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Global Veterinary Community

**Vaccination
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Group**


Recommendations on vaccination for Latin American small animal practitioners: a report of the WSAVA Vaccination Guidelines Group

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Executive Summary

The World Small Animal Veterinary Association Vaccination Guidelines Group has produced global guidelines for small companion animal practitioners on best practice in canine and feline vaccination. Recognising that there are unique aspects of veterinary practice in certain geographical regions of the world, the Vaccination Guidelines Group undertook a regional project in Latin America between 2016 and 2019, culminating in the present document. The Vaccination Guidelines Group gathered scientific and demographic data during visits to Argentina, Brazil and Mexico, by discussion with national key opinion leaders, visiting veterinary practices and review of the scientific literature. A questionnaire survey was completed by 1390 veterinarians in five Latin American countries and the Vaccination Guidelines Group delivered continuing education at seven events attended by over 3500 veterinarians.

The Vaccination Guidelines Group recognised numerous challenges in Latin America, for example: (1) lack of national oversight of the veterinary profession, (2) extraordinary growth in private veterinary schools of undetermined quality, (3) socioeconomic constraints on client engagement with preventive health care, (4) high regional prevalence of some key infectious diseases (*e.g.* feline leukaemia virus infection, canine visceral leishmaniosis), (5) almost complete lack of minimal antigen vaccine products as available in other markets, (6) relative lack of vaccine products with extended duration of immunity as available in other markets, (7) availability of vaccine products withdrawn from other markets (*e.g.* *Giardia* vaccine) or unique to Latin America (*e.g.* some *Leishmania* vaccines), (8) accessibility of vaccines directly by pet owners or breeders such that vaccination is not delivered under veterinary supervision, (9) limited availability of continuing education in veterinary vaccinology and lack of compulsion for continuing professional development and (10) limited peer-reviewed published scientific data on small companion animal infectious diseases (with the exception of leishmaniosis) and lack of support for such academic research.

In this document, the Vaccination Guidelines Group summarises the findings of this project and assesses in evidence-based fashion the scientific literature pertaining to companion animal vaccine-preventable diseases in Latin America. The Vaccination Guidelines Group makes some recommendations on undergraduate and postgraduate education and academic research. Recognising that current product availability in Latin America does not permit veterinarians in these countries to vaccinate according to the global World Small Animal Veterinary Association guidelines, the Vaccination Guidelines Group makes a series of “pragmatic” recommendations as to what might be currently achievable, and a series of “aspirational” recommendations as to what might be desirable for the future. The concept of “vaccine husbandry” is addressed *via* some simple guidelines for the management of vaccine products in the practice. Finally, the Vaccination Guidelines Group emphasises the global trend towards delivery of vaccination as one part of an “annual health check” or “health care plan” that reviews holistically the preventive health care needs of the individual

pet animal. Latin American practitioners should transition towards these important new practices that are now well embedded in more developed veterinary markets.

The document also includes 70 frequently asked questions and their answers; these were posed to the Vaccination Guidelines Group during our continuing education events and small group discussions and should address many of the issues surrounding delivery of vaccination in the Latin American countries. Spanish and Portuguese translations of this document will be made freely available from the on-line resource pages of the Vaccination Guidelines Group.

INTRODUCTION

The World Small Animal Veterinary Association (WSAVA) Vaccination Guidelines Group (VGG) was established in 2004 with the remit of providing globally applicable evidence-based advice for small companion animal veterinary practitioners on best practice for vaccination of pet dogs and cats. The VGG first released global vaccination guidelines for veterinarians in 2007 and these were updated in 2010 and 2016 (Day *et al.* 2016) and translated into multiple languages. The main body of the WSAVA vaccination guidelines are most applicable to pet cats and dogs living predominantly in and around their owners' homes (rather than living 100% outdoors or in large, closely-packed groups), but advice is also given on vaccination in a shelter setting. The 2010 and 2016 revisions were accompanied by a separate document providing information on vaccination for the owners and breeders of dogs and cats and by a series of infectious disease "fact sheets" designed to be used by veterinarians during consultation with clients (<https://www.wsava.org/guidelines/vaccination-guidelines>).

From 2012 to 2014 the VGG worked on a regional project focussing on the vaccination requirements of small companion animals in Asia (Day *et al.* 2015). Following from the success of that project the VGG embarked on a second regional project in Latin America (LATAM) between 2016 and 2019. The present paper represents the final outcome from this LATAM project. It summarises the key challenges faced by small companion animal veterinary practitioners in LATAM and makes a series of recommendations for future actions that might benefit the profession, pet owners and dogs and cats in these countries. The manuscript will be made available in Spanish and Portuguese translation *via* the VGG webpages (see above).

The VGG recognises that LATAM is a vast and diverse region comprised of numerous countries with distinctly different geography, climate, culture and socioeconomics; all of which may impact on the keeping of companion animals, the prevalence and distribution of key companion animal infectious diseases and the accessibility of veterinary preventive health care for those animal populations. The VGG could not visit every country in the region, but, as described below, gathered extensive data on which to base our comments and recommendations. We believe that the majority of these recommendations will have applicability across the LATAM region.

METHODOLOGY

The membership of the VGG was changed for the LATAM project. Emeritus Professor M. J. Day and Professor R. A. Squires were joined by Professors C. Crawford and M. Marcondes; the latter recruited as a regional expert in small companion animal infectious disease and vaccinology. The principle aim of the project was to gather as much information and scientific evidence concerning small companion animal practice, vaccine-preventable infectious diseases and vaccination of dogs and cats as possible, to form a firm basis for the recommendations to be made subsequently. To that end, the VGG undertook three fact-finding visits to Argentina (Buenos Aires and Rosario in 2016), Brazil (São Paulo and Rio de Janeiro in 2017) and Mexico (Mexico City, Guadalajara and Monterrey in 2018). Each of these visits was similarly structured and involved formal small group discussions with key opinion leaders (KoLs) including (1) first opinion veterinary practitioners, (2) representatives of small animal veterinary associations, (3) academic veterinarians involved in companion animal infectious disease research and the teaching of microbiology, immunology, clinical medicine and vaccinology, (4) government officials responsible for the assessment and licensing of small companion animal vaccines and (5) representatives of national and international vaccine manufacturers and distributors. The formal meetings were supplemented with site visits to veterinary practices in each of the seven cities; these were purposely selected to show a range of sizes and standards. Scientific literature relevant to the VGG mission was collected by on-line database searching and directly from academics participating in KoL meetings. During 2019, the VGG met to discuss findings and draft this final report.

In order to expand the information gained from these face-to-face meetings, the VGG developed a questionnaire for distribution among first opinion practitioners in the target countries (Appendix). The questionnaire was designed using "Google forms" (<https://www.google.com/intl/en-GB/forms/about/>) and was accessed and completed on-line. The questionnaire was made available in Portuguese and Spanish and was completed anonymously with instruction that only one veterinarian from each practice should undertake the survey. The responses were analysed (using tools in the Google survey programme) and summarised. Through the survey, the VGG gathered information about (1) the demographics of the responding practitioners, (2) veterinary practices and their access to diagnostic laboratories, (3) canine and feline infectious diseases seen in the practices and (4) canine and feline vaccines and vaccination protocols used in the practices. Responses to the surveys were received from 175 practitioners in Argentina, 579 in Brazil and

552 in Mexico. A small number of responses was received following release of the survey in Ecuador (n = 51) and Costa Rica (n = 33). The survey was made available to other WSAVA member associations within the region (Colombia, Cuba, El Salvador, Guatemala, Peru, Uruguay and Venezuela), but there was no uptake from those associations.

One of the aims of the project was to deliver continuing education (CE) in small companion animal vaccinology to practitioners in LATAM. Therefore, in each of the seven cities visited, VGG members provided a half-day of CE consisting of a series of lectures accompanied by written (and translated) notes. At each event, the results of the national questionnaire survey were presented. Over the course of the project, these events brought the VGG in direct contact with over 3500 LATAM practitioners with attendances of 150 in Argentina, 1200 in Brazil and over 2000 in Mexico. These large figures were achieved by live-streaming one of the events in Brazil *via* Facebook and by professional filming and on-line delivery (for a 30-day period) in Mexico. During the active discussion sessions that formed part of each meeting a number of “frequently asked questions” emerged and these (with answers) are given at the end of this document.

Evidence-based vaccination guidelines

The 2016 WSAVA global vaccination guidelines were formulated using the principles of evidence-based veterinary medicine. Recommendations, wherever possible, were made on the basis of scientific evidence. The VGG recognised that the quality of such evidence is variable and developed a novel classification scheme for grading the quality of evidence related to vaccinology. We have applied the same scheme to statements and recommendations made in the current document. The VGG classification is as follows:

Category 1 evidence: a recommendation supported by peer-reviewed scientific publication of either experimental or field data. Evidence within this category might still be of variable scientific quality despite peer review, as the peer review process does not conform to a universal standard.

Category 2 evidence: a recommendation supported by unpublished commercially sensitive studies submitted as part of a regulatory package for licensed veterinary vaccines. The assumption for this level of evidence is that information appearing on the datasheets of licensed products has been through competent peer review by regulatory authorities.

Category 3 evidence: a recommendation supported by commercial or independent experimental or field data that have not been published in the peer reviewed scientific literature or were not included in a formal regulatory package and subjected to scrutiny by regulators.

Category 4 evidence: a recommendation unsupported by experimental or field data, but assumed from knowledge of the “first principles” of microbiology and immunology or supported by widely-held expert opinion.

Throughout this document, statements may be followed by a qualifier [EB1], [EB2], [EB3] or [EB4] reflecting an “evidence base” of category 1, 2, 3 or 4, respectively. For each occasion of use only the most rigorous level of evidence available will be given.

CURRENT SITUATION IN LATIN AMERICA

The increasing trend for keeping pet animals in Latin America

There is little doubt that LATAM is experiencing remarkable growth in pet ownership and the associated pet care industry. A 2016 survey by GfK Global of 27,000 consumers in 22 different countries revealed that LATAM has the highest level of global pet ownership. Eighty percent of the online population surveyed in Argentina and Mexico, and 75% of the surveyed population of Brazil, owned a pet. Of the pet owners, 66% in Argentina, 64% in Mexico and 58% in Brazil owned dogs and 32, 24 and 28%, respectively, owned cats (https://www.gfk.com/fileadmin/user_upload/country_one_pager/NL/documents/Global-GfK-survey_Pet-Ownership_2016.pdf). There are no accurate figures for national dog and cat populations. In 2014, there were an estimated 52.2 million dogs and 22.1 million cats in Brazil (Conceição 2016) and Argentinian KoLs estimated up to 10 million dogs and 3 million cats in Argentina. In some regions, many of these animals will be free roaming rather than being owned–housed pets. With such growth should come an increasing demand for veterinary services and preventive health care for companion animals, including providing protection from infectious disease for the individual animal and animal population (“herd immunity”) by vaccination.

The veterinary profession and veterinary education in Latin America

The VGG discussed these demographics with academic and association colleagues in Argentina, Brazil and Mexico. We met with academic administrators and teacher/researchers from several veterinary schools in each country. A general observation was that it appeared challenging to provide accurate and up-to-date data on the demographics of the profession in the absence of national (as opposed to provincial or state) professional regulatory authorities who might ensure the quality of veterinary education, register veterinary graduates, maintain registers of practicing veterinarians and ensure that they undertake continuing professional development. Some estimates were given for the numbers of veterinarians in Argentina (21,000), Brazil (130,000 active veterinarians) and Mexico (45,000).

The numbers of veterinary schools were estimated at 21 in Argentina and 45 in Mexico and these are within a mixture of public and private universities. The most extraordinary growth in veterinary schools has occurred in Brazil where a marked rise in the

number of private institutions offering a veterinary curriculum means that there are currently thought to be over 400 schools in the country (Brazilian Federal Council of Veterinary Medicine, personal communication). Sixty-three of these are in state- or federally-funded public universities with the remainder being in the private sector. There are no centralised national curricula and the content and standard of teaching appears to be very variable. There were wide differences in the proportions of the curricula devoted to teaching of companion animal infectious diseases, immunology and vaccinology. Similarly, approaches to teaching the clinical application of vaccination in the consultation room setting were inconsistent.

CE is not mandatory for veterinarians and there is no scheme for recording or recognising participation in professional development. Opportunities for CE are provided through association congresses, private commercial congresses and lectures (physical and by online webinar) provided by industry. In Brazil, in particular, industry has an active programme for delivering CE in vaccinology by supporting lectures on the subject. In LATAM, many veterinary practices are small and run by single veterinarians. This creates a challenge for those veterinarians to be able to leave their practice in order to attend CE events.

Many of the academic colleagues with whom the VGG met were engaged in and publishing scientific research on companion animal infectious diseases. These studies form the evidence-based scientific literature for LATAM and where appropriate they are referenced in this document. The global challenge of obtaining research funding for companion animal studies applies equally in LATAM, but because of the zoonotic significance of canine visceral leishmaniosis, this is a particularly well-investigated disease in Brazil. At the practice level there are many issues with the diagnosis of companion animal infectious diseases. Most practices have access to point-of-care serological infectious disease diagnostic test kits, but not to diagnostic laboratories offering alternative methodologies. There is often misunderstanding of the limitations of the test kits used and the most appropriate methods for confirming a diagnosis of infectious disease.

Small animal vaccine-preventable infectious diseases in Latin America

Latin America encompasses a vast land mass (over 20 million km² in area) comprising 20 countries and a human population of over 650 million. More importantly, when considering infectious disease frequencies, it includes parts of north, south and central America as well as some Caribbean islands. It extends a vast distance from north to south, spanning the equator and including temperate, subtropical and tropical climatic zones. The region includes ecosystems ranging from desert to high mountains to tropical rain forest. It would therefore be expected that infectious disease frequencies would vary markedly from region to region within this vast, diversified area. Disease frequencies in some parts of Latin America have been studied thoroughly (and shown, indeed, to vary widely) while many other areas have not been studied at all.

The VGG obtained information on the nature and prevalence of vaccine-preventable canine and feline infectious diseases in LATAM *via* three methods: (1) review of the peer-reviewed scientific literature, (2) by discussion with key opinion leaders in small group meetings and (3) by questionnaire survey of veterinarians as described above.

The results of the questionnaire survey clearly showed that, in the five countries surveyed, the major canine vaccine-preventable infectious diseases are recognised by veterinary practitioners, in particular infections caused by canine distemper virus (CDV) (recognised by 88 to 96% of respondents), canine parvovirus type 2 (CPV2) (recognised by 88 to 94% of respondents) and *Leptospira* spp. (recognised by 49 to 68% of respondents) (Table 1). The canine infectious respiratory disease complex (CIRDC; “kennel cough”) is also widely recognised (by 88 to 98% of respondents). Although canine rabies is variably controlled in the LATAM countries (see below), cases are still recognised in all countries (by 6 to 12% of respondents). Not surprisingly, cases of canine visceral leishmaniosis (CVL) are most often recognised in Brazil (by 58% of respondents) but appear to occur also in the other four countries (recognised by 3 to 11% of respondents). The data in Tables 1 and 2 are of uncertain accuracy. They represent responses from veterinarians as to whether they recognise, clinically, these diseases in their practices and do not explore how robustly these diseases might have been diagnosed or confirmed microbiologically.

Table 1. Overview of major canine infectious disease agents reported to be present in veterinary practices in five LATAM countries

Disease/disease agent	Practitioners reporting in Argentina (%)	Practitioners reporting in Brazil (%)	Practitioners reporting in Mexico (%)	Practitioners reporting in Ecuador (%)	Practitioners reporting in Costa Rica (%)
CDV	89.1	91.7	94.4	96.1	87.9
CAV	29.1	16.8	35.1	39.2	18.2
CPV2	89.7	87.6	92.2	94.1	93.9
Leptospirosis	62.3	68.3	63.3	49.0	51.5
Canine infectious respiratory disease complex	97.7	87.8	86.2	92.1	90.1
Rabies	5.7	8.9	11.6	5.9	9.1
Canine visceral leishmaniosis	11.4	58.2	9.5	3.9	3.0
Number of survey respondents	175	579	552	51	33

CDV Canine distemper virus, CAV Canine adenovirus-1 or -2, CPV2 Canine parvovirus-2 variants.

Table 2. Overview of major feline infectious disease agents reported to be present in veterinary practices in five LATAM countries

Disease/disease agent	Practitioners reporting in Argentina (%)	Practitioners reporting in Brazil (%)	Practitioners reporting in Mexico (%)	Practitioners reporting in Ecuador (%)	Practitioners reporting in Costa Rica (%)
FPV	44.4	42.0	60.5	58.9	48.5
FHV1	78.1	94.9	44.1	41.2	30.3
FCV	78.1	54.8	63.3	56.9	60.6
<i>Chlamydia felis</i>	42.0	49.5	25.2	17.6	21.2
Feline leukaemia virus	63.3	82.1	84.6	88.2	96.9
Feline immunodeficiency virus	72.2	82.3	57.6	80.4	90.9
Feline infectious peritonitis	62.1	67.6	56.7	47.1	75.6
Rabies	4.7	7.8	7.3	1.9	9.1
Number of survey respondents	175	579	552	51	33

FPV Feline parvovirus, FHV1 Feline herpesvirus-1, FCV Feline calicivirus.

For the major vaccine-preventable feline infectious diseases, veterinarians in the five countries clearly reported recognising infections caused by feline parvovirus (FPV) (42 to 60% of respondents), feline herpesvirus type 1 (FHV1) (30 to 95% of respondents), feline calicivirus (FCV) (55 to 78% of respondents) and *Chlamydia felis* (18 to 50% of respondents). There appears to be widespread recognition of feline retroviral diseases and elsewhere we describe the high prevalence of these infections in certain regions. Respondents to the survey recognised feline leukaemia virus (FeLV) infection (63 to 97% of respondents) and feline immunodeficiency virus (FIV) infection (57 to 91% of respondents) in their practices. Although a vaccine against feline infectious peritonitis (FIP) is not available in most parts of the world, including LATAM, we also gathered data on FIP infection, which was recognised by 47 to 76% of respondents. Cases of rabies in cats were reported by 2 to 9% of respondents. The same qualification concerning the robustness of these data (see above) applies to the information on feline infectious diseases.

A summary of the relevant LATAM published scientific literature on these canine and feline infectious diseases is given in the sections below. High-quality epidemiological studies evaluating the distribution of infectious diseases in LATAM are scarce and although there are some reports, just a few published studies defined the diseases based on clinical presentation with confirmatory laboratory diagnostics. Confirmatory tests are not always available in many parts of LATAM, especially in places where there is no veterinary diagnostic laboratory and practitioners may use human diagnostic laboratories. Moreover, diagnostic tests, especially molecular analyses (*i.e.* reverse transcriptase polymerase chain reaction; RT-PCR), are sometimes too expensive, making the practitioner rely only on physical examination and sometimes also simple haematological examination.

Canine infectious diseases in LATAM

Although diseases such as those caused by CDV and CPV2 infection are preventable by vaccination, in many LATAM countries they are still a problem because vaccination rates (*i.e.* “herd immunity”) are too low and there is a high number of free-roaming dogs that have never been vaccinated (Hartmann *et al.* 2007) [EB1]. Another problem is that in some LATAM countries there is no requirement that vaccination be performed only by veterinarians. Therefore, vaccination without clinical examination or without consideration of the quality and viability of the vaccine product is a common practice. It is also possible for a pet owner to purchase a vaccine from an agricultural merchant, without proper storage and handling, and administer it in their own home, without clinical examination by a veterinarian and without adequate transportation or maintenance of the product. Regular clinical examination by a veterinarian including adequate vaccination of dogs with core vaccines is still an uncommon procedure among dog owners in many parts of LATAM. Although there are no formal prevalence studies in most of the LATAM countries, there are theses and abstracts of studies in university library repositories, and some publications, showing that infectious diseases preventable by vaccination are still present in most of the countries.

Canine distemper virus

A meta-analysis of cross-sectional studies addressing the global prevalence of CDV showed that most of the articles from LATAM were from Brazil, Argentina and Chile (Costa *et al.* 2019) [EB1]. The prevalence of canine distemper in Brazil was <10% to 41-50%, and in Argentina from 31-40% to >70% when diagnosis was based on molecular studies. When studies were based on serology, seroprevalence ranged from 21-30% to 51-60% in Chile and from 10-20% to >70% in Brazil (Costa *et al.* 2019) [EB1]. In the south of Brazil, the seroprevalence of CDV was reported to be 27.3% (223/817) in non-vaccinated dogs (Dezengrini *et al.* 2007) [EB1]. A study conducted between 2003 and 2004 in Argentina found 73.8% of cases (73/99) were confirmed by RT-PCR in dogs with clinical signs of the disease. Most of the dogs in that study were reportedly vaccinated against CDV, but had likely not received a full course of vaccination (Calderon *et al.* 2007) [EB1]. Other studies confirm that CDV is present in Brazil (Budaszewski *et al.* 2014, Monteiro *et al.* 2016, Alves *et al.* 2018), Chile (Acosta-Jamett *et al.* 2011, 2015), Colombia (Espinal *et al.* 2014), Cuba (González-Chávez *et al.* 2017), Ecuador (DiGangi *et al.* 2019) including the Galápagos Islands (Levy *et al.* 2008, Diaz *et al.* 2016) and Mexico (Damián *et al.* 2005, Rodríguez-Tovar *et al.* 2007) [EB1].

Canine parvovirus

CPV2 infection is still seen frequently in LATAM countries. In the South of Brazil the seroprevalence of CPV2 exposure was reported to be 68.7% (561/817) in non-vaccinated dogs (Dezengrini *et al.* 2007) [EB1]. A study conducted with 104 dogs with diarrhoea in Brazil identified CPV2 by PCR in faecal samples of 34.6% (36/104) of the dogs (Gizzi *et al.* 2014) [EB1]. Other studies show that CPV2 is present in Argentina (Calderón *et al.* 2011, 2015), Brazil (Alves *et al.* 2018, Headley *et al.* 2018), Chile (Acosta-Jamett *et al.* 2015), Colombia (Duque-García *et al.* 2017), Cuba (Pino-Rodríguez *et al.* 2018), Ecuador (Levy *et al.* 2008, Aldaz *et al.* 2013, De la Torre *et al.* 2018, DiGangi *et al.* 2019), Mexico (Ortega *et al.* 2017) and Uruguay (Pérez *et al.* 2007, Puentes *et al.* 2012, Maya *et al.* 2013) [EB1].

Canine adenovirus

Although many veterinarians report that they see cases of canine infectious hepatitis (caused by canine adenovirus type 1; CAV1) in LATAM countries, case reports with confirmation of the diagnosis are rare. One case report from Argentina made a diagnosis based on history, macroscopic and microscopic evaluation and presence of hepatic inclusion bodies (Lértora & Burna 2003) [EB1]. In Brazil, necropsy reports from 5361 dogs over a 43-year period (1964 to 2006) were reviewed and 62 (1.2%) cases of infectious canine hepatitis were diagnosed based on history, macroscopic and microscopic evaluation and the presence of hepatic inclusion bodies (Inkelmann *et al.* 2007) [EB1]. A follow-up immunohistochemical study of 27 cases confirmed the presence of CAV1 antigen (Inkelmann *et al.* 2008) [EB1]. Another study conducted in the same State, in the South of Brazil, evaluating cases from 1996 to 2009, reported 23 immunohistochemically-confirmed diagnoses of canine infectious hepatitis out of a total of 6993 dog necropsy examinations, representing 0.34% of the evaluated dogs (Oliveira *et al.* 2011) [EB1]. In Brazil, there are also some confirmed cases of CAV1 infection (Headley *et al.* 2013, 2018, 2019) [EB1].

Canine infectious respiratory disease complex

A study conducted in three shelters in the South of Brazil showed, by PCR from nasal swabs, that CAV2 was present as a single infection in 5.4 and 7.8% of the dogs in two shelters, while canine parainfluenza virus (CPiV; parainfluenza virus type 5) was found in 29.7 and 8.6% of the dogs, respectively. CAV2 was present as a coinfection with CDV in 2.7% of the dogs, CAV2 with CPiV in 22.9% of the dogs, CPiV and CDV in 4% of the dogs and CAV2, CDV and CPiV in 13.5% of the dogs in one of the shelters (Monteiro *et al.* 2016) [EB1].

A study evaluating lung samples obtained from dogs that died from acute or subacute pneumonia in Mexico from 1996 to 2003, identified, by immunohistochemistry, CAV2 in 57.1% (20/35) and CPiV in 51.4% (18/35) of the dogs (Damián *et al.* 2005) [EB1]. In the Galápagos Islands, where canine and feline vaccines are prohibited, a seroprevalence for CAV of 67.3% (64/95) and for CPiV of 100% (95/95) was reported in dogs (Levy *et al.* 2008) [EB1].

There is little information regarding the prevalence of *Bordetella bronchiseptica* infection in dogs in LATAM countries. *B. bronchiseptica* strains were isolated in 8.5% (11/130) of the nasal swabs obtained from 130 dogs in Mexico (González *et al.* 2006) [EB1].

Leptospirosis

Although there are many studies showing a high seroprevalence of leptospirosis in dogs in LATAM countries, there are few publications where the agent was isolated in order to identify the serovar causing the disease. The microscopic agglutination test (MAT) is the diagnostic test of choice for canine leptospirosis; however, it has poor ability to confirm the infecting serovar. Studies involving isolation of leptospires from dogs are recommended for epidemiological purposes, as well as for selection of antigens for diagnostic assay development and vaccine design (Sykes *et al.* 2010) [EB1]. During the VGG visits to LATAM countries, another commonly reported situation was the diagnosis of leptospirosis based on testing a single blood sample, sometimes considering the serovar with the highest titre as that causing the infection. Although, in the presence of clinical signs, a single titre ≥ 800 can suggest infection, it cannot confirm a diagnosis. MAT must be performed with paired serum samples collected 1 to 2 weeks apart. A fourfold change in titre supports a recent infection (Sykes *et al.* 2010) [EB1]. The serogroup with the highest titre has been interpreted as the infecting serogroup; however, the highest MAT titre can vary over time, indicating that the MAT does not reliably predict the infecting serogroup in acutely infected animals (Schuller *et al.* 2015) [EB1]. Another problem in LATAM countries is the lack of standardisation and quality control in laboratories performing MAT for diagnosis of leptospirosis, resulting in variation in results.

Leptospirosis in dogs is caused primarily by *Leptospira interrogans* and *Leptospira kirschneri* (Sykes *et al.* 2010) [EB1]. However, *Leptospira noguchii* (Silva *et al.* 2009) [EB1] and *Leptospira santarosai* (Miotto *et al.* 2016) [EB1] were also isolated from dogs in Brazil. *Leptospira interrogans* serovars most frequently isolated from both sick and apparently healthy dogs in Brazil were Canicola and Copenhageni (Yasuda *et al.* 1980, Rodrigues *et al.* 2007, Miraglia *et al.* 2013, Hagiwara *et al.* 2015) [EB1]. *L. interrogans* serovar Pomona was isolated from a number of dogs in one report (Yasuda *et al.* 1980) [EB1]. *L. interrogans* serovar Copenhageni was also the predominant serovar in isolates from suspected canine leptospirosis cases in Trinidad and Tobago (Suepaul *et al.* 2010).

Canine rabies virus infection

Cases of human and canine rabies have been reduced by nearly 90% over the past 20 years in LATAM countries following active mass vaccination programmes (Schneider *et al.* 2011) [EB1]. Although Costa Rica, French Guyana, Guyana, Panama, Suriname and

Uruguay are free of dog rabies, other countries still report cases (Velasco-Villa *et al.* 2017) [EB1]. According to the Pan-American Health Organisation (PAHO) Epidemiologic Surveillance System for Rabies, during 2010 to 2012, Bolivia and Haiti had the highest incidence of human rabies transmitted by dogs in the Western Hemisphere: 15% (6/40) and 40% (16/40) of all cases, respectively (Vigilato *et al.* 2013) [EB1].

Canine visceral leishmaniosis

Canine visceral leishmaniosis (CVL) is widespread from Mexico to Argentina, with autochthonous cases reported in many countries. The number of infected dogs in LATAM is estimated in millions, and there are high infection rates, especially in Brazil (Marcondes & Day 2019). Most epidemiological studies are conducted using serology, but the application of PCR in endemic areas has confirmed that the prevalence of infection in dogs is much higher than the seroprevalence (Baneth *et al.* 2008). The seroprevalence of CVL in endemic areas of Brazil ranges from 3.1 to 36.0% (Rosypal *et al.* 2007, Belo *et al.* 2017, Marcondes & Day 2019) [EB1].

The seroprevalence of CVL increased in Paraguay between 2005 to 2016, with values ranging from 23% to 32% (Miret *et al.* 2010, Portillo *et al.* 2011) [EB1]. Most cases were concentrated around the capital of the country, Asunción, where the seroprevalence reached 69% in stray dogs in 2010 (Miret *et al.* 2011) [EB1]. In 2006, when the first case of CVL was reported in Argentina, the prevalence of CVL (based on serology and/or PCR) was 57.3% (Cruz *et al.* 2010) [EB1].

In Uruguay, a survey in Salto, a city on the border with Argentina, found 22% seroprevalence for *Leishmania* spp. (Satragno *et al.* 2017) [EB1]. Studies of the seroprevalence of CVL in Mexico, Venezuela and Colombia have reported levels between 1.7 and 15.7% (Arjona-Jiménez *et al.* 2012, López-Céspedes *et al.* 2012), 5.6 and 40.0%, (Zerpa *et al.* 2000, 2001, 2003, Feliciangeli *et al.* 2005) and 1.6 and 36.0% (Fernández *et al.* 2002, Cortés 2006, Rosypal *et al.* 2007, Paternina-Gómez *et al.* 2013), respectively [EB1].

Feline infectious diseases in LATAM

Feline parvovirus

Few studies have been published in peer-reviewed journals with a confirmed diagnosis of this disease. In the south of Brazil 69.1% (67/97) of cats tested were seropositive for FPV; 100% (11/11) of vaccinated cats, 66.6% (34/51) of unvaccinated cats and 62.8% (22/35) of cats with unknown vaccination history (Johann *et al.* 2009) [EB1]. From 1996 to 2012, 1850 cats had necropsy examination at a university hospital in southern Brazil. Of these, 33 (1.78%) had a diagnosis of FPV infection confirmed by immunohistochemistry (Castro *et al.* 2014) [EB1]. A study conducted in Brazil (2004 to 2005) of 51 faecal samples from 46 diarrhoeic and five asymptomatic unvaccinated domestic cats, confirmed FPV infection by PCR in six (11.76%) cats (Garcia *et al.* 2011) [EB1].

Feline upper respiratory tract infection

Few studies have been published in peer-reviewed journals with a confirmed diagnosis of FHV1, FCV or *C. felis* infection. A study of 302 cats from the South of Brazil with and without clinical signs of respiratory disease, reported isolation of FHV1 and FCV with PCR confirmation in 11.2% (34/302) and 8.6% (26/302) of the cats, respectively (Henzel *et al.* 2012) [EB1]. In another study of 108 unvaccinated kittens with and without conjunctivitis in Brazil, 57.4% (62/108) had infection with FHV1, 37.0% (40/108) with FCV and 24.1% (26/108) with *C. felis*, confirmed by PCR (Baumworcel *et al.* 2017) [EB1]. *C. felis* was also identified by PCR in 6.2% (9/145) (Seki *et al.* 2010) [EB1] and in 58% (18/31) (Gonsales *et al.* 2013) [EB1] of cats with clinical signs in two studies in Brazil.

Feline retroviruses

Most studies on the prevalence of FeLV and FIV infection come from Brazil. Although studies are available from university repositories in countries such as Argentina, Chile, Guatemala and Mexico describing high prevalence of FeLV infection, few of these have been published in peer-reviewed journals. In developed countries the prevalence of FeLV infection is usually low, but in some LATAM countries the prevalence appears to be high.

The prevalence of FeLV infection reported in Brazil varies according to the region studied, with values of 0.33% (1/302) by enzyme-linked immunosorbent assay (ELISA) (Sobrinho *et al.* 2011), 1.1% (1/90) by ELISA (Marcondes *et al.* 2018), 2.6% (6/230) by immunochromatography (Lacerda *et al.* 2017), 11.52% (126/1094) by immunofluorescence antibody test (IFAT) (Almeida *et al.* 2012), 22.26% (55/247) by ELISA (Biezus *et al.* 2019), 32.5% (13/40) by ELISA (Teixeira *et al.* 2007), 38.3% (46/120) by IFAT (Meinerz *et al.* 2010) and 47.5% (507/1072) by PCR (Coelho *et al.* 2011) [EB1]. Leukaemia was associated with FeLV infection in 78.4% (29/37) of the cases in a study conducted in Brazil (Cristo *et al.* 2019a,b) [EB1].

FIV prevalence in Brazil appears to be lower than that of FeLV, with studies showing values of 3.33% (15/450) by PCR (Caxito *et al.* 2006), 4.14% (6/145) by PCR (Teixeira *et al.* 2007), 5.5% (5/90) by ELISA (Marcondes *et al.* 2018), 5.63% (17/302) by ELISA (Sobrinho *et al.* 2011), 5.84% (16/247) by ELISA (Biezus *et al.* 2019), 6.1% (14/230) by immunochromatography (Lacerda *et al.* 2017), 6.1% (9/148) by ELISA and PCR (Teixeira *et al.* 2019) and 14.7% (67/454) by PCR (Lara *et al.* 2008) [EB1]. In a study conducted in southern Brazil with 40 cats showing clinical signs of FIV infection, 15 (37.5%) had the infection confirmed by PCR (Caldas *et al.* 2000) [EB1].

In Argentina, cats with clinical signs compatible with retrovirus infection were evaluated and FIV infection was confirmed by immunochromatography in 21.45% (55/255) and by PCR in 20.34% (52/255) of the cats, while FeLV prevalence was 7.64% (14/255) by immunochromatography and 11.82% (30/255) by PCR (Novo *et al.* 2016) [EB1].

In the Yucatan peninsula of Mexico, the seroprevalence of retrovirus exposure in a population of cats was reported to be 2.5% (5/227) for FIV and 7.5% (17/227) for FeLV (Ortega-Pacheco *et al.* 2014) [EB1].

A study conducted on a Chilean island found a prevalence of infection, by PCR, for FeLV of 33% (26/78) (Mora *et al.* 2015) [EB1]. Seroprevalence of retroviral exposure in a cross-sectional survey of a convenience sample of domestic cats from Costa Rica's greater metropolitan area was 16.7% (17/102) for FeLV and 8.8% (9/102) for FIV (Blanco *et al.* 2009) [EB1]. Seroprevalence of retrovirus exposure for cats living in a shelter in Venezuela was 2.1% (2/95) for FeLV and 3.1% (3/95) for FIV (Pino *et al.* 2015) [EB1]. A study conducted in Colombia found a seroprevalence of 10.7% (184/1718) for FIV (Molina *et al.* 2016) and a study in Guatemala reported a seroprevalence of 16.7% (5/30) for FeLV (Lickey *et al.* 2005) [EB1].

Canine rabies virus infection

Rabies in cats has been reported in 15 LATAM countries (Argentina, Bolivia, Brazil, Chile, Colombia, Cuba, Dominican Republic, El Salvador, Honduras, Mexico, Nicaragua, Paraguay, Peru and Venezuela) from 2005 to 2015 (Velasco-Villa *et al.* 2017) [EB1].

Vaccines and vaccination practice in Latin America

Information on vaccines and vaccination practice was derived from our KoL meetings, the questionnaire survey and practice visits. It is recognised that there is under-vaccination of the companion animal populations in the LATAM countries; *e.g.* our Argentinian KoLs estimated that only 20 to 35% of owned pets were vaccinated and KoLs from Brazil suggested that 17% of dogs and 6 to 9% of cats had an annual veterinary visit (and vaccination).

Small companion animal vaccines are available to practicing veterinarians throughout LATAM. There are two major sources for these products. The majority of vaccines are produced by the major global manufacturers and are either the same or related products to those marketed in other regions and countries by those manufacturers. Such products are supported by North American and/or European licensing dossiers describing their quality, safety and efficacy, and often by independent peer-reviewed scientific literature. In this document, we will refer to such products as “international vaccines” or “quality assured vaccines.” The second source of vaccines is, less commonly, national manufacturers of specific products. The VGG was unable to assess the quality, safety and efficacy of such products, which are generally unsupported by independent peer-reviewed scientific literature. For that reason, all of the recommendations made in this document (with the single exception of *Leishmania* vaccines in Brazil, which will be discussed specifically below) relate only to international quality assured vaccine products.

However, although the majority of vaccine products are derived from the international manufacturers, there are different and much lesser product ranges available in the LATAM countries compared with markets in, for example, the United States or Europe. There are: (1) fewer products from a manufacturer's range made available, (2) unique products from an international manufacturer that are unavailable in other regions (*e.g.* the *Giardia* vaccine, which has been removed from most global markets with the exception of LATAM and will be discussed specifically below), (3) a trend to large multiantigen vaccines rather than the lesser antigen combinations that are now widely available elsewhere and (4) distinct differences with respect to licensed duration of immunity of the same vaccine product between markets elsewhere and markets in LATAM. All of these factors make it very difficult for veterinarians in LATAM to vaccinate in accordance with the current WSAVA global vaccination guidelines. In particular, the delivery of core vaccines to adult dogs and cats no more frequently than every 3 years is challenging when it is not possible to obtain three-component core vaccines (*e.g.* a combination of CDV, CAV and CPV2 or a combination of FPV, FHV1 and FCV) and these are admixed with multiple non-core antigens in large multicomponent combinations. The challenge is compounded when the licensed duration of immunity (DOI) for individual core antigens is 1-year, when the identical products in other markets carry a minimum DOI claim of 3 years. As we have found elsewhere, there was a reluctance to accept that a 1-year licensed product might be used “off label” every 3 years (with informed client consent) even though the identical product is authorised in this way in other regions. This “transition stage” in the use of core vaccines was more readily embraced by veterinarians in North America and Europe than it has been, or likely will be, in markets such as LATAM.

As we found in Asia, there are also challenges around rabies vaccination of individual pet animals in the practice setting (as opposed to government-run mass vaccination campaigns). Rabies vaccination is mandated by law to occur on an annual basis and currently the international inactivated rabies vaccines carry a 1-year licensed DOI in most LATAM countries. However, the identical products in other global markets now have a 3-year licensed DOI. In order to progress in LATAM, manufacturers and regulators will need to work to extend the label claim for DOI of these products, and at the same time, the veterinary professional associations will need to lobby for changes in the law (as has already happened in many other countries) so the law becomes consistent with the science.

Moreover, there remains a fundamental ethos in LATAM that a veterinary practice derives an important proportion of its income from the sale of vaccines to clients. Repeatedly on our practice visits, we noted large sign boards above the reception desk in practices that listed individual dog and cat vaccines and their prices. It was clear that clients, with or without the advice of the veterinarian, would need to select the vaccines that their pet received on the basis of what they could afford to pay. The concepts of the “annual

health check” and incorporating vaccination into a preventive health care programme for the individual pet (a practice “health care plan”) were novel to many members of the veterinary community in LATAM. Because of the perceived reliance on vaccine sales for underpinning practice income, there is also a current culture of “more is better.” Veterinarians almost exclusively deliver vaccination on an annual basis, using the vaccine product that contains the greatest antigen combination. Clients have been accustomed to visiting their veterinarian annually for a “vaccine booster.” Annual administration of large multicomponent vaccines are deemed preferable because the client has been led to expect that this approach is superior. We were told repeatedly that veterinarians would “lose their clients” if they did not offer annual multicomponent vaccination with the highest number of antigens possible. There is something of a “vicious cycle” to this concept, because manufacturers continue to supply and promote multicomponent products that may include (for the dog) anything up to 10 different antigens.

A further issue faced by veterinarians in LATAM is that companion animal vaccination is not restricted to the veterinary practice. Pet stores are able to vaccinate puppies and kittens before sale and owners may obtain vaccines directly for administration to their pets using poorly-considered vaccination schedules.

As the VGG had seen during our Asian project, there are also common and simple issues related to “vaccine husbandry” in LATAM veterinary practices. These largely relate to the in-practice storage of vaccines which often takes place in multiuse domestic refrigerators with no temperature monitoring and storage of multiple medicines (and often food and drink for human consumption). During our Asian project, the VGG produced some simple guidelines for effective vaccine husbandry and these are replicated and extended in the current document (Table 3) for the benefit of LATAM practitioners.

Although the 2016 WSAVA global vaccination guidelines have been translated into Spanish and Portuguese, and are freely available from the WSAVA website, it was clear that most veterinarians (except for the KoLs) were not aware of these and had not read them. During our country visits there was often publicity in the veterinary press concerning the WSAVA project and the translations were promoted at our CE events.

Contemporaneous with the VGG LATAM project has been a project run by the Federación Iberoamericana de Asociaciones de Pequeños Animales Veterinarios (FIAVAC). The project is managed by the Comité Latinoamericano de Vacunología en Animales de Compañía (COLAVAC) and aims to produce vaccination guidelines that consider the epidemiological and cultural idiosyncrasies of veterinary practice in LATAM. The establishment of COLAVAC is entirely within the spirit of WSAVA vaccination guidelines. The 2016 WSAVA guidelines clearly state that “These guidelines are not a mandatory edict, but rather should be used by national associations and individual veterinary practices to develop vaccination schedules relevant to the local situation.” COLAVAC is, therefore, an example of precisely that recommendation and we congratulate FIAVAC on this important initiative. COLAVAC guidelines have now been released for Brazil, Argentina and Mexico (<http://www.fiavac.org/guias.php>) and recently, in a scientific journal, for Peru (Rubio *et al.* 2018); however, readers will note that the guidelines differ in their recommendations for use of the same vaccines in the three countries, and sometimes differ from the recommendations made by the VGG in the present manuscript. There are some important reasons that might account for the latter observation and these relate to the ideal working practices for an expert group that produces practice guidelines. Firstly, such expert groups must be completely independent of industry and should not include industry representatives on committees or have input or right of veto from industry sponsors. As readers may see from the Conflict of

Table 3. Vaccine husbandry: key points for veterinary practitioners

- Vaccines should be kept in a designated refrigerator that is only used for storage of drugs and vaccines (not foodstuff or drinks)
- The electricity supply to a vaccine refrigerator should be safeguarded against inadvertent breaks by use of a switchless electric socket or a plug clearly marked “do not switch off”
- Vaccines (and particularly adjuvanted vaccines) have an optimum storage temperature that is usually between 2 and 8°C (domestic refrigerators should be maintained at 4°C). These products should not be frozen or positioned adjacent to the freezer compartment of the refrigerator, and refrigerator temperature should be monitored regularly by use of a maximum–minimum thermometer located in the main body of the refrigerator. Ideally, the temperature of the refrigerator should be charted in a log book on a daily basis
- Vaccines should be stored in the refrigerator with adequate room for air to circulate enabling a constant temperature to be maintained around the products
- Vaccines should be stored in the refrigerator within the manufacturer’s packaging
- Certain shelves should be designated for specific vaccines and the location of vaccines listed outside the refrigerator. This will minimise the time the door is kept open while accessing vaccines
- Correct stocks of vaccines should be maintained, without overstocking
- Stock should be rotated so new stock is placed at the back
- Vaccines transported into the field should also be subject to continuation of the “cold chain.” They should be transported in a cold box, but not put in direct contact with ice or ice packs
- Freeze-dried vaccines should be reconstituted immediately before use with appropriate diluent or liquid vaccine given concurrently (as per manufacturer’s recommendations). It is bad practice and contraindicated to make up first thing in the morning the vaccines anticipated to be used during the day. Some vaccine components (e.g. CDV, FHV-1) are particularly labile in this regard and so these vaccines may not induce adequate immunity if not reconstituted just before use
- Vaccines should only be mixed together in the same syringe if this is specified as acceptable in the manufacturer’s data sheets
- Syringes and needles for vaccines should not be reutilized
- Vaccine injection sites should not be sterilised with alcohol or other disinfectant as this may inactivate infectious (MLV) vaccines
- Vaccines should be “in date” and precise details of batch numbers, components and site of injection should be noted in the animal’s medical record

Interest statement that ends the present manuscript, the VGG is considered an entirely independent academic committee. Secondly, guidelines should be evidence-based and supported wherever possible by peer-reviewed published scientific literature. The VGG developed an evidence-based hierarchy for the science of vaccinology (Day *et al.* 2016), which is applied to its global and now regional guidelines. Finally, guidelines documents themselves should undergo scientific peer-review and be published in a creditable scientific journal rather than an industry magazine. VGG documents have always undergone such independent scrutiny and are published in the official scientific Journal of the WSAVA, the *Journal of Small Animal Practice*.

VGG RECOMMENDATIONS FOR LATIN AMERICA

Education

It is challenging to make recommendations regarding undergraduate education in an environment where there is such diversity in resources and standards between state-funded and private veterinary schools and a lack of any form of national curriculum. There is concern from the veterinary profession itself in the standards that might apply to the rapidly growing market in private veterinary education. The VGG can only emphasise the importance of solid grounding in the traditional teaching of veterinary immunology and microbiology as it pertains to small companion animal infectious disease and vaccinology, and to the development of tuition in client communication and delivery of vaccination in a clinical setting that must occur during the clinical years of a veterinary programme. Those academics who teach such curricular elements should be encouraged to be well-versed in the WSAVA global vaccination guidelines.

There is also clearly a huge need for postgraduate CE in small companion animal vaccinology. This is, to a large extent, the responsibility of the professional associations and veterinary industry and it is encouraging to see some of the initiatives for these subjects being incorporated into congress programmes and forming the content for postgraduate seminars in LATAM countries. The use of electronic delivery of tuition (*i.e.* via webinars) is also becoming more widespread in LATAM and vaccinology should comprise a valuable component of such programmes. The WSAVA itself hopes to further develop an on-line platform for delivery of CE in the near future and vaccination guidelines will form part of that content. It would be beneficial if discussions could be held in LATAM about moving towards compulsory continuing professional development for re-registration purposes for veterinary professionals.

Research

As can be seen from the summary of peer-reviewed scientific data related to small companion animal infectious diseases and vaccinology presented above, there is a marked lack of relevant information available to the veterinary profession in LATAM. Given the very large numbers of academic institutions and academic staff devoted to tuition in microbiology and immunology, it is disappointing that there are few active research programmes in this important area of veterinary medicine. It is likely that this reflects a number of possible contributing factors: (1) that in private institutions there is a focus on teaching rather than research, (2) that it is challenging to obtain research funding for investigation of small companion animal infectious disease that does not have zoonotic potential (*e.g.* CVL, leptospirosis and canine rabies), (3) that greater academic kudos might be derived from investigating diseases of production animals and (4) that diagnostic laboratory infrastructure for undertaking infectious disease surveillance programmes is lacking. Although much of the scientific literature reviewed by the VGG was generated in Brazil, it is alarming to see, in that country, the current climate of governmental cuts in support for tertiary education and research, in particular for programmes that support the training of the next generation of veterinary research scientists *via* MSc and PhD studies.

The VGG strongly supports the performance of clinically relevant research into small companion animal infectious diseases. In particular, developing a clear understanding of the regional prevalence of different infectious agents and the classification of infectious agents circulating in the field (*e.g.* specific serovars of pathogenic leptospires). There are clearly some distinctive aspects of infectious disease epidemiology in LATAM, in particular the observed higher prevalence of feline retroviral infections. Only by generating current surveillance and molecular phylogeny data will there be advances in clinical diagnostics, vaccine availability and disease control. As we suggested in Asia, there may be mutual benefit to academic researchers in veterinary schools working more closely with industry in order to generate clinically relevant data that might be used to introduce new vaccine products into LATAM for the benefit of the profession and the animals for which we care.

Vaccine supply

As will become clear from the recommendations made below, there is a particular challenge facing the implementation of global vaccination guidelines in LATAM. This relates very simply to the lack of minimal-antigen product ranges that are widely available in North America, Europe and other markets, and enable veterinarians in those countries to vaccinate in accordance with WSAVA guidelines. Until there is a shift away from large multi-antigen vaccines (containing anything up to 10 different antigens) towards trivalent or bivalent core vaccines with monovalent or bivalent non-core vaccines, it will be challenging for LATAM practitioners to embrace the new standards in vaccinology that are now well-embedded in many other markets. Once such product ranges are more widely available (currently only in Argentina), it will then require significant education as to how they are best used in practice and

a radical change in ethos to embrace the concept of preventive health care delivered through an annual health check or health care plan, as opposed to the deliberate marketing of vaccine products as commercial drivers of central importance in veterinary practice.

An important challenge in making such changes lies in identifying who has responsibility for driving change. Arguably, veterinary industry should lead in bringing revamped product ranges to LATAM, but this cannot happen without the support of the veterinary profession *via* the professional associations and without some flexibility in vaccine licensing requirements. With respect to the latter, the VGG supports the acceptance of licensure studies performed for other markets in obtaining new licences in new markets. At very least, not having to perform additional studies for products that are already licensed in North American or European markets would provide significant animal welfare benefits.

There remains the significant challenge of veterinary vaccines being available directly to owners and breeders out with the veterinary practice. A change in emphasis from the veterinary practice simply selling vaccines to selling a holistic preventive health care package based in professional advice will be required in order to re-educate the pet-owning public and attract them back to the veterinary practice.

Canine vaccination: Aspirational protocols

The VGG recommends that veterinarians in LATAM implement the basic principles of evidence-based companion animal vaccinology presented in the 2016 WSAVA global vaccination guidelines (Table 4; Day *et al.* 2016) [EB1]. Understanding the concept of core *versus* non-core vaccines is fundamental to application of the vaccination guidelines in practice. Core vaccines are those that every dog, regardless of location or lifestyle, must receive for protection against infections that cause significant morbidity or severe or fatal disease. Core vaccines contain CDV, CAV2 and CPV2, preferably as modified live viruses (modified live vaccine; MLV). In countries where canine rabies remains an endemic disease, inactivated rabies vaccine is also regarded as a core vaccine for every dog. Non-core vaccines are those considered for individual animals whose geographical location or lifestyle puts them at risk for specific infections. Non-core vaccines are not required for every animal and should not be used where there is no evidence for existence of a related disease or when the risk for exposure is minimal. Non-core vaccines include *Leptospira* vaccines and vaccines designed to protect against elements of CIRDC, which usually contain *B. bronchiseptica* with or without CPiV. The WSAVA global guidelines classify some vaccines as not recommended for any dog because there is insufficient scientific evidence to justify their use. These include the inactivated canine enteric (non-pantropic) coronavirus (enteric CCoV) vaccine and the *Giardia* vaccine when used to either prevent or treat infection.

Table 4. An aspirational vaccination programme for LATAM practitioners

Type of vaccine	Puppy or kitten vaccination	Adult animal revaccination
Quality-assured core MLV vaccines For dogs including CDV, CAV and CPV2 For cats including FPV, FCV and FHV1	Start at 6 to 8 weeks of age then every 2 to 4 weeks until 16 weeks of age or older [EB1] Core vaccination may be started earlier, but never earlier than 4 weeks of age with MLV products. For puppies a product containing high-titre CDV and CPV2 may be used at 4 to 6 weeks (if available) before switching to trivalent core vaccine at 8 weeks or older [EB1] A fourth vaccine should be given between 6 to 12 months of age OR 12 months after the third vaccine OR at 12 months of age [EB4]	Revaccination with core, quality-assured MLV vaccines should be no more frequent than every 3 years [EB1]. Serology might be used to monitor protective immunity (for CDV, CAV, CPV2 and FPV) and to aid decision making on revaccination intervals [EB1] The single exception to this may be cats at high risk of contracting upper respiratory virus, in which these components may be given annually [EB1]
Quality-assured canine rabies vaccine for client-owned pet dogs or cats (note this does not refer to mass vaccination campaigns)	According to manufacturer's recommendations; one dose from 12 weeks of age [EB1] The VGG recommends that in high risk areas (<i>i.e.</i> NOT most areas of LATAM) a second dose may be given 2 to 4 weeks later A second vaccine in non-high-risk areas should be given 12 months later or at 12 months of age	Quality-assured canine rabies vaccines all carry a 3-year licensed DOI in many countries outside of LATAM [EB1]
Non-core vaccines Examples for dogs: <i>Leptospira</i> , canine infectious respiratory disease complex ("kennel cough") and <i>Leishmania</i> Examples for cats: feline leukaemia virus or <i>C. felis</i> (vaccines against feline immunodeficiency virus and <i>Bordetella</i> [for cats] are not available in LATAM)	Give according to manufacturer's recommendations: generally two doses 2 to 4 weeks apart. Injectable non-core vaccines and oral CIRDC vaccines are generally given from 8 weeks of age. Intranasal CIRDC vaccines may be given earlier (follow manufacturer's recommendations) [EB1]	Non-core vaccines are generally given annually unless the datasheet specifically recommends otherwise. FeLV vaccines may be given every 2 or years to adult cats (and some quality-assured FeLV vaccines carry a licensed 2- or 3-year DOI in markets outside of LATAM) [EB1]
Not recommended vaccines These include vaccines against coronavirus (canine or feline), <i>Giardia</i> and <i>Microsporium canis</i>		

The generic information in this table should be read in conjunction with the more detailed recommendations provided in the current WSAVA vaccination guidelines (Day *et al.* 2016). Vaccination according to WSAVA guidelines is possible only where available product ranges separate core from non-core vaccine components. Note that these recommendations apply only to quality-assured vaccines, most of which are produced by large, international companies.

CCoV is considered of minor clinical importance as a primary enteric pathogen, causing only mild diarrhoea in puppies. More severe enteric disease occurs with CCoV and CPV2 coinfection (Decaro *et al.* 2004) [EB1]. Published studies have demonstrated that commercial inactivated enteric CCoV vaccines induce only transient serum antibody responses and do not reduce viral infection or faecal shedding of virus compared with non-vaccinated dogs (Pratelli *et al.* 2003, de Castro *et al.* 2010) [EB1]. Moreover, injectable CCoV vaccine does not lead to elevation of faecal CCoV-specific IgA antibody concentration, which is believed to underlie immune protection (Decaro *et al.* 2004) [EB1].

Similarly, dogs vaccinated with a commercial inactivated *Giardia* vaccine were not protected from *Giardia* infection in that there were no differences in parasite cyst or antigen detection rates or the occurrence of diarrhoea between vaccinated and unvaccinated dogs (Anderson *et al.* 2004, Lund *et al.* 2010) [EB1]. In addition, treatment of *Giardia*-infected animals with a commercial inactivated *Giardia* vaccine was not effective in eliminating cyst production (Anderson *et al.* 2004) [EB1].

The WSAVA guidelines recommend revaccination of puppies with international MLV core vaccines at timed intervals over the first 4 months of age to overcome interference by maternally-derived antibody (MDA) [EB1]. The guidelines also recommend that a final MLV core vaccine is given between 6 months to 1 year of age in order to ensure that all puppies receive at least one dose of vaccine that is able to confer immunity in the absence of MDA [EB4]. Development of protective immunity is not dependent on the number of MLV core vaccines given during the puppy vaccination series, but rather when they are given. For adult animals, there is ample evidence supporting revaccination with quality-assured international MLV core vaccines no more frequently than every 3 years (Abdelmagid *et al.* 2004, Bohm *et al.* 2004, Mouzin *et al.* 2004, Gore *et al.* 2005, Schultz 2006, Larson & Schultz 2007, Mitchell *et al.* 2012, Killely *et al.* 2018) [EB1]. While regulatory authorities in LATAM countries require annual revaccination with international MLV core vaccines licensed elsewhere for use at 3-year intervals, this practice is regarded as inappropriate use of client financial resources that are better applied to annual wellness examinations, routine parasite prophylaxis, and treatment of medical issues. Increasing the frequency of vaccination with MLV core vaccines does not confer greater protection to an individual animal. Increasing the number of animals that are properly vaccinated is much more important to ensure protection through population or “herd” immunity than vaccinating each animal more often. Even though the 3-year DOI datasheets for quality-assured international MLV core vaccines are not currently accepted by LATAM countries, the VGG encourages the national and local regulatory authorities to permit practitioners to use these vaccines according to the WSAVA guidelines as “off-label use” products with informed client consent. This approach has been used successfully in other countries pending acceptance of the quality-assured international vaccine datasheets by the national and local authorities.

Canine vaccination: Pragmatic protocols

Issues with vaccine product availability, product licensed DOI, and knowledge of disease prevalence and exposure risks hampers adoption of the WSAVA global vaccine guidelines by practitioners in LATAM countries. In many of these countries, there is limited availability of quality-assured multicomponent and single-component international vaccines allowing separate use of MLV core antigens *versus* non-core antigens. The paucity of peer-reviewed studies on specific disease prevalence in LATAM countries presents challenges for practitioners in making evidence-based decisions on what non-core vaccines are appropriate for individual animals in different regions.

LATAM practitioners and their national associations should lobby industry and government regulators for access to quality-assured international canine vaccines that contain just the MLV core components (CDV, CPV2, CAV2) or the non-core components (*Leptospira*, CPiV, *Bordetella*). This will allow for administration of the MLV core vaccine every 3 years and for separate annual vaccination with non-core vaccines for individual dogs at risk. Currently, most quality-assured international vaccines available in LATAM countries contain MLV core antigens (CDV, CAV2, CPV2) combined with non-core antigens (*Leptospira*) and non-recommended antigens (*i.e.* enteric CCoV). Practitioners can follow some pragmatic recommendations presented in Table 5 to transition from giving these multicomponent vaccines every year to every dog to using the core and non-core vaccines separately according to the WSAVA guidelines. Included in this transitional pragmatic protocol is the “off-label” administration with client consent of MLV core vaccine components every 3 years to adult dogs instead of annually. The VGG recognises that practitioner use of this pragmatic protocol is limited by local product availability.

For clients that can only afford one vaccine for their dog, the recommended approach is to choose a quality-assured international vaccine containing the MLV core components and give that vaccine at a time when the single dose can induce long-lasting protective immunity in the absence of maternal antibody interference (*i.e.* at 4 months of age or older).

Canine leishmaniosis in LATAM

Canine visceral leishmaniosis (CVL) caused by *Leishmania infantum* is one of the most significant zoonotic diseases in LATAM and the geographical distribution of CVL is expanding in the region. CVL is widespread from Mexico to Argentina, with autochthonous cases reported in many countries (Marcondes & Day 2019) [EB1]. Although vaccines can prevent active infection and the risk of development of clinical disease in some dogs, some vaccinated dogs can become progressively infected and transmit the parasite to the sand fly vectors even in the absence of clinical signs (Bongiorno *et al.* 2013, Fernandes *et al.* 2014, Oliva *et al.* 2014, Regina-Silva *et al.* 2016) [EB1]. Therefore, for animals living in endemic areas, from an epidemiological viewpoint, it is more important to use

Table 5. A pragmatic vaccination programme for LATAM practitioners in 2019

Type of vaccine	Aim	Puppy or kitten vaccination	Adult animal revaccination
Core vaccines for dogs and cats	Select a quality-assured MLV product that allows the <i>minimum combination</i> of core antigens to be given (CDV, CAV, CPV2 for dogs; FPV, FHV1, FCV for cats) Use an alternative diluent rather than reconstitute with a non-core vaccine if that non-core vaccine is not essential for that animal	Start at 6 to 8 weeks of age then every 2 to 4 weeks until 16 weeks of age or older [EB1] Core vaccination may be started earlier, but never earlier than 4 weeks of age with MLV products. For puppies a product containing high-titre CDV and CPV2 may be used at 4 to 6 weeks (if available) before switching to trivalent core vaccine at 8 weeks or older [EB1] A fourth vaccine should be given between 6 to 12 months of age OR 12 months after the third vaccine OR at 12 months of age [EB4]	Discuss with clients the new global approach to core revaccination and obtain consent for administration of core quality-assured MLV vaccine no more often than every 3 years [EB1] The single exception to this may be cats at very high risk of contracting upper respiratory virus. These cats might be vaccinated annually, but be aware that the FPV component of the vaccine combination is not actually required [EB1]
Quality-assured canine rabies vaccine for client-owned pet dogs or cats (note this does not refer to mass vaccination campaigns)	Select a quality-assured international product if available	According to manufacturer's recommendations; one dose from 12 weeks of age [EB1] The VGG recommends that in high risk areas (<i>i.e.</i> NOT most parts of LATAM) a second dose may be given 2 to 4 weeks later A second vaccine in non-high-risk areas should be given 12 months later or at 12 months of age	Conform to local legal requirements for annual revaccination, but continue to actively lobby associations and governments to allow triennial revaccination using quality-assured products with a licensed 3-year DOI. Continue to lobby industry to register these products with a 3-year DOI in your country
Non-core vaccines Examples for dogs: <i>Leptospira</i> , canine infectious respiratory disease complex (kennel cough) and <i>Leishmania</i> Examples for cats: feline leukaemia virus or <i>C. felis</i> (feline immunodeficiency virus and <i>Bordetella</i> vaccines [for cats] are not available in LATAM)	Discuss the individual animal's lifestyle and exposure risk with the client – is the vaccine really necessary for this animal? Chose a quality-assured product which contains just the desired antigen or the antigen in the least possible combination with other non-essential components	Give according to manufacturer's recommendations: generally two doses 2 to 4 weeks apart. Injectable non-core vaccines and oral CIRDC vaccines are generally given from 8 weeks of age. Intranasal CIRDC vaccines may be given earlier (follow manufacturer's recommendations) [EB1]	Non-core vaccines are generally given annually unless the datasheet specifically recommends otherwise; FeLV vaccines need not be administered to adult cats on an annual basis (see Table 4)
Not recommended vaccines These include vaccines against coronavirus (canine or feline), <i>Giardia</i> and <i>Microsporium canis</i>	Consider whether there is sufficient scientific evidence to support their use		

The generic information in this table should be read in conjunction with the more detailed recommendations provided in the current WSAVA vaccination guidelines (Day *et al.* 2016). Note that these recommendations apply only to quality-assured vaccines, most of which are produced by large, international companies.

insecticides, especially collars, to prevent sand fly bites, than it is to vaccinate (Sevá *et al.* 2016, Lopes *et al.* 2018) [EB1]. Whenever possible, the two measures should be combined, in order to provide a high level of protection not only for dogs, but for other animals and people that share the same environment. It is important to highlight that a previous history of vaccination does not exclude a diagnosis of CVL in dogs with clinical signs or clinicopathological abnormalities suggestive of the disease.

Currently in LATAM there are only two licensed vaccines against CVL. One contains the recombinant A2 protein of *L. donovani* in an adjuvant, licensed in Brazil and Paraguay, and the other consists of purified excreted–secreted proteins of *L. infantum* (LiESP) in an adjuvant, and is licensed in Paraguay and Argentina. The vaccination protocol for puppies includes three doses given 3 weeks apart and an annual booster. The A2 vaccine can be used in dogs from 4 months of age and the LiESP vaccine from 6 months of age. Adult dogs that have never been vaccinated receive the same protocol. Vaccines against CVL should only be considered for dogs living in endemic areas, where they are at risk of being infected. According to the manufacturer's recommendations, only seronegative dogs should be vaccinated; however, many dogs can be infected without seroconversion, and therefore, be improperly vaccinated.

Canine rabies in LATAM

It is clear that large-scale mass vaccination programmes conducted over recent decades have succeeded in controlling canine rabies virus infection in dogs and cats (and therefore the human population) in many LATAM countries. There are, however, remaining “hot spots” for disease and low numbers of individual cases are recorded in countries with good overall control. In most LATAM countries there is ongoing surveillance and legally-mandated annual canine rabies vaccination. This may be delivered by mass vaccination field campaigns run by government or non-governmental organisations or through the veterinary practice for individual client-owned pet animals. Vigilance and continued vaccination to maintain herd immunity are essential at this time for maintaining control of canine rabies. As discussed above, there is a disconnect between the law and the science pertaining to rabies vaccines. There is no doubt that

in mass vaccination field campaigns (particularly where these aim to vaccinate free roaming stray or community owned dogs) annual revaccination is essential to account for population turnover. However, for a client owned, veterinarian-visiting individual pet animal, vaccination with an international quality-assured canine rabies vaccine should confer a minimum 3 year duration of immunity (Day *et al.* 2016) [EB1]. A move to licensing those vaccines with a 3-year DOI as the same products have in the USA, Canada and Europe would help address this anomaly.

Feline vaccination: Aspirational protocols

When aspiring to produce an optimised vaccination protocol for cats in a particular locale, the immensity and diversity of Latin America must be borne in mind. Nevertheless, it is possible to provide broad advice to LATAM veterinarians based on what has been learned about feline infectious diseases in the region and beyond, and by considering what vaccines are commercially available in LATAM.

Veterinarians in all LATAM countries are encouraged to follow the fundamental advice provided in the latest WSAVA vaccination guidelines (Day *et al.* 2016) (Table 4). As these guidelines make clear, there are core vaccines that, in an ideal world, all pet kittens should receive and all adult cats should receive sufficiently frequently to ensure protection throughout life. These vaccines protect against infectious agents that can cause severe illness or death, especially in kittens. In all countries, vaccines against FPV, FHV1 and FCV are considered core (Scherk *et al.* 2013, Day *et al.* 2016) [EB1]. In countries where rabies is endemic, rabies vaccines are also regarded as core (Scherk *et al.* 2013, Day *et al.* 2016) [EB1]. In addition, there are non-core vaccines. Not every kitten or cat need necessarily receive every one of the non-core vaccines. Use of these vaccines should be based on an informed risk–benefit analysis, based on knowledge of local disease frequencies and the lifestyle of the individual cat (Day *et al.* 2016) [EB1]. Non-core vaccines protect against infectious agents that may be encountered frequently in some areas, but are known to be rare or absent in other places (*e.g.* FeLV). Some non-core vaccines (*e.g.* those against *C. felis* infection) protect against disease agents that are generally less pathogenic than those covered by the core vaccines or are treatable using antibiotics. The VGG categorises one feline vaccine (against FIP) as “not recommended.” Although this is a commercially-available vaccine in some countries (not in LATAM), the VGG has judged that there is insufficient evidence of benefit to recommend its routine use.

In some LATAM countries (*e.g.* Brazil) FeLV has been reported to be highly prevalent in some regions (*i.e.* the southeast and deep south of the country) and much less prevalent in others, such as the north (Almeida *et al.* 2012, Lacerda *et al.* 2017, Biezus *et al.* 2019, Cristo *et al.* 2019a,b) [EB1]. Overall, FeLV prevalence in Brazil seems to be considerably higher than in many other countries where its prevalence has been studied (Galdo Novo *et al.* 2016) [EB1]. In Mexico, FeLV prevalence has been shown to exceed that of FIV in Merida, tropical Mexico, but does not match the very high prevalence values reported from various parts of Brazil (Ortega-Pacheco *et al.* 2014) [EB1]. Therefore, it is recommended that LATAM veterinarians seek to establish FeLV prevalence in their local area, to allow evidence-based decisions to be made about the recommended use (or otherwise) of FeLV vaccines. This is the essence of how non-core vaccines should be used.

High-quality, MLV FPV vaccines have been shown to provide long-lasting, robust immunity to a large majority of vaccinated cats when used in accordance with WSAVA VGG guidelines (Gore *et al.* 2006, Barrs 2019) [EB1]. As a precaution, revaccination every 3 years is generally recommended. Vaccinating more frequently than every 3 years with high-quality MLV FPV vaccines is unlikely to provide any improvement in the degree of protection provided by these vaccines and may increase the risk of adverse reactions. It is far more important to ensure that a large proportion of the target population is vaccinated (*i.e.* to increase the overall herd immunity) than it is to increase the frequency of revaccination of individual animals in the population at risk. Indeed, the unhelpful annual revaccination of cats against FPV with products, known to provide many years of protection, should be viewed as poor use of potentially limited client financial resources. These could be better applied to address other health issues in the pet and perhaps could be used to purchase non-core vaccines, if use of one or more of those is supported by evidence and hence justifiable in that locale.

High-quality MLV vaccines against FCV and FHV1 do not provide such robust or long-lasting protection as do the FPV vaccines just mentioned (Jas *et al.* 2015) [EB1]. The immunity conferred by these vaccines cannot prevent infection or development of the carrier state. Nevertheless, for cats living “low risk” lifestyles (*i.e.* indoor only cats that do not visit boarding catteries) vaccination every 3 years is considered to provide sufficient protection (Scherk *et al.* 2013, Day *et al.* 2016) [EB4]. For cats at higher risk of FCV or FHV infection (*i.e.* cats with outdoor access or cats regularly visiting a boarding cattery), annual revaccination is recommended [EB4]. In some countries, it is possible to purchase vaccines that contain only FCV and FHV1, so that trivalent vaccines can be used every 3 years (FCV, FHV1, FPV) and a bivalent vaccine (FHV1, FCV), if needed, in each of the intervening years. Unfortunately, such products are not, as yet, consistently available throughout the world.

Rabies vaccines must be used in accordance with local regulations. Notably, some international quality assured rabies vaccines for use in cats provide protection for at least 3 years (Jas *et al.* 2012) [EB1]. In the USA, regulations requiring annual revaccination of cats, despite evidence of much longer-lasting protection by some vaccines, were challenged and changed as a consequence of effective political lobbying by the veterinary profession and pet owners.

A crucial feature of an idealised vaccination protocol for cats in any country would include a finish to the kitten series no earlier than 16 weeks of age. This is because evidence has accumulated in recent years indicating that a sizeable minority of kittens have significant amounts of interfering maternal antibodies against some of the vaccine components, even at up to 20 weeks of age (Digangi

et al. 2012, Jakel *et al.* 2012a,b) [EB1]. A 16 weeks or later finish is consistent with this scientific evidence and with the current WSAVA vaccination guidelines, as well as with guidelines from other organisations.

Vaccine products available in LATAM countries may not carry datasheet recommendations for use as described in this section. It would be helpful if local regulations and guidance from veterinary professional organisations enabled practitioners to use vaccines “off label” with informed client consent. This approach was used for years by veterinarians in other countries, before datasheet recommendations were eventually updated. The VGG hopes that, in due course, quality assured core MLV vaccines produced by large, international pharmaceutical companies will have datasheet changes made in the LATAM countries.

Feline vaccination: Pragmatic protocols

Small animal practitioners in LATAM countries are currently unable to adopt the WSAVA vaccination guidelines in full. This is for a number of reasons. Firstly, rational use of non-core vaccines is hampered in many parts of LATAM by a lack of information about disease frequencies. Conversely, for some regions, excellent, detailed information is available. Where evidence is lacking, veterinarians often decide to take a precautionary approach. This can lead to unnecessary overuse of non-core vaccines. More research and surveillance would enable more informed, selective use of non-core vaccines.

Secondly, in many LATAM countries there is limited product availability. In particular, core vaccines licensed and approved for biennial, triennial or less frequent use are unavailable in many LATAM countries. In part, this may be because of a lack of locally-generated evidence for extended DOI and a requirement for such evidence from local regulatory authorities. Yet multiple strands of evidence, generated in numerous countries, support a view that feline core vaccines can be used in LATAM countries similarly, and with as much confidence, as in other parts of the world. Although current datasheets for many quality assured MLV core vaccines recommend annual revaccination of adult animals, the very same vaccines are given triennially in many other countries, including some with high infectious disease pressure.

Another challenge concerning product availability in LATAM is a paucity or lack of monovalent non-core vaccines. For example, in some countries, *C. felis* vaccines are only available in combination with the core FPV, FHV1 and FCV components and FeLV is only available in combination with the preceding four. Therefore, there exist 3-component, 4-component and 5-component feline vaccines, but few or no monovalent, non-core products. A veterinarian who wished to protect against FeLV as well as the core agents, but perceived no need to protect against *C. felis*, might thus be forced to administer the *C. felis* component, even if it was judged superfluous.

Veterinary practitioners and regional associations should therefore continue to lobby industry and government regulators for changes that would bring recommendations concerning use of quality assured vaccine products into line with those that apply and are used in many other parts of the world. Table 5 presents some pragmatic recommendations concerning use of feline vaccines that are intended to assist LATAM practitioners to head in the recommended direction.

Application of preventive health care plans with an annual health check to Latin America

As discussed earlier in this document it was clear from our discussions and practice visits in LATAM that the dominant culture in veterinary practice is that veterinarians sell vaccines to clients, that the sale of vaccines is the main driver for client attendance at the veterinary practice, and that vaccine sales underpin a large component of veterinary practice income. Indeed, some 25 years ago, these were global principles that also applied to veterinary practice in North America, western Europe, Australia, New Zealand, South Africa and other developed markets.

In the latter markets, in 2019, this culture has now been substantially replaced by a new way of promoting veterinary services (including vaccines) to clients. There has been a progressive move away from the concept of the “annual vaccination booster” or the “vaccine booster consultation” towards the implementation of holistic preventive health care packages delivered in part by an “annual health check” consultation. In more developed markets, this has now been extended to delivery of a practice “health care plan” for which a client might pay a regular monthly fee to cover numerous elements of preventive health care for their pets. The annual health check consultation is considered to require a longer period of time than a general consultation and provides the opportunity for the veterinarian to engage with the client to discuss in detail the overall health and wellbeing of the companion animal family member. Elements of the health check consultation (or of an annual health care plan) might include consideration of nutrition, dental health, behavioural issues, endo- and ectoparasite control, vector-borne diseases testing and which vaccines (core or non-core) might be delivered during this annual visit. Indeed, in many mature markets, annual assessment of the need for core revaccination (CDV, CAV and CPV2 for dogs and FPV for cats) is now determined by in-practice serological testing (“titre testing”) to determine whether an animal is already protected and therefore need not be revaccinated. The WSAVA global vaccination guidelines mention the value of serological testing and provide strong support for this approach. There is increasing literature to support the use of such serological tests in veterinary practice (*e.g.* Killey *et al.* 2018) [EB1]. Moreover, there is a substantial literature that evaluates the annual health check consultation and advises on the content, timing and approach to such a consultation (*e.g.* Belshaw *et al.* 2019) [EB1].

Implementing this new approach to delivery of companion animal preventive health care may be daunting for many LATAM practitioners. However, these changes need to be embraced in order for the profession in LATAM countries to keep pace with colleagues in more developed markets. Whilst there may be a longer transition period for veterinarians working with economically constrained clients, these new concepts should be more readily embraced by those working in areas of relative prosperity.

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Conflict of interest

The work of the VGG has been supported financially by MSD Animal Health who are global partners with the WSAVA. The VGG is an entirely independent group of academic experts who have authored this manuscript without consultation with industry. Representatives of the sponsoring company do not attend VGG meetings. The company does not have the right of veto over VGG recommendations.

FREQUENTLY ASKED QUESTIONS

Questions about vaccine products

1. Why does the VGG not recommend enteric canine coronavirus vaccine when I routinely identify this organism on faecal testing?

The VGG does not recommend this vaccine because there is insufficient scientific evidence to justify its use. The evidence that canine enteric coronavirus is a primary pathogen leading to intestinal disease in adult dogs is weak; the diarrhoea associated with infection is mild unless there is concurrent infection with CPV2. Experimentally, the virus causes only mild diarrhoea, if any, in dogs over 6 weeks of age and vaccination against CPV2 alone appeared to protect against challenge by both viruses. There is no evidence that available vaccines would protect against pathogenic, mutant forms of the virus that occasionally arise and have been described. There is even less evidence that the vaccine can protect against infection in the field and injectable vaccine does not appear to induce protective faecal IgA antibodies (Decaro *et al.* 2004). Brazilian data shows no difference in the identification of canine enteric coronavirus by PCR from the faeces of normal dogs and dogs with diarrhoea (Gizzi *et al.* 2014) [EB1].

2. Giardia vaccine is widely used throughout LATAM. Why does the VGG not recommend this vaccine?

The VGG does not recommend this vaccine because there is insufficient scientific evidence to justify its use. The evidence that the vaccine can prevent either shedding or infection is weak. One large field study of 6000 dogs showed that vaccinated puppies were actually more likely to have diarrhoea than unvaccinated puppies, and there was no difference between these groups with respect to cyst or antigen detection (Lund *et al.* 2010) [EB1]. The disease in dogs is not life-threatening, is rarely zoonotic, is of low prevalence and responds to therapy; for these reasons the vaccine is not recommended for client-owned dogs. It is not known whether the vaccine can cross-protect against strains of *Giardia* other than those used in challenge studies. Brazilian data shows no difference in the identification of *Giardia* by PCR from the faeces of normal dogs and dogs with diarrhoea (Gizzi *et al.* 2014) [EB1]. It is notable that the vaccine has been withdrawn from all markets globally with the exception of those in LATAM.

3. Are there any advantages to using intranasal rather than parenteral vaccines to protect against elements of the canine infectious respiratory disease complex?

Although published studies addressing this question do not always agree, the VGG is of the belief that, immunologically, vaccination *via* a mucosal route is more likely to generate relevant protective immunity (specifically the production of mucosal IgA and IgG antibodies as opposed to systemic IgG antibodies) for pathogens that infect *via* the same mucosae (Larson *et al.* 2013) [EB1]. Intranasal vaccination may have the added benefit of a rapid onset of immunity that may relate to a non-specific stimulation of innate immunity (*via* Toll-like receptor engagement and local cytokine/chemokine production) [EB4]. This may be beneficial when a dog is to be exposed in the short term to an environment where there is a risk of exposure to elements of the canine infectious respiratory disease complex (CIRDC). Intranasal vaccines may be used in puppies as early as 3 weeks of age as a single dose, with annual revaccination required. Intranasal vaccines are available (depending on the market and not all in LATAM) that are specific for *B. bronchiseptica* (Bb) alone or Bb in combination with CPiV, or Bb in combination with CPiV and CAV2.

4. I have heard that there are now oral vaccines against elements of the canine infectious respiratory disease complex – Why do we not have these in my country?

Oral vaccines against Bb are available in Australia, North America and Europe. These products have the advantage of ease of application, but contain only a single antigen (Bb) and may not share the same rapid onset of immunity as intranasal products. They may be given to puppies from 8 weeks of age and require annual revaccination. There is variation in the scientific literature as to whether

the oral and intranasal Bb vaccines confer equivalent protection, or whether protection is better with intranasal products (Larson *et al.* 2013, Ellis *et al.* 2016a, Scott-Garrard *et al.* 2018) [EB1]. As to why these products are not available in LATAM, you would need to ask the manufacturers and regulatory authorities responsible for vaccine licensure.

5. Does the VGG recommend use of a *Leishmania* vaccine?

The VGG classifies *Leishmania infantum* vaccines as non-core, meaning that their use should be restricted to dogs at risk in areas endemic for the infection. *Leishmania* vaccines are only available in Brazil, Argentina and Paraguay. These vaccines should be regarded as one tool in the prevention of canine visceral leishmaniasis. Control of the access of susceptible dogs to sand flies (*e.g.* by housing indoors during the times of greatest sand fly activity) and the use of sand fly preventives (*e.g.* collars) is far more important than vaccination (Sevá *et al.* 2016, Lopes *et al.* 2018) [EB1]. Vaccines do not produce sterilising immunity; they may prevent or lessen the severity of clinical signs in infected animals, but do not always prevent infection and so even vaccinated dogs may act as a reservoir for *Leishmania* (Regina-Silva *et al.* 2016) [EB1]. Dogs should be tested before vaccination as vaccination of a dog that is already infected is of no benefit in the prevention of infection and a waste of vaccine.

6. Why do we not have a *Borrelia* vaccine in our country?

Borrelia of different species are associated with infection and disease of dogs and cats in North America and Europe through to Asia. *Borrelia* are transmitted by *Ixodes* spp. ticks and have wild mammal and avian reservoirs. In order to introduce a *Borrelia* vaccine to LATAM, there would need to be robust research studies into whether the pathogen exists in this region, whether there are competent tick vectors and wildlife reservoirs, and whether dogs and cats could become infected and go on to develop clinical signs of disease. In Brazil, studies have identified borreliosis in human patients with Brazilian Lyme-like disease or Baggio–Yoshinari syndrome (Yoshinari *et al.* 2003, Mantovani *et al.* 2012), and *Borrelia burgdorferi* sensu lato in asymptomatic humans (Gonçalves *et al.* 2015) and ticks from the genus *Dermacentor* (Gonçalves *et al.* 2013) [EB1]. Few reports relate to companion animals, and although anti-*Borrelia* antibodies have been found in dogs, to our knowledge the pathogen has not been isolated from sick dogs (Spolidorio *et al.* 2010, Nascimento *et al.* 2016) [EB1]. On that basis, there is currently no basis on which to justify introduction of a companion animal *Borrelia* vaccine to the region.

7. Can certain core vaccines ‘break through’ maternal immunity earlier than others and therefore establish protection in puppies?

Modern high-titre international quality-assured vaccines are more likely to be able to do this, which is why the VGG recommends use of such products. Where available, the use of high-titre combination CDV and CPV2 vaccines designed for use in young puppies is also recommended where core vaccination is started earlier than 8 weeks of age (see Tables 4 and 5). However, there is no guarantee that every puppy will make an early, active immune response to each vaccine antigen and so the global WSAVA guidelines should be followed: by giving the final early-life dose of core vaccine at 16 weeks of age or older with a follow-up vaccine between 6 and 12 months of age.

8. The VGG recommends use of core vaccines no more frequently than every 3 years, but the core vaccines in my country are licensed to be given annually. How can I give a product with a 1-year licensed duration of immunity every 3 years?

This situation was faced by veterinarians globally in the last two decades when guidelines recommendations were for adult core revaccination no more frequently than every 3 years, but products all had a licensed duration of immunity of 1 year. At that time, veterinarians were able to use the available products in accordance with guidelines simply by obtaining informed client consent (and documenting this in the medical record) for “off label” use of the product. There was never any legal claim brought successfully against a veterinarian for doing this, nor examples of dogs contracting infection because of extending vaccination intervals. Subsequently, in many markets globally, the identical core vaccines were relicensed with a 3-year DOI. Until this relicensing occurs in LATAM, veterinarians can adopt the same strategy that was used very successfully over the last 20 to 25 years in North America, Europe and other regions.

9. Do the current CPV vaccines provide protection against all of the circulating types of CPV?

Over the decades since the first identification of CPV2 in 1978, new biotypes of the virus (CPV2a, CPV2b and CPV2c) have emerged in many parts of the world, including LATAM. These virus variants are characterised by subtle changes in amino acid sequence in the VP2 protein. Most vaccines contain either CPV2 or CPV2b and questions have been raised as to whether these provide adequate cross-protection against new virus variants (specifically CPV2c). There are numerous studies that show such cross-protection occurs and that all current CPV vaccines remain efficacious in the field (*e.g.* Spibey *et al.* 2008, Wilson *et al.* 2014) [EB1]. Occasional reports occur of clinical parvovirus in vaccinated dogs, but this scenario generally relates to failure to vaccinate according to guidelines recommendations or vaccination of puppies that are already incubating the virulent virus.

10. Do we have good evidence concerning which serovars of *Leptospira* circulate in LATAM, on which to base decisions about the type of *Leptospira* vaccine to use in practice?

While there is no doubt that leptospirosis occurs in dogs in LATAM, there is minimal high-quality scientific evidence about the geographical distribution, causative serovars and clinical manifestations of the disease. The major weakness in many published studies is that the gold-standard for confirming clinical diagnosis (*i.e.* paired serology 2 weeks apart by the microscopic agglutination test [MAT]) and identifying the infecting serovar (isolation of the organism) has not been used. Available studies do suggest that the dominant serovars circulating in the field in LATAM may still be *L. interrogans* serovars Canicola and Copenhageni [EB1], and that consequently, the traditional canine “L2” vaccines containing these organisms might confer adequate protection. In North America and Europe, “L3” and “L4” vaccines have been marketed to help address a greater diversity of causative serovars in those regions. At present, there is insufficient evidence on which to formulate a specific LATAM vaccine or to recommend adoption of the North American L4 products in an evidence-based fashion.

11. Shouldn't *Leptospira* vaccines be core as we have a high prevalence of cases in animals and people in my country?

Where there is solid scientific evidence (see question 10) that leptospirosis is a significant clinical problem then it makes perfect sense to routinely vaccinate at-risk dogs to prevent a serious and potentially zoonotic infectious disease. However, it is simply not possible for the VGG to classify *Leptospira* vaccines as core in our global guidelines, because there are parts of the world in which the infection does not exist or is of very low prevalence. Moreover, the lifestyle of some individual dogs does place them at lower risk of encountering this infection. This is why the VGG promotes the use of non-core vaccines based on regional disease surveillance data coupled with a lifestyle history of the individual pet. LATAM practitioners must do their best to obtain reliable local data on *Leptospira* infection to help inform decision making about use of this vaccine.

12. What are the risk factors for exposure to *Leptospira* spp.?

Decision making about whether or not to use non-core *Leptospira* vaccines would be facilitated by robust surveillance data indicating whether *Leptospira* was prevalent in your geographical area and which serovars were circulating in the field. Unfortunately, such data are not available in most parts of the world. Consequently, the decision to vaccinate needs to be taken based on the lifestyle of the individual dog. Apartment dwelling dogs with limited and controlled access to outdoors are unlikely to require *Leptospira* vaccination. However, dogs with outdoor access and particularly those with access to water that might be contaminated *via* exposure to rodents or domestic livestock should be vaccinated. Even dogs kept in a yard may be at risk if small wildlife (*e.g.* rodents) can also access the yard.

13. The prevalence of FeLV appears to be relatively high in some parts of LATAM, as compared with USA and parts of Europe. What can we learn from the experience in those regions that might help us reduce the prevalence of FeLV here?

The prevalence of FeLV was much higher in Europe 30 to 40 years ago than it is today. It is thought that the combination of (1) diagnostic testing for FeLV (which has become considerably more convenient and accurate over those decades), (2) suitable management of cats found to be infected and (3) widespread vaccination against FeLV, have together led to the substantial decrease in FeLV prevalence in some countries (Studer *et al.* 2019) [EB1]. The first step in regions of LATAM where FeLV has not been well studied would be to determine local FeLV prevalence. If testing is considered impractical or too expensive, then it may help to recall that high prevalence of feline multicentric lymphoma, cranial mediastinal lymphoma and very severe non-regenerative anaemia are strong clues that FeLV may be prevalent in the area. In regions where many cats are known to become infected each year, client education and widespread vaccination should be practiced. Ideally, cats should be tested prior to first vaccination because there is no benefit to vaccinating a cat that is already infected when that dose of vaccine may benefit another animal.

14. How do I decide whether to use non-core FeLV vaccination in my practice?

This decision should be based on a risk–benefit analysis. If FeLV is known or highly suspected on the basis of good information to be prevalent in the town or region where you work, use of the non-core FeLV vaccine can be justified. For example, if there is a high prevalence of strongly FeLV-associated diseases, such as multicentric or cranial mediastinal lymphoma, increased pressure on owners to permit testing and vaccination against FeLV (in addition to use of core vaccine) is justified.

15. Should I choose modified-live or inactivated core vaccines for cats?

Each has its own advantages and disadvantages. If it is judged necessary to vaccinate a pregnant or immunosuppressed cat (*e.g.* a retrovirally-infected cat), an inactivated vaccine is considered safer from first principles (although the evidence for this is limited and recent studies suggest this may not be the case; Bergmann *et al.* 2018) [EB1]. Similarly, where there may be a multi-cat establishment without a history of upper respiratory tract infection, use of a killed product (from first principles) would reduce the risk of transfer of live vaccine virus. In some countries, inactivated vaccines are used in more cats than are MLV vaccines. In many other countries, MLV feline vaccines are used in far more cats than are inactivated vaccines. Although it is considered uncertain and controversial by some experts, there is evidence that adjuvant (present in inactivated and subunit vaccines but generally not in MLV vaccines) is implicated as being associated with development of the feline injection site sarcoma (FISS) (AbdelMageed *et al.* 2018, Kass 2018) [EB1]. This would be an important disadvantage of adjuvanted vaccines. There is some limited evidence that inactivated FHV1 vaccines provide more rapid onset of protection than do MLV FHV1 vaccines (Lappin 2012) [EB1]. Finally, where canine rabies is an endemic disease

and cats should receive rabies vaccination as core, use of inactivated adjuvanted vaccine is the only option, unless there is access to a recombinant product.

16. Does the VGG recommend recombinant vaccines for dogs and cats?

The VGG does not make recommendations about specific commercial brands of vaccine or generally about classes of vaccine. In some parts of the world there are recombinant virus-vectored vaccines available to protect against CDV, FeLV and rabies. In some circumstances these do have advantages: for example for use in wildlife species and as a means of avoiding use of adjuvanted rabies vaccine in cats, as these are one possible injectable product (of many vaccines and non-vaccine injectables) that have been associated with FISS (see Questions 15, 67 and 68). To our knowledge, such monovalent products are not available in LATAM.

17. In which countries is rabies vaccination given only every 3 years? Is there scientific evidence behind this practice?

Rabies vaccines are routinely administered to individual pet animals visiting the veterinarian only every 3 years in North America and Europe. In those regions the legal requirement is for triennial revaccination of adult dogs and cats. The international quality-assured rabies vaccines used in those regions all carry a licensed DOI of 3 years. The licence is based on firm scientific evidence and licensing studies (*e.g.* Lakshmanan *et al.* 2006) [EB1]; without such evidence the laws would not have been changed to allow 3-yearly revaccination. Unfortunately, the identical rabies vaccine products, used in Asia, Africa and LATAM are administered annually. This is because the regional or national laws have not changed and industry has not relicensed the products with a 3-year DOI as has occurred in North America and Europe. In LATAM, you are still legally obliged to give rabies vaccines on an annual basis; however, the veterinary profession should be lobbying for change in the laws and relicensing of the vaccine products. You should also note that this only applies to individual pet animals visiting the veterinarian for vaccination. In the context of mass vaccination campaigns in the field (as might be conducted by government authorities or non-governmental organisations), rabies vaccines are still administered annually to as many dogs as possible (including to free-roaming dogs). This is because there is generally high population turnover in free-roaming dog populations and annual revaccination is required to maintain herd immunity levels of 70% [EB1].

18. Is there a relationship between bodyweight and amount of antigen in a vaccine? Should smaller dogs receive less vaccine than larger animals?

This is a frequently asked question throughout the world. Vaccines are unlike pharmacological drugs and are not administered on a mg/kg basis. Vaccines contain a defined amount of antigen, which is the amount required to stimulate a primary or secondary immune response in an animal. Each individual person and animal has an “immunological repertoire” of antigen-specific T and B lymphocytes defined by T-cell and B-cell receptors (TCRs and BCRs). Burnett’s “clonal selection theory” proposed that each T and B cell carried a unique receptor specificity, but we now know that any one receptor is capable of recognising multiple epitopes (TCR “degeneracy” and BCR cross-reactivity). Any vaccine must therefore contain antigenic epitopes capable of being processed and presented to TCRs, or recognised conformationally by BCRs, and the aim of the vaccine is simply to be recognised by relevant antigen-specific lymphocytes such that these cells are stimulated to generate active immunity and immunological memory. It is therefore irrelevant how large or small the target animal might be; the vaccine simply needs to be able to activate the correct cells in the immunological repertoire. Vaccines are formulated with a sufficiency of antigen to achieve that aim. Having said that, there is some evidence that dogs of low bodyweight do tend to make higher serological responses to some antigens (Kennedy *et al.* 2007) and do have a higher incidence of post-vaccinal adverse events than larger dogs (Moore *et al.* 2005) [EB1]. However, at this time, there is no suggestion that vaccines will be formulated on the basis of bodyweight. In North America, some vaccines are available in 0.5 mL rather than 1.0 mL volumes, but the antigenic content of these products is similar. You should never split a vaccine dose between animals or administer anything less than a full dose of vaccine to an animal. This is “off label” use of the product and you would be liable if that animal subsequently developed infection post vaccination.

19. Does the VGG consider therapeutic vaccines such as the canine melanoma vaccine?

In the 21st century vaccination is no longer simply about inducing protection from infectious disease. Therapeutic “vaccines” are used to stimulate or modulate immune responses in cancer (*e.g.* use of the canine melanoma vaccine) or allergy (use of allergen-specific immunotherapy in atopic dermatitis) and in human medicine there is much active research into therapeutic vaccines for autoimmune diseases. The VGG does not consider these alternative uses for vaccination, which are generally the domain of veterinary specialists. Our focus is always on vaccines available globally for the prevention of infectious diseases in dogs and cats, and on products that are used widely in first-opinion veterinary practice.

20. What does the VGG think about the vaccine against *Microsporium canis* that is currently being used for dogs and cats in some parts of LATAM?

The VGG does not recommend the use of a vaccine to prevent dermatophytosis in dogs and cats since there are very few efficacy studies published. Although there are reports of success of anti-dermatophyte vaccines in cattle and fur-bearing animals, the response does not appear to be the same in cats, as these vaccines do not protect against challenge infection (Deboer & Moriello 1994, Deboer

et al. 2002, Frymus *et al.* 2013) [EB1]. A commercial vaccine consisting of killed *M. canis* was licensed in the USA for treatment of cats; however, this vaccine did not provide a more rapid cure of an established infection in vaccinated cats compared with unvaccinated controls. The product was withdrawn from the market (Frymus *et al.* 2013) [EB1].

Questions about vaccine delivery

21. Can I give core vaccination to puppies at 4 weeks of age if they are due to be sold at 6 weeks of age?

The first thing to say about this practice is that 6 weeks of age is really too young for puppies to be weaned, removed from their mothers and sold. In Europe it is now illegal to sell puppies that are under 8 weeks of age. The veterinary profession in LATAM should take ownership of this welfare issue and educate dog breeders as to appropriate times for weaning. Bringing together litters of puppies aged 4 to 6 weeks at weekend “puppy markets” is also a “recipe for disaster” in terms of infectious disease transmission and it should also be beholden on the veterinary profession to address this welfare issue. If the bitch that has produced the litter was well-vaccinated, it is likely that she will have a high concentration of serum antibodies against core antigens (CDV, CAV and CPV2) and that these will transfer to the puppies in colostrum. In such a circumstance it is unlikely that either a 4-week-old or 6-week-old puppy will respond to core vaccination, although the chances of this are improved if high-titre combination CDV and CPV2 vaccines designed for use in young puppies are applied. However, in LATAM, it is perhaps more likely that the bitch will not have been well vaccinated and it is therefore correct to attempt to provide protection to puppies as early as possible. The most appropriate way to do this would be with a vaccine containing CDV and CPV and designed for use in young puppies as described above. Such a product might be administered from 4 weeks of age; however, MLV vaccines should NEVER be given any earlier than then as they may produce infection and malformation in neonatal animals. After 6 weeks of age, puppies may be vaccinated every 2 to 4 weeks (switching to a trivalent CDV, CAV and CPV2 vaccine at 8 weeks old). The most important dose of core vaccine is actually that given at 16 weeks of age or older, when all puppies should have lost maternally-derived antibodies and be capable of responding to vaccine. This should be followed by a fourth core vaccination given between 26 and 52 weeks of age (ideally at the earlier end of that range).

22. If puppies or kittens were known not to take in colostrum, when may I vaccinate them?

It is difficult to be absolutely certain that a litter of puppies or kittens did not obtain colostrum; or that certain individuals within the litter did not obtain colostrum. However, if this is suspected, the first advice would be to implement excellent husbandry by providing as clean and isolated an environment as possible. The use of “artificial colostrum” formulated of milk replacer and serum or plasma from a well-vaccinated adult animal might also be considered in the first 24 hours of life. It is known experimentally that colostrum-deprived animals are capable of making an immune response to core vaccine very early in life (Chappuis 1998) [EB1]; however, MLV vaccines should never be used any earlier than 4 weeks of age as they may induce infection or developmental defects in the neonatal animal. Core vaccination in this situation might start at 4 weeks of age. Although in theory, a colostrum-deprived animal should be capable of responding to a single canine core vaccine or a single dose of FPV vaccine (because there is no inhibition from MDA), it would be pragmatic to proceed through the recommended WSAVA protocol for puppies or kittens. Even in a colostrum-deprived kitten, at least two doses of FHV1 and FCV vaccine would be recommended. At 4 weeks of age, the use of core CDV and CPV2 vaccine designed for young puppies would be recommended.

23. How many doses of core vaccine should I give to a puppy?

This depends on the circumstances and the age the puppy is first presented for core vaccination. Initial vaccination would ideally be given whilst the puppies were still with the bitch and arranged by the breeder. In Europe, for example, where puppies cannot be sold until after 8 weeks of age and where bitches are likely to be well vaccinated, a breeder might arrange for core vaccination at 8 to 9 weeks of age and then responsibility for subsequent vaccines passes to the new owner. In LATAM, where a puppy might be obtained much earlier in life, core vaccination might begin as early as 4 to 6 weeks of age (see recommendations above). According to WSAVA guidelines, puppies may receive core vaccines every 2 to 4 weeks, with the final early-life dose of vaccine being given at 16 weeks of age or older. So the actual number of core vaccines will depend on the age of starting and the frequency of administration. A “standard” protocol in North America or Europe might involve core vaccination at 8, 12 and 16 weeks of age with a fourth core vaccine at 26 weeks of age. In LATAM this protocol might be adapted to account for an earlier onset of core vaccination.

24. Can we use serological testing to determine when to vaccinate a puppy, rather than giving multiple doses of vaccine?

There are in-practice serological test kits available on the market that can detect the presence of serum antibody to CDV, CAV and CPV2. However, these are designed to inform decision making about revaccination of adult dogs, rather than determine the optimum time for vaccination of puppies. It is simply not practical (and has welfare implications) to repeatedly blood sample very young puppies and, more importantly, until 16 weeks of age, it is not possible to discriminate between MDA and antibody produced endogenously by the puppy’s own immune system in response to vaccination. So, the answer to the question is “no” it is not possible to use these test kits to determine the optimum time for puppy vaccination. However, the test kits could be used to determine the need for a core vaccine given between 26 and 52 weeks of age (according to WSAVA guidelines). If a puppy is tested at 20 weeks of

age (*i.e.* 4 weeks after receiving the last core vaccine at 16 weeks of age or older) and is seropositive (for CDV, CAV and CPV2), then those antibodies must reflect the puppy's own immune response and indicate that immunological protection has been induced. In that circumstance, the puppy would not require another vaccine at 26 to 52 weeks of age and may go straight into the adult revaccination schedule.

25. Do some breeds of dog transfer more maternally-derived antibody to puppies than others?

There is no evidence that transfer of MDA is breed associated or related to body size. Transfer does depend on husbandry factors such as the bitch herself being a “good mother” and being able to suckle all her puppies in the crucial window of the first 24 hours of life (although some studies suggest that “gut closure” to absorption of MDA may occur even earlier than this). However, the level of MDA may vary between different bitches, depending on how well they have been vaccinated. Concentrations of MDA might also vary for the three major vaccinal antigens (CDV, CAV and CPV2) for any one bitch. There are, however, some breeds of dog (*e.g.* rottweilers, dobermanns) that may more likely include genetic “low responders” or “non-responders” to individual vaccine antigens (Day *et al.* 2016). It is well recognised in North America and Europe that certain individual rottweilers are more susceptible to CPV2 infection (Houston *et al.* 1996), which is suggested to reflect inadequate vaccinal immune responses; however, in one study dogs of this breed responded adequately to vaccination (Coyne 2000). Rottweilers also make lesser serological responses to rabies vaccine (Kennedy *et al.* 2007) [EB1]. Serological testing might be used to identify non-responder animals and ideally they would not be used for breeding purposes as they would not be able to transfer adequate MDA to any puppies.

26. Do all puppies in a litter receive the same amount of maternally-derived antibody from the mother?

In an ideal world this would be the case, but it is clear that within a large litter, individual puppies must proactively find a teat in order to take in an adequate amount of colostrum within the first 24 hours of life. Smaller or weaker puppies within a litter may not be able to achieve this and will therefore have taken in less MDA. These animals will be protected from infection for a lesser period of time during early life, but, in contrast, should be capable of making an endogenous immune response to core vaccines earlier than littermates that suckled more successfully and acquired a greater volume of colostrum.

27. Do puppies born to a mother that is revaccinated annually with core vaccines receive more maternally-derived antibody than puppies born to a mother that is revaccinated every 3 years?

There is no evidence that this is the case. Adult dogs that receive triennial core revaccination are known to have stable protective antibody titres during each 3-year revaccination cycle and experimental data have shown that puppies appropriately vaccinated in early life (and then never again as adults) maintain a plateau of protective antibody titres against CDV, CAV and CPV2 (Schultz 2006) [EB1]. There is a wealth of serological data that shows that annual core revaccination of adult dogs is unnecessary and that protective antibody titres are maintained perfectly adequately with triennial (or longer) core revaccination (Abdelmagid *et al.* 2004, Bohm *et al.* 2004, Mouzin *et al.* 2004, Gore *et al.* 2005, Schultz 2006, Larson & Schultz 2007, Mitchell *et al.* 2012, Killey *et al.* 2018) [EB1]. Some veterinarians like to vaccinate breeding bitches just before they are mated, but there is no evidence that this provides higher quality MDA than in bitches receiving a standard triennial core revaccination protocol.

28. How can we safely socialise puppies if they are potentially susceptible to infection (because they are in the “window of susceptibility”) at the optimum time for socialisation?

The window for effectively socialising puppies overlaps with the “window of susceptibility” to infectious disease (*i.e.* the short period when puppies no longer have sufficient MDA to confer full protection against infection, but still have sufficient MDA to block the ability of MLV core vaccines to induce an endogenous immune response) (Cutler *et al.* 2017) [EB1]. There is therefore a theoretical risk that engaging puppies in socialisation activity (*e.g.* attending a puppy class, exposing a puppy to the outdoors) might allow them to acquire infectious disease. This is a dilemma for the veterinarian; however, we must encourage socialisation as behavioural issues are a major factor in the relinquishment of pet dogs later in life. There are certain practical measures that can be taken to minimise risk: (1) holding puppy classes in relatively clean environments, (2) ensuring that all puppy and adult participants are vaccinated and (3) ensuring the puppy receives the full WSAVA recommended course of core vaccination. One study from the USA monitored puppies attending puppy classes and did not record a single incidence of infection (Stepita *et al.* 2013) [EB1]; so with common sense the risks are small.

29. How long after the last vaccination do you need to wait to be able to walk with a puppy on the street?

The worst case scenario might be that a puppy had blocking MDA that prevented generation of an endogenous immune response to core vaccine until the vaccination given at 16 weeks of age or older. Within days of that core vaccination the puppy will have generated some immunity, with maximal serum antibody titres likely being achieved around 2 weeks post vaccination. Of course many puppies will have responded at an earlier age to core vaccination and in LATAM where the process of core vaccination might begin even earlier, one might expect protection to be conferred at an earlier age. As walking on the street is part of the socialisation process, the answer overlaps with the question above. Common sense should prevail and exposure risk should be minimised during early life. For example, taking such a young puppy to a dog area in a park would not be recommended.

30. If the only chance to vaccinate an animal is while it is being neutered, should we do it?

There is no evidence that delivering a vaccine to an animal during neutering will fail to engender an active immune response. Anaesthetic agents per se are not immunosuppressive and the transient stress and inflammation associated with the surgical procedure will not affect the induction of vaccinal immunity [EB4]. The only reason for avoiding vaccination during neutering relates to the possible very rare occurrence of a vaccine-associated type I hypersensitivity reaction, which might potentially involve an unstarved animal vomiting and aspirating during surgery. This has nothing to do with the efficacy of the vaccine in inducing a protective immune response. One study has shown that vaccines administered to kittens during early neutering did not affect the immune response to the vaccines (Reese *et al.* 2008) [EB1].

31. Why should shelter puppies be vaccinated every 2 weeks from 6 weeks of age to 20 weeks of age if it has been shown that puppies may have persistent maternally-derived antibody until 16 weeks of age?

Shelters are generally high risk environments with high population density of animals of unknown vaccination and infectious disease exposure history. In the case of puppies entering a shelter, the vaccination history of the dam will also generally be unknown. In order to optimise protection for puppies in such an environment, the VGG recommends this core vaccination schedule where it can be afforded by the shelter. The shelter environment is usually distinctly different from that of a breeding establishment and, subsequently, the new home of an individual puppy.

32. If a dog sneezes after application of an intranasal vaccine, is it necessary to reapply the vaccine?

No, this is not necessary. These products are formulated with an “overage” of antigen content to allow for the possible loss of some of the product during administration. If in any doubt, you should contact the manufacturer of the vaccine.

33. Can I give multiple vaccines (e.g. core combination, rabies and CIRDC vaccine) on the same day, especially to small breed dogs? Or should I spread the vaccines over separate weeks?

The immune system is capable of responding to (or actively tolerating) many thousands of different antigens at any one time. The mucocutaneous surfaces of the body are naturally interacting with very large numbers of antigens (*e.g.* from the microbiome, dietary antigen, inhaled antigen) in a continual process. Therefore, immunologically speaking, the delivery of multiple vaccine antigens on one occasion poses no problem to the immune system [EB4]. For multicomponent vaccines, a requirement of licensing is that it be demonstrated that each component is able to induce a protective immune response. Manufacturers also often demonstrate “compatibility” of their own product ranges which are licensed to be co-administered [EB2]. For these reasons, there is no immunological sense in staggering vaccine delivery over different weeks. This would necessitate multiple visits by the client and may increase the likelihood of crucial vaccinations being “missed” from the schedule. One piece of practical advice is that where multiple different injections are to be given (*e.g.* core vaccine with a separate rabies vaccine), that these be given into different subcutaneous sites so that different draining lymph nodes are targeted for immune priming. Two studies from the USA counter this, in that they show for both dogs (particularly of low bodyweight) and cats that there is a greater likelihood of adverse reactions post vaccination when increasing numbers of antigens are delivered at any one time (Moore *et al.* 2005, 2007) [EB1]. Vaccinating according to WSAVA guidelines minimises the number of antigens that might be delivered on one practice visit.

34. How long should I wait to vaccinate a dog after it has recovered from an immunosuppressive disease such as distemper or ehrlichiosis?

A fundamental principle of vaccination is that any animal that is clinically ill should not be vaccinated and vaccination should be delayed until the animal has recovered. If a dog has really recovered from a CDV infection, then it will have natural immunity to reinfection; probably better immunity than might be induced by a vaccine. Consequently, that dog could be tested and if seropositive would not require CDV revaccination. However, because the CDV antigen is generally mixed with other core vaccinal antigens, that dog will likely receive standard core revaccination in the future. If it is essential to revaccinate a dog recovered from CDV infection, then a period of 4 weeks post recovery should allow immune function to recover. The situation with *Ehrlichia canis* infection is more complex because the disease may have acute and chronic stages and treated dogs may still harbour the infectious agent such that disease can recur following any future stressful event. Again, if a dog has been diagnosed and appropriately treated, it should have been clinically normal for at least 4 weeks before any consideration of vaccination is made. In both circumstances, performing a simple haematological and serum biochemical examination might also indicate that an immunological recovery has been made (*i.e.* normalisation of leucocyte counts and serum gamma globulin concentration).

35. If a dog has recovered from distemper and is then vaccinated against distemper, could that vaccine induce neurological signs?

The simple answer is “no.” As above (Question 34), if a dog has naturally recovered from CDV infection it will have robust natural immunity against reinfection and in reality does not require CDV vaccine (but will likely receive it as part of a multiantigen core vaccine). Remember that the viruses in core vaccines are attenuated and therefore incapable of inducing tissue pathology and clinical

disease. There is one recent report and some historical cases of post vaccinal CDV encephalitis in puppies (Fairley *et al.* 2015) [EB1], but this is a very rare occurrence.

36. A dog rescued from the street is taken into a house where there are young puppies still undergoing their early life vaccinations. The dog shows signs of CDV infection after a few days in the new home. Should the puppies be vaccinated immediately, rather than waiting until their next scheduled vaccination day?

It would always be good practice to isolate such a newly introduced adult dog from the puppies wherever possible (until the puppies had completed their core vaccination schedule). Remembering that it is impossible to know precisely when each puppy might have a “window of susceptibility”, some puppies might already be immune and others not at the time of introduction. If the puppies are within a 2 to 4 week interval between core vaccines, then in this scenario, there is no harm in revaccinating them earlier than the schedule might have otherwise been and then readjusting the schedule up to the vaccine given at 16 weeks of age or older. However, until the 16 week or older vaccine, there is no guarantee of protection in all cases.

37. Should dogs that have recovered from parvovirus or distemper infection be vaccinated against those diseases?

A dog that has recovered from natural infection with either CDV or CPV2 will have developed robust immune protection and will be seropositive for the relevant virus. This natural immunity is actually even better than the immunity that might be achieved by vaccination. So, while a recovered dog would likely not require vaccination against that particular pathogen, because core vaccines are formulated as a trivalent product, it will still require vaccination to ensure protection against the other two pathogens (*e.g.* a dog recovered from CDV infection would still require vaccination against CAV and CPV2).

38. How long should I wait after a dog has finished a course of glucocorticotherapy to vaccinate?

This depends on the dose of glucocorticoids given. An anti-inflammatory dose (*e.g.* 0.5 to 1.0 mg/kg of prednisolone) will not impair the ability of the immune system to respond to vaccination. An immunosuppressive dose (*e.g.* 2 to 4 mg/kg of prednisolone), particularly if combined with other immunosuppressive agents, is designed to impair immune function. Consequently, vaccination should not be delivered until at least 4 weeks after the glucocorticoid has been tapered and then stopped [EB4]. The dog should, of course, also be clinically healthy following the cessation of such therapy. Although there are no formal studies of the effects of glucocorticotherapy on canine vaccination, there is a study of the effect of ciclosporin treatment on feline vaccinal immune responses. Whilst being treated with ciclosporin, cats were able to make adequate protective immune responses to previously seen vaccinal antigens (FPV, FHV1, FCV, FeLV and rabies), but the drug impaired the immune response to first-time vaccination with FIV vaccine (Roberts *et al.* 2015) [EB1].

39. Can I vaccinate while a dog is receiving chemotherapy? If not, how long do I have to wait after finishing chemotherapy before vaccinating?

Dogs receiving powerful immunosuppressive chemotherapeutic drugs should not be vaccinated. These drugs impair immune function by targeting rapidly-dividing immune cells in addition to the target cancer cells. At least 4 weeks should elapse after stopping such therapy before any vaccines are given. The dog should be clinically recovered and ideally a haematological and serum biochemical evaluation would indicate recovery in immune function.

40. Is it necessary to revaccinate a dog after completing a course of chemotherapy?

Although chemotherapeutic drugs will affect immune function (see question 39), they do not ablate the immune system or destroy memory lymphocytes. Therefore, there is no need to routinely revaccinate dogs after completing chemotherapy other than in their normal cycle of core or non-core revaccination. A dog finishing chemotherapy could be serologically tested for the presence of protective antibodies against core vaccine antigens if there was any concern over its level of protection. Human patients receiving chemotherapy are not revaccinated at the end of their treatment protocols.

41. How long should I wait after a dog has had surgery before I vaccinate?

There is nothing about the process of surgery and administering an anaesthetic agent per se that would interfere with the ability of the immune system to respond to vaccination [EB4]. However, depending on the nature of the surgery, in the post-surgical recovery period dogs may be clinically unwell and receiving a variety of medical treatments. From first principles it makes sense to wait until the dog is clinically healthy and finished post-operative medical treatment before revaccinating.

42. Until which age should I vaccinate an elderly dog? Should elderly dogs be vaccinated every year with core vaccines because their immune system might not function as well as when they were younger?

For core vaccines (CDV, CAV and CPV2) there is good evidence that appropriate puppy vaccination induces lifelong protective immunity without regular adult revaccination. There are also studies that show that geriatric dogs (*i.e.* dogs over 10 years of age) maintain protective levels of antibody against these three core viral antigens and that these antibody levels do not decline with age as part of the phenomenon of “immunosenescence” (HogenEsch *et al.* 2004) [EB1]. In contrast, it is also known that delivering a new

vaccine (*i.e.* one not previously given) to an older dog leads to a less effective primary immune response than might have been made earlier in life (Day 2010) [EB1]. Therefore, there is no evidence that geriatric dogs require any more frequent core revaccination than younger adults; geriatric dogs can be safely maintained on the standard triennial core revaccination programme. Where core revaccination is determined by serological testing (titre testing), the VGG recommends that this might be performed annually (rather than triennially) in geriatric dogs; simply to provide reassurance that revaccination is not required [EB4].

43. How many doses of vaccine should a Rottweiler receive? Do they need to get more doses of CPV2 than other dogs?

Rottweilers are a breed that is well recognised to contain a higher than average frequency of genetic low responders and non-responders to CPV2 and rabies vaccines. There is no reason to vaccinate Rottweilers any more frequently than other breeds of dog. If they are of this genetic type, that means that they lack the immunological ability to ever respond to the particular antigen (*e.g.* CPV2); that means that no matter how frequently they are vaccinated, they will not respond to vaccination. This situation is one in which serological testing is of practical benefit. Test kits will be able to determine whether a Rottweiler is seronegative to CPV2 after vaccination (note that this does not apply to rabies). Such a dog would therefore be at risk of contracting infection and appropriate measures might be taken to minimise that risk. More importantly, such dogs should not be used for breeding purposes.

44. Are there any breed-specific vaccination protocols for dogs?

There is no evidence that any canine breed or breed group requires any specific vaccination protocol. There has been discussion about small breed dogs (see Question 18) and whether rottweilers might require a different core vaccination protocol given the possibility of breed-related poor response to CPV2 and rabies vaccines (see Questions 25 and 43). Related young dogs of the Weimaraner breed are susceptible to a complex syndrome involving hypertrophic osteopathy, chronic recurrent infection and serum IgG deficiency. There is a suggestion that onset of this clinical syndrome might be influenced by vaccination (Harrus *et al.* 2002) and there has been some discussion about vaccination protocols for dogs of this breed. However, overall there is insufficient evidence to advise anything except standard core and non-core vaccination, according to guidelines recommendations, for all breeds of dog.

45. If a dog misses an annual *Leptospira* vaccine by more than 3 months, do I need to give one or two doses of vaccine to re-establish immunity?

If a dog has missed its annual *Leptospira* booster vaccine by a period of up to 3 months, a single “booster” dose of vaccine should be sufficient. If the annual revaccination is delayed by more than 3 months (*i.e.* a 15-month interval since the last vaccine) then two doses of vaccine (given 2 to 4 weeks apart) should be given to re-establish immunity and then annual boosters thereafter. Some manufacturers may advise that protection may extend to 18 months before a new primary course of vaccination is required, but the VGG adopts a more cautious outlook when considering all vaccines in a generic fashion.

46. Can vaccination affect the interpretation of *Leptospira* titres in a dog?

Yes, vaccination will lead to generation of an antibody response post vaccination; however, this may not persist for very long and post vaccinal titres may decline or even disappear by 4 months post vaccination, even though the dog remains protected for the full 12 months cover of the vaccine. Although post vaccination titres tend to be low, they may persist for more than 4 months at high levels if the dog is exposed to field strains. Also, cross-reactivity with non-vaccinal serovars can occur (Sykes *et al.* 2010) [EB1]. Because of this, if attempting to confirm a diagnosis of leptospirosis in a clinically ill dog, the timing of any previous vaccination must be considered. This is one of the major reasons why the clinical diagnosis of leptospirosis can only be achieved properly by assessment of MAT testing on paired serum samples taken 2 weeks apart. Vaccinal antibodies will not show an increased titre, but antibodies against a potentially infecting serovar should show a four-fold elevation in titre.

It is important to highlight that dogs can develop titres against serovars not included in vaccines, and sometimes the highest titre is against a non-vaccinal serovar. Positive titres to non-vaccinal serovars should be interpreted with caution if a vaccinated dog develops clinical signs consistent with leptospirosis (Barr *et al.* 2005, Martin *et al.* 2014) [EB1].

47. Should I use *Leptospira* vaccines every 6 months or annually in an at-risk dog?

A dog at high-risk for leptospirosis might be one that has regular access to water environments where there may be contamination by rodents or farming environments with livestock. Even urban dogs may therefore be at risk. In early versions of the WSAVA global guidelines, the VGG made the recommendation that 6-monthly revaccination against leptospirosis be considered for high-risk dogs. We subsequently removed that recommendation as there was insufficient scientific evidence to support it. Therefore, even high-risk dogs require only annual revaccination against leptospirosis.

48. Is it preferable to use a large multi-antigen vaccine as a single injection or give separate injections of small combination or single antigen vaccines?

The VGG would always recommend the use of small antigen combination vaccines (*e.g.* a trivalent or bivalent core vaccine with separate non-core vaccines) in order to have the flexibility to vaccinate individual animals according to WSAVA guidelines.

As described above, such product ranges allow delivery of the minimum essential antigenic components for that individual animal based on a lifestyle assessment of its exposure risk. Giving multiple injections of smaller antigen component vaccines is far preferable to giving a single injection of large multicomponent vaccine containing antigens that are not required or not recommended for that animal. This is one of the greatest challenges in LATAM; ensuring that the small antigen component product ranges available in other markets are brought to LATAM, in order to allow veterinarians to vaccinate according to WSAVA guidelines.

49. How many doses of vaccine should we give to an adult dog or cat without previous vaccination history?

For core vaccines and rabies vaccine, a single dose of MLV international quality assured vaccine will induce protective immunity in an adult animal. Remember that adult animals do not have blocking MDA like puppies and kittens. The one exception to this rule might be for adult cats in the case of FHV1 and FCV vaccines, where to be sure of the best response, two doses (2 to 4 weeks apart) might be given. This is easy to achieve where there is access to a trivalent (FPV, FHV1 and FCV) and bivalent (FHV1 and FCV) vaccine, but in LATAM, where only trivalent products are marketed, this would necessitate giving an additional (unnecessary) FPV vaccine. Moreover, serological testing could be used to determine whether an adult dog actually required any vaccination against CDV, CAV and CPV2 or whether an adult cat required any vaccination against FPV (note that at the time of writing the feline test is not available in LATAM). In the case of non-core vaccines, these will all require two doses given 2 to 4 weeks apart, followed by boosters at the recommended interval.

50. I am concerned that in LATAM, where few animals are vaccinated and there is a high prevalence of infectious disease, that vaccinating every 3 years against CPV and CDV is insufficient. Should I continue to give annual core vaccination to dogs?

In LATAM, it is far more important to try to increase herd immunity than it is to increase the vaccination load of individual animals. The more dogs and cats that are vaccinated within the population, the more difficult it is for infectious disease to spread within that population. Veterinarians must understand that giving a core vaccine to an animal induces protective immunity. There are no degrees of protective immunity. The presence of antibody against core vaccine antigens, no matter what the titre, indicates that the animal has immunological protection and immunological memory and any exposure to the pathogen results in a rapid secondary (memory) immune response. It is simply not possible to make an individual animal MORE immune by giving more frequent vaccination. In fact, immunologically speaking and from first principles, repeated vaccination above the recommended levels is more likely to induce immunological “tolerance” (failure to respond) than immunological protection [EB4]. Therefore, triennial core revaccination according to WSAVA guidelines is perfectly adequate, even for the most high-risk of dogs. Precious vaccine doses would better be used to improve herd immunity than be wasted on an already well protected animal.

51. My clients cannot send their dog to a boarding kennel unless it has been vaccinated against *Giardia*; so how can the VGG classify the *Giardia* vaccine as not recommended?

Here, the veterinary professional needs to ask the question “who is making this regulation”? In many countries (including in North America and Europe) the lay owners of boarding kennels and catteries make these rules on the basis that historically, that is what they have always done. These well-meaning individuals are not scientifically trained veterinarians and are generally unaware of the scientific advances in veterinary vaccinology over the past decades. It should be up to the veterinary profession to educate this community and assist them with developing regulations that are consistent with modern science.

52. If adult cats acquire resistance to FeLV, until what age should we revaccinate them against FeLV?

It is generally accepted that adult cats do develop some level of natural resistance against FeLV infection; therefore, it is considered more important to establish immunity by vaccination of kittens than it is adult cats [EB4]. Any kitten that may have an at-risk lifestyle (*i.e.* indoor–outdoor access, living in a multi-cat environment) might benefit from FeLV vaccination, especially where that kitten also lives in an area known to have high prevalence of infection (see main text of this document for where this is known in LATAM). For adult cats, the VGG currently recommends FeLV revaccination only every 2 or 3 years, rather than annually. That should be continued lifelong.

53. Should you vaccinate a cat (for FeLV) that tests positive for FeLV?

No. In-practice diagnostic tests for FeLV detect viral antigen. So a true positive result indicates that the cat is currently infected with FeLV or fighting off a recent infection. Some cats successfully rid themselves of FeLV. Others become persistently or progressively infected. So the cat that tests positive should be retested immediately using a test from a different manufacturer to rule out a false positive result. If a second positive result is obtained, the cat should be retested in 4 to 6 months' time. If the cat remains positive 4 to 6 months later, progressive infection is likely. It is important to highlight that negative antigen tests can occur in infected cats without viraemia, which means that sometimes you may be vaccinating an asymptomatic but FeLV-infected cat. In this case the vaccine will not cause any harm, but is also unlikely to confer any benefit to the cat.

54. Should indoor only cats be vaccinated against FeLV?

The risk factors for FeLV infection include outdoor access and exposure to other cats where virus might be transmitted *via* salivary secretions (*e.g.* licking, mutual grooming, shared food and water bowls, or biting as part of fighting behaviour). An indoor only cat that may only leave the indoor environment for an annual veterinary visit would not be a candidate for non-core vaccination, including against FeLV. Of course, considering that FeLV vaccination is most effectively used in kittens, making this decision about the predicted future lifestyle of the cat is sometimes difficult for the owners. If there is any suggestion that the cat might have outdoor access during its future lifetime, or that it will live with other cats that have outdoor access, there is sense in considering FeLV vaccination in early life; particularly in areas of high prevalence of the infection.

55. If a household has a FeLV-positive cat and the family decides to adopt a new kitten, how should that kitten be vaccinated against FeLV?

Ideally, the known FeLV-infected cat would be housed indoors in isolation and the owners should be advised against introducing any other cat to the household. However, in the situation described, if unavoidable, the new kitten should certainly be vaccinated against FeLV as soon as possible and ideally before introduction into the household. Standard kitten FeLV vaccination with two doses given 2 to 4 weeks apart beginning at 8 weeks of age and then a 12-month booster is required.

56. Can you vaccinate a pregnant animal?

Ideally, pregnant animals should not be vaccinated. In the case of core vaccines where transfer of MDA is required, normally vaccinated adult dams should have adequate titres of antibody for transfer and it should not even be necessary to revaccinate immediately before the dam becomes pregnant. Unless indicated specifically by the manufacturer that vaccination is safe during pregnancy (and some products do carry this claim), there are also theoretical risks to the foetus with respect to the use of MLV vaccines in the pregnant animal. Non-core vaccines should also not be given during pregnancy; non-core vaccines tend not to induce protective antibody transferred in colostrum in that way that occurs with core vaccines.

57. Should you swab the skin with alcohol before injecting a vaccine?

There is absolutely no evidence to support this procedure even though it remains widely practiced. There is a risk that alcohol may inactivate a proportion of MLV virus particles in a vaccine and so such swabbing is actually contraindicated. Although the skin carries a normal microflora, needle injection is highly unlikely to result in any subcutaneous infection by “carriage” of organisms into the skin microenvironment. You should also note that in human medicine, sites of injectable vaccine delivery are no longer alcohol swabbed, according to WHO and CDC recommendations (*e.g.* WHO Best Practices for Injections and Related Procedures Toolkit; accessible on-line) [EB1].

58. Can I give a vaccine straight out of the refrigerator or do I need to warm it up first?

There is no harm in lightly warming a dose of vaccine (*i.e.* by holding it in the hand) IMMEDIATELY before use, but this is really not required. One study of feline injection site sarcoma suggested that delivery of cold vaccine may be a risk factor for the tumour (Kass *et al.* 2003) [EB1]. However, vaccines should NEVER be over-warmed or kept at room temperature for more than 1 hour. This is because some of the viral components of MLV vaccines are thermo-intolerant and the efficacy of the vaccine will be impaired by warming. Vaccines should never be reconstituted early in the morning for use throughout the day. Vaccines should always be stored appropriately (refer to Table 3).

59. In my country, maintaining the cold chain is a problem. How long can a vaccine be kept at room temperature before it can no longer be given to an animal?

For MLV vaccines even 1 to 2 hours at room temperature (and room temperature may fluctuate widely depending on geographical region and season) is sufficient to begin to inactivate some of the virus components of the vaccine. More problematic to the veterinary practice is when there may be a power cut and the vaccine refrigerator may be without power for prolonged periods of time. In this context, the recommendation would always be to contact the manufacturer of the vaccines to ask for advice. Recent studies suggest that international killed rabies vaccines may actually be quite thermotolerant, but these studies are done against the background of mass vaccination in the field and not from the perspective of practicing quality veterinary medicine in the veterinary clinic (Lankester *et al.* 2016) [EB1].

60. Should puppies and kittens be dewormed before receiving a vaccine?

This is a commonly-held belief that is perpetuated in many parts of the world. Virtually all puppies and kittens are born with endoparasites and current recommendations are that regular deworming starts at 2 weeks of age in puppies and 3 weeks of age in kittens (*e.g.* ESCCAP Guidelines; <https://www.esccap.org/guidelines/>), which is naturally earlier than the administration of core vaccines (from 4 to 6 weeks of age). However, if a puppy or kitten is presented for vaccination, but clearly carries a massive parasite burden to the extent of being severely anaemic and clinically ill, then of course vaccination might best be delayed until the animal

is healthy. However, most parasitized puppies and kittens remain apparently healthy. There is currently no evidence to suggest that carrying a “normal” burden of parasites interferes with the ability of a puppy (or kitten) to respond to vaccination. In fact, it may be more important to provide protection against life-threatening viral disease than to worry about any possible effect of parasitism on vaccination. However, immunologically speaking, there is now much research that shows that parasite infestation can influence the nature of immune responses by skewing immunity towards a T regulatory response associated with immunological suppression and a T helper 2 type response dominated by humoral rather than cell-mediated immunity and this has also been shown for the dog (Junginger *et al.* 2017) [EB1]. There are experimental studies in mice and pigs that show that endoparasitism impairs vaccinal immune responses (Urban *et al.* 2007) [EB1], but what is currently lacking is any evidence that endoparasite infestation impairs canine or feline vaccinal immune responses. Deworming is clearly an important part of preventive health care for dogs and cats (and has public health implications), but there is currently no basis for delaying vaccination for susceptible animals until deworming has been completed.

61. Should we as veterinarians be vaccinated against rabies? Are there any other occupational diseases we should be vaccinated against?

Any veterinarian who practices in a rabies endemic country, who deals with animals that may be imported from rabies endemic countries or who deals with wild animals (particularly bats) should be routinely vaccinated against rabies according to current recommendations for people. Rabies is a fatal disease and no veterinarian at risk of exposure should be unprotected. From the perspective of companion animal practice, there are no other zoonotic diseases for which human vaccination is available or recommended.

Questions about adverse events

62. How do we persuade clients who are reluctant to accept vaccination for their pets because they are concerned about potential adverse events?

This relates to what is now known as “vaccination hesitancy” and is of increasing concern in both human and veterinary medicine throughout the world. Active lobby groups with strong internet presence promote a culture of fear related to the potential adverse events associated with vaccination of children and pets. The tragedy in human medicine is that such activity has seen a decline in herd immunity for common childhood diseases in recent years, with outbreaks and deaths of once-controlled diseases such as measles. There is no doubt that veterinarians are now also regularly confronted by clients who will refuse vaccination for their pets. It is our professional responsibility to calmly explain the rationale for vaccination, the importance of individual and herd immunity, and the safety of vaccines with very low prevalence of adverse events. This is one reason why the VGG has produced a companion document to the global veterinary guidelines, written in lay language for the pet owner and breeder (unfortunately only in English). This is a factual source of information to which clients concerned about vaccines might be directed. At the time of writing, the VGG is also conducting a global survey of vaccination hesitancy in small companion animal practice. The results of the survey will be presented during 2020.

63. How common are adverse events post vaccination and what type of adverse events may we see in practice?

A wide range of adverse events has been recognised post vaccination. Most of these are transient and mild (*e.g.* type I hypersensitivity reactions immediately post vaccination), but some may induce more severe disease (*e.g.* immune-mediated haemolytic anaemia, feline injection site sarcoma). The single most common “reaction” is mild lethargy, anorexia and pyrexia for 2 to 3 days post vaccination. This is actually not an adverse reaction, but more an indication that the vaccine has stimulated immune and inflammatory pathways as part of generating the protective immune response. It is difficult to obtain accurate data on the frequency of adverse reactions post vaccination. Reviewing all of the global information, we can say that there are somewhere between 30 and 50 adverse reactions (mostly mild and transient) for every 10,000 vaccinations given in practice (Moore *et al.* 2005, 2007, Miyaji *et al.* 2012) [EB1]. The risk of contracting life-threatening infectious disease (particularly in environments such as in LATAM) far outweighs the risk of adverse events.

64. If an animal has had an allergic reaction post-vaccination in the past, should you ever vaccinate them again?

Theoretically, if a reaction was due to an IgE-mediated type I hypersensitivity reaction, the animal is immunologically sensitised and is likely to be affected by the same type of reaction on subsequent exposure to the same antigen. In reality, this does not always happen and sometimes such reactions occur only once. If the reaction has occurred in a puppy or kitten that has not yet received the full course of early life vaccines, then that animal must be revaccinated in order to receive the full schedule of core vaccines. You might consider whether non-core vaccines are justified for that animal, and as an adult, serological testing might be used to inform the need for core vaccines. There are certain practical measures that might be taken to avoid the occurrence of such reactions for second or subsequent times. Switching brand of vaccine may or may not have an effect. There is no harm in giving a dose of antihistamine or anti-inflammatory dose of glucocorticoid immediately before vaccination; this will not interfere with the efficacy of the vaccine. The animal may best be kept in the clinic and monitored for several hours post vaccination, rather than being sent home.

65. If an animal has had an allergic reaction post-vaccination in the past, can you use glucocorticoids before giving future vaccines in order to prevent such reactions occurring again?

Yes, glucocorticoid at an anti-inflammatory dose may be used, as may a dose of antihistamine. There is no guarantee that this will prevent the reaction occurring again, but there should be no interference with the efficacy of the vaccine.

66. If a dog has recovered from an immune-mediated disease that may have been triggered by vaccination; how should I revaccinate it in the future?

Immune-mediated or autoimmune diseases are complex multifactorial disorders involving triggering factors acting on a background of immune dysregulation in a genetically susceptible individual. Recognised trigger factors for canine immune-mediated diseases include underlying infection, neoplasia, chronic inflammation or recent exposure to drugs or vaccines. The evidence for vaccine-associated autoimmunity in the dog is limited and restricted to clinical observations of immune-mediated disease beginning 2 to 4 weeks post vaccination in the absence of any other possible triggers. The most common disorder linked to vaccination is immune-mediated haemolytic anaemia (IMHA) with conflicting evidence related to immune-mediated thrombocytopenia (IMTP) or immune-mediated polyarthritis. That said, because vaccination is a potential trigger, and because immune-mediated diseases have a relapsing and remitting pattern, careful consideration should be given to revaccination protocols for any dog that has been successfully treated and recovered from an immune-mediated disorder. Core revaccination might be avoided if the dog is serologically tested and shown to already have immunity. Non-core vaccines should be carefully selected, weighing the balance between disease exposure risk and risk of relapse of immune-mediated disease. It may not be possible (legally) to avoid rabies revaccination; however, in some US states it is possible for the veterinarian to authorise “medical exemption” from rabies revaccination. Although these precautions are sensible (from first principles), two recent studies actually show no significant ill-effect when dogs recovered from IMHA or IMTP were revaccinated (Ellis *et al.* 2016b, Moon & Veir 2019) [EB1].

67. What is the evidence that adjuvanted vaccines are a cause of the feline injection site sarcoma (FISS)?

Vaccines are just one of a long list of injectable products that have been associated with FISS. There is something unique about cat (*versus* dog) subcutis, which means that repeated injection (of anything) may establish a state of chronic inflammation that might at some point transform into neoplastic disease. The cat, in general, appears more susceptible to developing sarcomas following localised trauma or chronic inflammation (Morrison 2012) [EB1]. Whether adjuvant in vaccines makes vaccines any more likely to induce this reaction is a contentious debate. There is no doubt that adjuvant induces a long-lasting localised chronic inflammatory reaction at the injection site (much more so than non-adjuvanted vaccines) (Day *et al.* 2007) [EB1], but it is suggested that any vaccine is capable of inducing this reaction. In practical terms, the advice is to minimise the use of all vaccines in cats (*i.e.* by vaccinating according to WSAVA guidelines) and wherever possible to minimise the use of adjuvanted vaccine as a precaution. Consideration should also be given to the site of administration of vaccines to cats (see Question 68).

68. What is the best anatomical location for vaccinating a cat in order to reduce the risk of feline injection site sarcoma?

There is no specific anatomical location in which a cat might be injected that will reduce the risk of sarcoma developing. However, there are strategies that might be adopted that will aid in the management of sarcoma, should it occur. There are several different options recommended by different organisations and authors. These include administration as far distal as possible subcutaneously into the hindlimbs and forelimbs, administration into the skin of the lateral abdomen and administration as far distal as possible into the tail. The WSAVA does not recommend a single option, but suggests that at very least the scruff of the neck is not used and that vaccination sites may be rotated each time and that those sites be recorded in the animal’s medical record.

69. Does the VGG recommend serological testing of adult dogs and cats instead of core revaccination?

Yes, the VGG is supportive of the use of in-practice serological testing to determine whether adult dogs are protected (*i.e.* have serum antibody) against CDV, CAV and CVP2, and whether adult cats are protected against FPV (at the time of writing the feline test is not available in LATAM). Note that serology cannot predict protection against FHV1 or FCV, or against any non-core vaccine antigens. Serological testing for the efficacy of rabies vaccination is often required for the purposes of pet travel, but in this instance, testing is generally performed within a defined period post vaccination (*e.g.* 4 weeks) and serological testing is not used in general practice to demonstrate protection from rabies because titres can decline after the recommended testing interval. You should select a well-validated test kit supported by peer-reviewed scientific literature. Serology might be performed annually or triennially during the annual health check consultation. Many owners, particularly those concerned about the safety of vaccines (see question 62) will prefer this option for their pets.

70. Are there kits to evaluate antibody titres in cats?

Yes, one manufacturer makes an in-house test kit to measure FPV, FHV1 and FCV antibodies in the serum of cats (Mende *et al.* 2014), but at the time of writing this test is not available in LATAM [EB1]. Note that only antibody against FPV is predictive of protection; antibody against the upper respiratory tract viruses does not correlate with protection.

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APPENDIX: THE WSAVA QUESTIONNAIRE SURVEY



WSAVA
Global Veterinary Community

**Vaccination
Guidelines
Group**


WSAVA VACCINATION GUIDELINES GROUP

FOCUS ON LATIN AMERICA PROJECT 2016 to 2019

Dear Colleague,

I am sure that you are aware of the WSAVA Vaccination Guidelines Group (VGG) and the work we have done since 2004 in introducing global recommendations for the vaccination of dogs and cats. In 2016 the VGG starts an exciting new project that focuses on endemic infectious diseases and vaccination in Latin America. The VGG will be making a series of fact-finding visits to countries in the region to meet with a spectrum of veterinary professionals (practitioners, industry, academia and governmental) to formulate recommendations for best-practice vaccination of pet dogs and cats in this part of the world.

In advance of these visits, the VGG would like to obtain and analyse information on the perceptions of small animal practitioners working in these countries with respect to infectious disease and vaccination of dogs and cats.

Accordingly, we have prepared the attached short questionnaire and would be very appreciative of your time in completing this to help us in our endeavours. The data will remain confidential to the VGG and would only be published in anonymous and aggregated form.

I thank you for your assistance with our work and look forward to meeting you at one of the continuing education events that the VGG will be hosting in Latin America during this phase of our work.

Sincerely,

Emeritus Professor M. J. Day
BSc BVMS(Hons) PhD DSc Dr(hc) DiplECVP FASM FRCPATH FRCVS

Chairman, WSAVA Vaccination Guidelines Group.

QUESTIONNAIRE

ALL INFORMATION IS CONFIDENTIAL TO THE VGG

Please circle the appropriate answer or give information on the line

SECTION 1. ABOUT YOU

Are you: Male or Female

What is your age range?

20 to 30 years 31 to 40 years 41 to 50 years 51 to 60 years > 60 years

How long have you been a veterinarian?

<5 years 5 to 10 years 11 to 20 years 21 to 30 years > 30 years

Which veterinary school did you graduate from? _____

SECTION 2. ABOUT THE PRACTICE YOU WORK IN

Is your practice: rural or urban (city)

Is your practice: small animal only or mixed animal (including livestock)

How many veterinarians work in your practice?

Full time _____ Part time _____

How many support staff (nurses, receptionists, kennel staff) work in your practice?

Full time _____ Part time _____

Do you use a computerised medical records system? Yes No
 Do you see only day-patients? Yes No
 If no, do you have a hospital for patients staying overnight or longer? Yes No
 Approximately what proportion (%) of your patients is:
 dogs _____ cats _____ other species _____.
 Do you have access to a diagnostic laboratory? Onsite _____ University _____ Private _____

If you have your own practice laboratory onsite, what tests do you run in-house?

Haematology
 Serum biochemistry
 Cytological examination
 Antibody titres for vaccine-preventable diseases List:
 Others List:

SECTION 3. ABOUT CANINE INFECTIOUS DISEASES IN YOUR PRACTICE

Please tick which of the following infectious diseases you believe to be present in your area. For each one you indicate, please estimate how many cases you might diagnose in 1 year.

Disease	Seen in my practice	Estimated number of cases seen/year
Canine distemper (CDV)		
Canine hepatitis (adenovirus, CAV1)		
Canine parvovirus (CPV2)		
Rabies		
Leptospirosis		
Kennel cough (canine infectious respiratory disease complex)		

SECTION 4. ABOUT FELINE INFECTIOUS DISEASES IN YOUR PRACTICE

Please check which of the following infectious diseases you believe to be present in your area. For each one you indicate, please estimate how many cases you might diagnose in 1 year.

Disease	Present in my practice	Number of cases seen/year
Feline parvovirus (FPV)		
Feline herpesvirus (FHV)		
Feline calicivirus (FCV)		
Rabies		
Feline leukaemia virus (FeLV)		
Feline immunodeficiency virus (FIV)		
Feline infectious peritonitis (FIP)		
<i>Chlamydia felis</i> infection		

SECTION 5. ABOUT THE VACCINES YOU HAVE IN YOUR PRACTICE

Tick which of the following types of vaccine you have in your practice:

For Dogs	For Cats
Combined CDV, CAV2 and CPV2 vaccine	Combined FPV, FHV and FCV vaccine
Combined CDV, CAV2, CPV2, CPi	Combined FPV, FHV, FCV and <i>Chlamydia</i> vaccine
Combined CDV, CAV2, CPV2, CPi, <i>Leptospira</i>	Combined FPV, FHV, FCV, <i>Chlamydia</i> and FeLV vaccine
Combined CDV, CAV2, CPV2, CPi, CCv	
Combined CDV, CAV2, CPV2, CPi, CCv, <i>Leptospira</i>	
Combined CPV2, CCv	
Combined CPV2, CDV	
<i>Giardia</i> vaccine	
Rabies vaccine	Rabies vaccine
Combined <i>Bordetella</i> /Canine Parainfluenza	
Intranasal ___ parenteral ___	
Leptospirosis vaccine	FeLV vaccine
Visceral leishmaniosis vaccine	FIV vaccine
Others (please name)	Others (please name)

Do all of your canine vaccines come from a single manufacturer? Yes No

Which manufacturer/s? _____

Do all of your feline vaccines come from a single manufacturer? Yes No

Which manufacturer/s? _____

SECTION 6. ABOUT VACCINATING DOGS IN YOUR PRACTICE

What proportion (%) of your canine patients has ever been vaccinated with the CORE canine vaccines (CDV, CAV and CPV)? ____

At what age do you first vaccinate a puppy? _____

How many times would you vaccinate a puppy and how long in weeks is the interval between vaccinations? _____

At what age do you give the last “puppy vaccination”? _____

Do you revaccinate at approximately 1 year after finishing the puppy vaccinations? Yes No

How often do you give CORE vaccines to adult dogs? (Circle the appropriate choice below)

Every 6 months Annually (every year) Triennially (every 3 years) Less often (>3 years)

Is rabies vaccination for dogs a legal requirement in your area? Yes No

At what age do you give the first dose of rabies vaccine to a puppy? _____

Do you give a second dose of rabies vaccine to a puppy? If so, at what age? _____

Do you recommend revaccinating adult dogs against rabies? If so, how frequently should they be revaccinated? _____

Do you use other vaccines in addition to the core vaccines (CDV, CAV2 and CPV2) in adult dogs? If so, which ones and how frequently do you give them (i.e. annually? More or less often?) _____

SECTION 6. ABOUT VACCINATING CATS IN YOUR PRACTICE

Approximately what proportion (%) of your feline patients has ever been vaccinated with the CORE feline vaccines (FPV, FHV and FCV)? _____

At what age do you first vaccinate a kitten? _____

How many times would you vaccinate a kitten and how long in weeks is the interval between vaccinations? _____

At what age do you give the last “kitten vaccination”? _____

Do you revaccinate at 1 year after finishing the kitten vaccinations? Yes No

How often do you give CORE vaccines to adult cats? (Circle the appropriate choice below)

6 monthly annually (every year) triennially (every 3 years) longer (>3 years)

Is rabies vaccination a legal requirement for cats in your area? _____

At what age do you give the first dose of rabies vaccine to a kitten? _____

Do you give a second dose of rabies vaccine to a kitten? If so, at what age? _____

Do you recommend revaccinating adult cats against rabies? If so, how frequently should they be revaccinated? _____

Do you use other vaccines in addition to the core vaccines (FPV/FCV/FHV1) in adult cats? If so, which ones and how frequently do you give them (i.e. annually? More or less often?) _____

IS THERE ANYTHING ELSE YOU WOULD LIKE TO TELL US ABOUT INFECTIOUS DISEASES OR VACCINATION PRACTICES IN YOUR AREA?

FINALLY

Do you have important diseases in your area for which there are currently no vaccines available? Yes No

If yes, what are the diseases: _____

Would you use a vaccine if it were available? Yes No

**THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE
IT WILL PROVIDE VALUABLE INFORMATION FOR THE VGG TO HELP FORMULATE RECOMMENDATIONS
FOR VACCINATION IN LATAM**

These WSAVA vaccination guidelines have been published as submitted to JSAP and have been through an abridged peer-review process.