to the death of the animal.

Q. Can I give intranasally a killed *Bordetella* vaccine intended for subcutaneous injection?
A. No. This will not stimulate an effective immune response and may cause unnecessary discomfort.

Q. If a puppy sneezes after an intranasal vaccination, is it necessary to vaccinate again?
A. Sneezing, with loss of some of the vaccine, is commonly observed after the use of intranasal products. These vaccines have been designed to allow for partial loss of the product and so it should not be necessary to revaccinate unless it is clear that none or very little of the product was delivered successfully.

Q. What precautions are necessary when using injectable MLV FHV/FCV vaccines in cats?
A. Avoid aerosolising any of the modified live FHV/FCV vaccines intended for subcutaneous or intramuscular injection. For example, do not flick the syringe and attempt to squirt out any tiny air bubbles, this is quite unnecessary. Aerosolised vaccine in the consulting room may come into contact with the cat's mucosae (*e.g.* conjunctival and oronasal) and this can cause disease. These live vaccines are designed to be safe when administered parenterally, not via mucosae. If some of the vaccine leaks from the injection site into the cat's fur, as much as possible should be removed (*e.g.* using a dry paper towel) and then an antiseptic should be applied to the affected area of skin and fur before a final cleaning step.

Q. If an animal receives the first dose of a vaccine that requires two doses to immunise (*e.g.* a *Leptospira* bacterin or a FeLV vaccine), and it does not return for the second dose within 6 weeks, is there any immunity?
A. It is safest to assume not. A single dose of a two-dose vaccine should be assumed not to provide any immunity. The first dose is for priming the immune system, the second for immunising. If a second dose is not given within 6 weeks of the first, the regime needs to be started again, making sure the two doses are given within 2 to 4 weeks of each other, as per the product leaflet. After those two doses, revaccination with a single dose can be done at yearly or greater intervals (as per the product leaflet) to boost the response.

Q. If a dog or cat received its last core MLV vaccine more than 3 years ago, do I need to recommend starting the series of vaccinations again (*i.e.* two doses 2 to 4 weeks apart)?
A. No, this should not be necessary. For the MLV core vaccines, multiple doses are only required for puppies or kittens because they have MDA. The VGG is aware that many product leaflets do advise re-starting a vaccination series with two doses, but there is little to no evidence that this is necessary. For MLV vaccines, a single dose should be sufficient.

Q. If a puppy or kitten fails to receive any colostrum will it have any passive antibody protection from the dam?

A. Depending on the antibody titre of the dam they will have little or, more likely, no protection. Approximately, 95% or more of the MDA in the blood of a newborn puppy or kitten that suckled normally is obtained from the colostrum. It is absorbed via the intestine into the systemic circulation for up to 24 hours after birth, but especially in the first 4 hours. It is important that puppies and kittens suckle successfully in the first few hours after birth.

Q. At what age can one safely stop vaccinating old dogs?
A. It is not appropriate to stop vaccinating dogs that have reached a certain, advanced age. For the core MLV vaccines, the current recommendation is for lifelong revaccination no more frequently than every 3 years. If a *Leptospira* vaccine or one or more non-core vaccines are chosen for use, these generally need to be given annually.

Q. What vaccination protocol is recommended for an unvaccinated adult dog?
A. Core MLV vaccine to protect against CDV, CAV-1 and CPV, plus vaccination to protect against rabies and leptospirosis in endemic areas. A single dose of the rabies and MLV core vaccine is sufficient, but two doses of the *Leptospira* vaccine must be given to immunise. Revaccination against CDV, CAV-1 and CPV should be repeated no more frequently than every 3 years thereafter. Annual revaccination against leptospirosis is needed. Revaccination against rabies should be as per local regulations or product leaflet. Non-core vaccines (*e.g.* parainfluenza virus, *Bordetella* and others) should be selected based on a risk–benefit analysis for each individual animal. Killed non-core vaccines would require two doses given 2 to 4 weeks apart with annual boosters thereafter.

Q. What vaccination protocol is recommended for an unvaccinated adult cat?
A. For an adult cat that may never have been vaccinated, the VGG recommends vaccination with two doses of core MLV vaccine (FPV, FCV, FHV), 2 to 4 weeks apart, plus one dose of rabies vaccine in endemic areas. Young cats <1 year of age, or older cats that have outdoor access, or live indoors with other cats that have outdoor access, should also be vaccinated against FeLV (two initial doses, followed by booster revaccination every 2 to 3 years, as per the product leaflet). For cats that have low-risk lifestyles, revaccination with the core, trivalent MLV vaccine should be no more frequent than every 3 years. For cats that have high-risk lifestyles, revaccination no more frequently than every 3 years for FPV and annually for FHV and FCV is recommended. However, in some countries, bivalent vaccines containing only FHV and FCV are unavailable. In these countries, cats that have high-risk lifestyles would need to receive trivalent (FPV, FCV, FHV) vaccine annually. Non-core vaccines (*e.g. Chlamydia*) should be selected based on a risk–benefit analysis for each individual animal. Non-core vaccines generally require two doses given 2 to 4 weeks apart with annual boosters thereafter.

Q. Why do core MLV vaccines for dogs contain CAV-2 rather than CAV-1? Isn't CAV-1 more important and more pathogenic?
A. In the past, core MLV vaccines for dogs did contain CAV-1 and occasionally caused transient "blue eye" or corneal oedema, an uncommon and distressing adverse effect. Modern core MLV vaccines for dogs that contain CAV-2 provide strong cross-protection against CAV-1 and do not cause corneal oedema. Hence, CAV-2 has replaced CAV-1 in core MLV vaccines for dogs.

Q. How should I approach vaccination of breeding bitches and queens?
A. Although there is scant evidence that vaccination during pregnancy causes harm, it is generally recommended to avoid vaccinating breeding bitches and queens during their pregnancies, if possible. Rather, they should ideally be scheduled for any needed vaccination before they become pregnant. If core vaccines are needed during pregnancy, historically, inactivated vaccines were recommended rather than MLV vaccines, although an increasing number of canine MLV vaccines are now approved for use in pregnancy, if deemed essential. Breeding bitches and queens need core vaccines like all other cats and dogs. Non-core vaccines should be used based on a risk–benefit analysis. Some experts recommend annual rather than triennial revaccination of breeding bitches with MLV core vaccines to maximise antibody concentrations in their colostrum. However, giving additional MLV core vaccine doses to already immune bitches during pregnancy will only enhance serum antibody levels in a minority. There may be a greater risk of using MLV core vaccines in pregnant queens, compared with bitches (FPV is the main concern). No MLV core vaccines are approved for such use in queens. Some MLV vaccines state a specific contraindication for use in pregnancy in their product leaflets. This is most likely because the relevant safety trials have not been performed in pregnant bitches or queens rather than that harm has been documented. The vaccine manufacturer would need to be consulted for further details.

Q. What is the current situation regarding canine influenza viruses around the world? Do I need to vaccinate?
A. There is an excellent page about canine influenza on the Centers for Disease Control and Prevention website: https://www.cdc.gov/flu/other/canine-flu/keyfacts.html.

Canine influenza A H3N8 virus spread from horses to dogs and then adapted to its new host and was able to spread between dogs to cause respiratory illness, especially in group-housed dogs. Subsequently this virus was detected in dogs across much of the USA. A vaccine was developed to protect dogs against this virus and remains commercially available. However, it is considered that this virus may no longer be circulating among dogs in USA and may be extinct.

Canine influenza A H3N2 viruses originally spread from birds to dogs, adapted to their new host and became able to spread among dogs, causing respiratory illness. Canine H3N2 viruses have also been transmitted from infected dogs to domestic cats. A canine H3N2 virus was first detected in dogs in South Korea in 2007 and is endemic in several countries in Southeast Asia. This virus was subsequently introduced into the USA and Canada by importation of infected dogs from countries where this virus was endemic, and circulates sporadically in the USA. Vaccines developed to protect dogs against canine influenza A H3N2 viruses are commercially available.

Q. Is it a good idea to give a MLV vaccine to a wild or exotic species or to a domestic species other than the one that the vaccine is licensed to protect?
A. No, never give a MLV vaccine unless it has been shown to be safe in the species you aim to protect. Many MLV vaccines have caused disease and death when used in animal species other than those for which they were originally licensed. Even worse, the vaccine could be shed from the wild animals, spread among them and regain virulence through multiple passages. This could cause disease even in the target species for which the vaccine was originally developed.

A safe and effective recombinant, canarypoxvirus-vectored CDV vaccine licensed for use in ferrets is available in certain countries. This vaccine has also been suggested as the off-label distemper vaccine of choice in many wild and exotic species as it doesn't contain any live distemper virus.

Q. Can homeopathic "nosodes" immunise pets successfully?
A. No. Nosodes cannot be expected to prevent any infectious disease. There is very scant evidence of safety and efficacy. In a small number of publications, nosodes have been shown to lack efficacy (Rieder & Robinson, 2015).

Questions about adverse events following vaccination

Q. What is an "adverse event following vaccination" (AEFV)?
A. An adverse event is any detrimental, unintended consequence that follows vaccine administration (including lack of protection). Local reactions such as pain and swelling at the injection site and minor systemic reactions such as lethargy, anorexia, fever and episodes of vomiting are commonly observed (Miyaji et al., 2012; Moore et al., 2005, 2007; Yoshida et al., 2021, 2022). Urticaria and anaphylaxis are less common (Tizard, 2021). More serious consequences (*e.g.* Feline Injection Site Sarcomas, FISS) are rare.

Q. How common are adverse events following vaccination (AEFV)?
A. AEFVs are uncommon but undoubtedly underreported, so it is difficult to be sure. Altered vaccine manufacturing approaches have been aimed at reducing the incidence of AEFVs.
A Japanese study of adverse reactions to canine non-rabies combined vaccines administered in 2006 to 2007 (Miyaji et al., 2012) reported on 57,300 vaccinations administered at 573 veterinary hospitals (the last 100 dogs vaccinated at each hospital). A total of 359 dogs had AEFVs, that is 62.7 per 10,000 vaccinated dogs. Death was observed in 1 dog, anaphylaxis in 41, gastrointestinal signs in 160, dermatological signs in 244 and other clinical signs in 106. A total of 83.3% of AEFVs were noticed within 12 hours of vaccination. In the dogs that developed anaphylaxis, it began within 60 minutes of vaccination in all of them and within 5 minutes in nearly half of them (46.3%).

In other studies carried out earlier in USA, AEFVs were somewhat less frequently observed. Adverse events of any kind (including very minor reactions) were documented within the first 3 days following vaccination in 38 of 10,000 vaccinated dogs (Moore et al., 2005). Adverse reactions of any kind (including very minor reactions) were documented within the first 30 days following vaccination in 52 of 10,000 vaccinated cats (Moore et al., 2007). However, some animals may have had reactions that were not reported to the practice, but were reported to other practices or emergency practices where the animal was seen.

Recent work in USA on a much larger population of dogs (nearly 5 million) has shown that members of some breeds have a much higher risk of acute AEFVs than does the general dog population (Moore et al., 2023). Dachshunds, Boston terriers, miniature Pinschers, French Bulldogs and Havanese were at higher risk. Smaller dogs that receive multiple vaccines per visit are at particular risk.

Q. Should a middle-aged dog with a previous history of a serious adverse event following vaccination be revaccinated? I am concerned about severe hives or facial oedema, anaphylaxis or immune-mediated disease.
A. Not necessarily. If the vaccine suggested to have caused the adverse reaction was a MLV core vaccine, and the dog was previously vaccinated according to these guidelines, then the dog is very likely to remain protected and revaccination is probably not needed. Gold standard serological testing could be considered if the owner is particularly worried. For rabies vaccines, the local authorities must be consulted in case antibody titre measurement or some other approach to avoiding use of that vaccine may be permitted. If a *Bordetella* injectable vaccine is implicated, an alternative vaccine (*e.g.* intranasal or oral) can be recommended. If a *Leptospira* vaccine is implicated, and the dog's lifestyle and geographical location places it at particularly high risk, then revac-

cination with one of the newer vaccines proven to contain very low concentrations of excipients such as bovine serum albumin might be considered.

If it is decided that vaccination is absolutely necessary, then switching to a different product may be helpful, although evidence in support of this suggestion is scant. This strategy may not be successful in part because hypersensitivity reactions are known to be related to excipients contained within the vaccine (*e.g.* traces of bovine serum albumin used in the culture process). These are common to many different products, although some products contain much less than others. The use of antihistamines or anti-inflammatory doses of glucocorticoid pre-revaccination is acceptable and should not interfere with the vaccinal immune response. Revaccinated susceptible animals should be closely monitored for up to 24 hours post-vaccination although such reactions (Type I hypersensitivity) generally occur within minutes to 1 hour of exposure. Other types of hypersensitivity (II, III or IV) can occur much later (*e.g.* hours to months).

Q Should an adult dog with a history of immune-mediated disease, even if there was no suspicion that this was triggered by a vaccine (so-called "non-associative disease"), be given a booster vaccine when it is due?
A The concern here is that vaccines are, by design, an antigenic stimulus and as such, could tip the balance of immune-homeostasis in a predisposed patient towards a relapse of autoimmunity (*e.g.* immune-mediated haemolytic anaemia, IMHA, thrombocytopenia, ITP or polyarthritis). Serological testing could be used here for CPV, CDV and CAV and potentially rabies (but you would need to check with regulatory authorities about rabies). If revaccination is planned, the following information should be considered in performing a risk–benefit analysis, and in interpreting any adverse outcomes subsequent to revaccination: all immune-mediated diseases have potential to relapse spontaneously, regardless of whether a booster is given. For the 3 immune-mediated diseases mentioned above, the relapse rates are markedly higher in the first few months following diagnosis. This is typically the period when the dog would be receiving higher doses of immunosuppressant drugs, with gradual tapering of the dose. Vaccines should not be given during this period to avoid further increasing the risk of disease relapse at this vulnerable time. After 12 months, the long-term rate of spontaneous relapse is much reduced (typically 10 to 15% of patients). In a recent review of IMHA, 22 of 44 dogs that had recovered from IMHA subsequently received boosters, with 4 dogs receiving more than one booster. One of the 22 dogs had a relapse of IMHA soon after a booster (Weingart et al., 2019). For ITP, one research abstract described an investigation of vaccine boosters as a potential cause of relapsing immune-mediated disease (Ellis, 2016). Twenty-two dogs in remission (no longer receiving immunosuppressant drugs) were followed long-term. Nine of these dogs did not receive booster vaccines. The other 12 did receive boosters, in some cases multiple boosters over multiple years. No dog in either group relapsed (Ellis, 2016). Should a relapse occur within 4 weeks of a booster vaccination, it should be kept in mind that temporal association does not prove causality, but this would certainly highlight a need for closer scrutiny over administration of further vaccines, and should be reported to the relevant authorities as an AEFV.

Q. Should I give a half dose or a ¼ dose of vaccine to small or tiny dogs to reduce the risk of them having an adverse reaction?
A. This is not recommended, despite some emerging evidence that small dogs are more prone to adverse reactions and seem to develop higher antibody titres in response to standard vaccine doses than do large and giant dogs. Severe, adverse reactions are uncommon, even in small and tiny dogs and risk of adverse reactions was more strongly linked to breed than to body size in one recent study that was published as an abstract (Moore et al., 2023). Some vaccines have undergone further development and refinement with marked reduction of the concentrations of excipient components thought to be associated with many adverse reactions (*e.g.* bovine serum albumin). Others have been reformulated to contain the same amount of antigen in a smaller volume (*e.g.* 0.5 mL) more suitable for tiny dogs. Further study of the needs of tiny dogs as compared with giant dogs is required. Meanwhile, VGG does not recommend giving small or tiny dogs less than a full dose.

Q. I understand that lack of efficacy is an important form of AEFV. Why do some dog breeding kennels continually have problems with dogs dying from CDV and CPV-2 infections?
A. The most likely cause for this scenario is that the breeding stock is not adequately vaccinated. Outbreaks might occur among puppies that did not obtain sufficient MDA as the bitch was not properly vaccinated. Conversely, where puppy vaccinations are not scheduled according to these guidelines (these guidelines advise a final puppy vaccination at 16 weeks of age or older) there is a risk that some puppies may be left unprotected because of long-term persistence of interfering MDA beyond 12 to 14 weeks of age. Good husbandry, hygiene, nutrition, avoidance of over-crowding and stress reduction all play a role in minimising disease outbreaks in kennels.

Q. Some puppies were vaccinated at 9 weeks of age against CPV and yet they developed parvoviral enteritis at 10 weeks of age. Why might this have happened? Did the vaccine cause the disease?
A. The most common reason for a young, vaccinated puppy to develop a vaccine-preventable disease shortly after vaccination is that the animal was already incubating the disease before it was vaccinated. It is also possible that these puppies might have been infected during their "window of susceptibility" when they no longer had sufficient MDA to fully protect them against virulent street virus but the MDA concentration or titre was still sufficient to interfere with their immune response to a recently administered vaccine.

Q. I have heard that "over-vaccination" of cats sometimes causes chronic kidney disease (CKD). Is this true?
A. CKD is a common and important disease of older cats yet only a few studies have explored risk factors. A questionnaire-based study published in 2016 showed an association between owner-reported annual/frequent revaccination of cats (>9 years of age) and development of azotaemic CKD (Finch et al., 2016). Age and severe periodontal disease were other, independent risk factors for development of azotaemic CKD. This study, which reported on 27 cats that developed azotaemic CKD out of a population of 148, did not prove causality but, rather, provided evidence of an association.

Several published laboratory studies have some bearing on the feasibility of a causal relationship between annual/frequent revaccination of cats and development of azotaemic CKD (Lappin et al., 2005; Lappin, Basaraba & Jensen, 2006a; Summers et al., 2022; Whittemore et al., 2010). Some feline vaccines that contain FPV, FCV and FHV are grown in cell culture on feline cells originally isolated from feline kidney tissue (so-called Crandell-Rees Feline Kidney Cells, CRFK). Feline proteins are likely present in these vaccines. It has been reported that parenteral injection of CRFK cell lysates, or of vaccines likely grown on CRFK cells, into experimental cats induces production of antibodies that can bind to feline renal cell extracts, various feline renal proteins and CRFK cells (Lappin et al., 2005; Lappin, Basaraba & Jensen, 2006a; Summers et al., 2022; Whittemore et al., 2010). Experimental hyper-inoculation of cats with a CRFK cell lysate (12 times in the first 50 weeks, then once more a year later) resulted in lymphoplasmacytic interstitial nephritis in three out of six cats (Lappin, Basaraba & Jensen, 2006a). However, in a more recent hyper-inoculation study that used a FPV/FCV/FHV vaccine rather than a cell lysate (eight vaccinations given over a 14-week period) hyper-vaccination did not induce CKD, nor interstitial nephritis (Summers et al., 2022).

Annual/frequent revaccination of adult cats has not been proven to cause CKD. Nevertheless, it is appropriate to avoid unnecessary overuse of vaccines, as emphasised throughout these guidelines.

Questions about the use of serological or "titre" testing to determine if an animal is protected against disease

Q. Should I feel obliged to start using serological or "titre" testing routinely in my practice?
A. No. This is a personal choice. Modern, quality-assured vaccines are safe. Some experts recommend routine revaccination on a schedule (*e.g.* triennially for the MLV vaccines in dogs) with little or no routine use of serological testing (Ellis et al., 2022). You may find yourself considering serological testing for the first time when dealing with a patient that is due for vaccination but is receiving potent immunosuppressive or antineoplastic medications. Alternatively, you may be dealing with a patient that has a previous history of a serious adverse event following vaccination.

Q. For which infectious disease agents can I use serological testing to try to predict if an animal is protected?
A. In dogs, CDV, CAV and CPV. In cats, FPV. Testing for anti-CDV and anti-CAV antibodies using a gold standard diagnostic laboratory test is likely to be more reliable than in-practice testing. Testing for antibodies against other infectious agents (*e.g. Leptospira*) is much less reliable as a predictor of protection.

Q. In general, what does a *positive* serological test result in an adult animal mean for these four viruses (CDV, CAV and CPV in dogs, FPV in cats)?
A. It means that antibody has been detected through testing. The immune response after natural exposure or vaccination is enormously complex, comprising far more than mere antibody production. Nevertheless, for these four viruses, presence of antibody is widely held to indicate protection in an animal that has mounted its own active immune response. Antibody is not the sole mediator of protection, but its presence in the serum of an animal over 20 weeks of age is held to indicate protection against these viruses. This is also true for rabies virus but not true for many other viruses.

Q. If a serological test result is *negative* for antibodies against any of these infectious disease agents (CDV, CAV and CPV in dogs, FPV in cats), what should I do?
A. Tell the owner that the test indicates that the animal may be unprotected and recommend immediate revaccination.

Q. How reliable is serological testing?
A. Let us consider only CDV, CAV and CPV in dogs and FPV in cats. There are gold standard serological tests that need to be done in diagnostic laboratories. These cannot be done in the practice. There are also commercially available in-practice diagnostic test kits produced by a range of manufacturers. These are obviously far more convenient.

It is thought that the gold standard tests yield more reliable results than the in-practice diagnostic test kits (although even this has occasionally been questioned). This is especially true for the detection of anti-CDV and anti-CAV antibodies. So, if you have ready access to gold standard testing by a diagnostic laboratory, it should provide you with the most reliable results clinically available.

The biggest concern regarding in-practice serological testing is said to relate to the specificity of these tests (Bergmann et al., 2020; Bergmann, Halzheu, et al., 2021a; Bergmann, Zablotski, et al., 2021b). A false positive result would suggest that the animal has antibody, and is protected, and therefore does not need to be vaccinated when, in fact, according to current guidelines, it should be vaccinated because the result was a *false* positive. Recently, several different in-practice diagnostic test kits were compared with gold standard tests in Germany

(Bergmann et al., 2020; Bergmann, Halzheu, et al., 2021a; Bergmann, Zablotski, et al., 2021b). The results raised concern about the reliability of some of the in-practice diagnostic test kits for some of the viruses (see the Serological Testing section of these guidelines).

Q. Are the reliability and ease-of-use of the available in-practice serological test kits much the same or do I need to be thoughtful about which one(s) I choose?
A. It is worth making yourself well informed about the differences. These kits have recently been studied and compared carefully (Bergmann et al., 2020; Bergmann, Halzheu, et al., 2021a; Bergmann, Zablotski, et al., 2021b). There are differences in ease-of-use and in performance relative to gold standard tests. The best of these tests performed very well relative to gold standard tests for detection of anti-CPV antibodies.

Q. Are these in-practice serological test kits more reliable at detecting antibodies against some viruses as compared with others? What about CPV?
A. Yes. This is a key point. Let us start by considering detection of CPV antibody in pet dogs because some in-practice test kits perform particularly well in this context. The best kit for detection of anti-CPV antibody was used to test 198 client-owned dogs (Bergmann et al., 2020). It produced 154 true positive results and only one false positive. This test kit did not produce a single false positive result when used on 43 specific pathogen-free dogs (CPV antibody negative). However, it did produce many false negative results in the client-owned dogs. Recall that negative test results should routinely prompt a recommendation to revaccinate. False negative test results lead to revaccination of animals that, in reality, have protective antibody. This may be wasteful but it is not usually harmful. Conversely, false positive test results will leave a potentially susceptible animal unprotected. This is a much more serious situation, so it is excellent that so few false positive results were detected in this study (Bergmann et al., 2020). The other three in-practice test kits for detection of anti-CPV antibody produced PPV and specificity results that were nearly as good as the best kit but there is a more important point to consider. The most important advantage of the best-performing test kit was not its slightly higher PPV, but its superior ability to provide reliable results even at low seroprevalences. Even if this kit had been used to test a population in which only 10% of the dogs were CPV-seropositive, it would still have generated a highly impressive PPV.

Q. By comparison, how do in-practice serological test kits for detection of anti-CDV and anti-CAV antibodies perform?
A. Much less reliably, according to some recent work (Bergmann, Halzheu, et al., 2021a; Bergmann, Zablotski, et al., 2021b). Specificity of a single in-practice kit for detection of anti-CAV antibody was low. Several in-practice kits for detection of anti-CDV antibody were unreliable, especially when testing healthy-looking dogs with chronic disease and acutely-ill dogs.

Q. I'm confused, what is a so-called "protective titre"?
A. You are not alone in being confused. This is a complicated topic.
A "protective titre" is an amount or concentration of antibody against disease X in blood sufficient to protect an animal from disease X. This phrase is most relevant and simplest to understand in young puppies and kittens that have not yet mounted their own active immune response against infectious disease agent X. In these puppies and kittens, maternally derived colostral antibodies are particularly important. If they have sufficient MDA (*i.e.* a "*protective* titre") they should be protected from a moderate virulent challenge. However, gold standard assays for MDA are sophisticated bioassays so results will differ somewhat from laboratory to laboratory. Viral challenge doses vary in nature. So animals predicted to be protected (but only just) according to one laboratory may be considered susceptible or (alternatively) reasonably well protected by other laboratories.

Things get more complicated in older animals that have mounted their own active immune response against infectious disease agent X. These animals should have developed cellular immunity as well as their own antibodies and memory cells. In large challenge studies conducted over a number of years that have not been published in detail (Schultz, 2006; Schultz et al., 2010) it was found that mere presence of antibody (not a particular titre) was sufficient to indicate robust immunity to the following viruses: CDV, CAV, CPV in dogs; FPV in cats. For these viruses (but not for others), presence of even low amounts of antibody was found to predict immunity to challenge. It is unfortunate that this large body of interesting work was not published in full detail. Subsequent studies of similar scale have not been carried out.

Q. How long after CPV/CDV vaccination should you wait before measuring protective antibody concentrations using in-clinic tests?
A. This question is most relevant for puppies, because adult dogs are more likely already to have serum antibodies present at the time of booster vaccination, regardless of how long an interval there has been since they were last vaccinated. If a puppy receives its final primary vaccine at 16 weeks of age, then it may be tested from 20 weeks of age onwards. Testing should be done no less than 4 weeks after the last vaccination. Any antibody present at that stage is very unlikely to be of passive, maternal origin and therefore indicates that the puppy is actively protected.

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Author contributions

Richard Adrian Squires: Conceptualization (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (lead); resources (equal); writing – original draft (equal); writing – review and editing (equal). **Cynda Crawford:** Conceptualization (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (supporting); resources (equal); writing – original draft (equal); writing – review and editing (equal). **Mary Marcondes:** Conceptualization (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (supporting); resources (equal); writing – original draft (equal); writing – review and editing (equal). **Nathaniel Whitley:** Conceptualization (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (supporting); resources (equal); writing – original draft (equal); writing – review and editing (equal).

Conflict of interest

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Abbreviations

AAFP	The American Association of Feline Practitioners
AAHA	The American Animal Hospital Association
Ab	antibody
ABCD	The Advisory Board on Cat Diseases
AEFV	adverse event following vaccination
CanL	canine leishmaniosis
CAV	canine adenovirus
CCoV	canine coronavirus
CDV	canine distemper virus
CIV	canine influenza virus
CKD	chronic kidney disease
CPiV	canine parainfluenza virus
CPV	canine parvovirus type 2 and its variants
DOI	duration of immunity
EB	evidence base
FAQ	frequently asked question
FCV	feline calicivirus
FeLV	feline leukaemia virus
FHV	feline herpesvirus-1
FIP	feline infectious peritonitis
FIV	feline immunodeficiency virus
FISS	feline injection site sarcoma
FPV	feline panleukopenia virus/feline parvovirus
Ig	immunoglobulin
IMHA	immune-mediated haemolytic anaemia
ITP	immune-mediated thrombocytopenia
LiESP	excreted-secreted proteins of *Leishmania infantum*
MDA	maternally derived antibody

mRNA	messenger RNA
MLV	modified live virus
NPV	negative predictive value
OA	overall accuracy
Osp	outer surface protein
PAW	pet animal welfare
PPV	positive predictive value
SPC	summary of product characteristics
VGG	Vaccination Guidelines Group
WHO	World Health Organization
WSAVA	World Small Animal Veterinary Association

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