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6 February 2012

Open Letter

World Small Animal Veterinary Association

Prof. Jolle Kirpensteijn	President
Prof. Peter Ihrke	President Elect
Dr Walt Ingwersen	Secretary
Prof. Richard Squires	Member of Scientific Advisory Committee (SAC), and Vaccination Guidelines Group
Prof. Michael Day	Chair of SAC, and Member of Vaccination Guidelines Group (VGG)
Prof. Ron Schultz	Member of Vaccination Guidelines Group (VGG)

Cc: Prof. Marian Horzinek, former Member of VGG
Prof. Hajime Tsujimoto, new Member of VGG
Dr Roger Clarke, Committee Member 'Animal Welfare'
Richard Ford, Canine Vaccination Task Force/American Animal Hospital Association (AAHA)

Cc: Australian Veterinary Association
Australian Veterinary Boards Council (AVBC)
Australian National Kennel Council (ANKC)

Cc: Wendye Slatyer, National Dog, Australia
Registered Breed Clubs in Australia

Gentlemen,

Re: Critique of the WSAVA VGG Vaccination Guidelines for Owners & Breeders of Dogs and Cats

It is disappointing, though not unexpected considering industry (Intervet) sponsorship, that the *Vaccination Guidelines for the Owners and Breeders of Dogs and Cats,* released by the World Small Animal Veterinary Association (WSAVA)'s Vaccination Guidelines Group (VGG) in September 2010 (and published online[1] in October 2010), trade science and animal welfare for commercial interest and vaccine sales.

These **consumer guidelines** are devoid of any references, and, instead of "science-based advice" to help the consumer of veterinary services make informed choices on the APPROPIRATE healthcare of their animals, the owners and breeders of dogs (and cats) are being intimidated by images of sick animals and an unpalatable amount of preaching which culminates in the central recommendation that

> **"...every adult dog needs to receive the core vaccines, but they need not be given more often than every three years"**

The **consumer guidelines** followed hot on the heels of the *"updated and expanded version"* of the Vaccination Guidelines for veterinarians (2010)[2] (**professional guidelines**) – originally launched at the 2007 annual congress of the WSAVA in Sydney which was hosted by the Australian member organisation, ASAVA, the small animal special interest group of the Australian Veterinary Association (AVA). The **professional guidelines** highlight that:

> **"Dogs that have responded to vaccination with MLV core vaccines maintain a solid immunity (immunological memory) for many years in the absence of any repeat vaccination. Following the 12 month booster, subsequent revaccinations are given at intervals of 3 years or longer, unless special conditions apply."**

[1] WSAVA Vaccination Guidelines Group; M.J. Day, M.C. Horzinek, R.D. Schultz "Vaccination Guidelines for the Owners and Breeders of Dogs and Cats" http://www.wsava.org/PDF/Misc/WSAVA_OwnerGuidelines_September2010.pdf
[2] M.J. Day, M.C. Horzinek, R.D. Schultz, Vaccination Guidelines Group/WSAVA "Guidelines for the Vaccination of Dogs and Cats", *Journal of Small Animal Practice, Vol. 51, June 2010* http://www.wsava.org/PDF/Misc/VaccinationGuidelines2010.pdf

What's magic about these 3 years? Nothing, it seems. In July 2003, just months after the release of the Canine Vaccination Guidelines by the American Animal Hospital Association (AAHA), the U.S. *DVM News Magazine* reported on "*Industry, profession questions AAHA vaccine guidelines…"*. Among those interviewed for the article in *DVM News Magazine* were Richard Ford and Ronald Schultz, members of the original AAHA Canine Vaccination Task Force, who explained that the 3-year interval was a compromise for practitioners:

- Ford: *"It's arbitrary. It's just completely arbitrary…"*
- Schultz: *"I thought if the veterinarian understood that if a killed rabies vaccine could work for three years that they could surely understand that a modified-live distemper, adeno or parvo (vaccine) could work for three years, minimum…Modified-live vaccines have a much longer duration of immunity than killed vaccines."*

From my extensive reading of the literature on canine vaccination, I gather that this compromise **is between the arbitrary, traditional annual vaccination practice and the medically sound approach to APPROPRIATELY vaccinate SUSCEPTIBLE animals ONCE or twice IN EARLY LIFE using modified-live virus (MLV) products**. As VGG member Schultz explained, in *Current and future canine and feline vaccination programs*, Veterinary Medicine/March 1998:

> *"An important question to ask yourself is: "What do we do to ensure that children who are vaccinated at an early age, usually less than 6 years of age, still have immunity at 20, 40, 60 or 90 years of age?" Nothing! We don't measure titers in people, and we don't routinely vaccinate adults. We rely on the memory cells of the immune system. Since vaccines for people are similar in many ways to canine or feline vaccines, since the immune system of a person is similar to that of an animal, and since immunity persists for the life of a person (average 70+ years), then why wouldn't immunity from canine and feline vaccines persist for 10 to 15 years? The answer is that many canine and feline vaccines do provide the same lifelong immunity."*

Such lifelong immunity, from the canine core vaccines (distemper, hepatitis and parvovirus) has been studied and documented – notably by VGG member Schultz:

- R.D. Schultz (2000): *Extract from* ***"Considerations in Designing Effective and Safe Vaccination Programs for Dog"***, in: Recent Advances in Canine Infectious Diseases. Carmichael L.E. (Ed.)/Published by International Veterinary Information Service (www.ivis.org):

Table 2. Duration of Immunity and Efficacy for Canine Vaccines Commercially Available in the United States.

Vaccine	Minimum Duration of Immunity	Estimate of Relative Efficacy (%)
Core		
Canine Distemper	≥7 yr[1]	>90
Canine Parvovirus-2	≥7 yr[1]	>90
Canine Adenovirus-2	≥7 yr[1]	>90

- R.D. Schultz *et al* - ***"Age and Long-term Protective Immunity in Dogs and Cats"****, J. Comp. Path 2010, Vol. 142":*

> "In our studies…the longest period of time after initial vaccination that dogs were sampled and that antibody was found to persist was 14 years [in natural environments]…In environments free from CDV and CPV-2, we have not been able to keep dogs for longer than 9 years, thus the minimum DOI as defined by antibody persistence was 9 years …"

It follows that the 'vaccination debate' is, quite simply, a commercial argument in which the very purpose of vaccination, i.e. the prophylaxis in the individual animal, has been completely abandoned. As VGG member Horzinek[3] emphasized

> ***"Vaccines protect against infectious disease, and a precondition for their use is a risk of infection."*** (emphasis added)

[3] Marian C. Horzinek "Vaccine use and disease prevalence in dogs and cats", *Veterinary Microbiology 117 (2006) 2-8*

I show in the following pages and attached tables that the presentation of vaccine "DOI" in both the **professional** and the **consumer guidelines** is misleading, actively aiding in the WILFUL misinterpretation of (re)vaccination requirements. For example, the hugely delayed AVA Policy (2009) on the vaccination of dogs and cats[4] (now down-graded to Position Statement, due to "conflicting views" among the industry body's members on the issue[5]; this change appears to have coincided with the recent addition of a vaccine manufacturer's representative to the ASAVA Committee[6]) states:

> ***"Current scientific consensus recommends that adult cats and dogs should be vaccinated with core vaccines triennially where applicable."*** (emphasis added)

The AVA highlights that

> *"Vaccination protocols should be determined…based on attributes such as duration of immunity of available vaccines…"* (emphasis added)

Horzinek clarifies:

> ***"The 'duration of immunity' (DOI) issue has dominated the veterinary literature** during the past decade, the polemics having been **inspired by industry claims aimed at achieving a marketing advantage**…After all, 'childhood diseases' have been so named because of their temporal limitation, and adults are not revaccinated…*
> ***it is moot to discuss the benefits of…vaccination intervals when immunological knowledge, independent experimental data and medical vaccinology have evidenced lifelong protection…"*** (emphasis added)
>
> (Horzinek & Thiry (2009), *"Vaccines and vaccination: The principles and the polemics"*, Journal of Feline Medicine and Surgery (2009) 11, 530-537)
>
> *"Scientific arguments (for the change in the immunization protocols) include…**vaccination-challenge data obtained by the industry in preparation of the product registration (which only established a minimum DOI)**."* (emphasis added)
>
> (M.C. Horzinek *"Vaccination Protocols for Companion Animals: The Veterinarian's Perspective"*, J. Comp. Path 2010, Vol. 142 S129-132)

The VGG's sponsor, Intervet (now MSD Animal Health), carried out one such "minimum DOI study". Within the framework of the study, 3-monthly serology preceded the sequential challenge of the test dogs with CAV-1, CPV-2 and CDV at 37, 38 and 39 months post-vaccination, and, as the results show (extract from published paper[7] below), the mean titres established at the manufacturer-determined end-point of 3 years were all **well above the threshold which is correlated with protection.** Based on the titres presented, this study confirmed solid seroconversion (which is defined as a four-fold or greater rise in titre compared with the pre-vaccination titre), resulting in robust immunity, and the (majority of) test dogs maintained antibody levels >1:80 for CPV-2 which is deemed protective:

TABLE 1. Geometric Mean Titers in Dogs Following Second Vaccination with CAV-2, CPV, and CDV

Virus Fraction (Assay)	*Prevaccination*	*Months after Vaccination*									
		1	*3*	*6*	*9*	*12*	*21*	*24*	*30*	*33*	*36*
CAV-2 (SN)	<2	89	153	964	497	672	368	379	332	256	357
CPV (HI)	<10	567	680	1,444	395	640	350	257	192	151	237
CDV (SN)	<2	402	781	195	110	241	201	48	144	100	193

HI = hemagglutination inhibition titers; SN = serum neutralization titer test.

[4] Australian Veterinary Association "Vaccination of dogs and cats", first ratified and published as POLICY in June 2009, now revised to POSITION STATEMENT (May 2011) http://www.ava.com.au/policy/67-vaccination-dogs-and-cats
[5] E-Ructations – AVA NSW Division Newsletter, 26 May 2011 http://www.ava.com.au/sites/default/files/May%20NSW%20newsletter.pdf
[6] http://www.asava.com.au/ASAVA/ASAVAWhatwedo/tabid/1499/Default.aspx
[7] Thomas C. Gore; Nallakannu Lakshmanan; Karen L. Duncan; Michael J.Coyne; MelissaA. Lum; Frank J.Sterner, Intervet Inc., "Three-Year Duration of Immunity in Dogs Following Vaccination Against Canine Adenovirus Type-1, Canine Parvovirus, and Canine Distemper Virus", *Veterinary Therapeutics, Vol. 6, No. 1, Spring 2005*

What this study proved is that the vaccine (Nobivac, which, like other MLV core vaccines, still uses the same 'proprietary' CPV-2 strain patented over 20 years ago – see pages 22-24 for more details) protects for LONGER THAN 3 YEARS. Thus, the manufacturer's label claim for revaccination every 3 years *"to maintain protection"* is incongruent with the data generated during the 'dedicated DOI study' and is not representative of the average dog's vaccination requirement for protection against disease.

Not only is there **no justification for a blanket revaccination recommendation at 3 years,** as WSAVA VGG/SAC members have confirmed, e.g.:

- Michael J. Day - ***"How I Vaccinate an Animal with Previous History of Adverse Reaction"**, Proceedings of 2010 WSAVA Congress, Geneva:*

  > "Although the licensed duration of immunity (DOI) for the core vaccine components (DHP [distemper, hepatitis (adenovirus 2), parvovirus 2]) is three years, **there is now evidence for a minimum DOI of 9 years for CDV and CPV**..." (emphasis added)

- Richard Squires - ***"Controversy and Confusion: Revaccination of adult dogs and cats – an update"**, Newsletter of AVA Queensland December 2010:*

  > "**Regardless of their labelling**...modified live versions of the "core" vaccines...are almost universally accepted to provide **very long lasting protection, for well over 3 years and possibly for life."** (emphasis added)

but, as separate studies have shown, persisting antibodies neutralise challenge virus --- as evidenced by the absence of clinical disease in the Intervet laboratory test dogs ---- and this, being the very principle of vaccination with MLV vaccines, quite logically extends to dogs in the field:

Schultz (1998)[8]:

> *"...we're not seeing an anamnestic response from most modified live or non-infectious products";*

Schultz (with Laurie Larson, 1996)[9]:

> *"After challenge...85% of the(se) vaccinates [puppies vaccinated at 8, 10, and 12 weeks] showed no increased response...This was expected because most vaccinates were actively immune at the time of challenge..."*

Martinod, Pfizer Central Research U.S. (1999)[10]:

> *"...most adult dogs have become immune through vaccination or natural infection and are (refractive) [likely to mean refractory = resistant] to boosting with modified live vaccines",*

and Böhm *et al* (2004)[11]:

> *"With all three diseases [CDV, CAV-1, CPV-2] there was no evidence that the proportion of protected dogs decreased with the time since their last vaccination...The observation that a booster vaccination did not increase the proportion of dogs protected against CPV agrees with the results of a study of dogs at a UK teaching hospital in which the vaccination status of adult dogs did not influence the presence or titre of CPV antibodies (Tennant and others 1991)."*[12]

THUS: *"The client is paying for something with no effect or with the potential for an adverse reaction." (Schultz, 1995)*[13]

> *"...most vaccinations administered to adult dogs and cats serve no beneficial 'immunological' purpose whatsoever." (Squires, 2009)*[14]

[8] Dr Ronald Schultz in DVM Vaccine Roundtable "*Safety, efficacy heart of vaccine use; experts discuss pros, cons"* DVM December 1988
[9] Laurie J. Larson; Ronald D. Schultz "High-titer canine parvovirus vaccine: Serologic response and challenge-of-immunity study", *Veterinary Medicine/March 1996*
[10] Serge Martinod, Pfizer Central Research, Groton/CT/USA "Vaccination Practices in Veterinary Medicine: Standardization versus Tailored to Needs?", *Advances in Veterinary Medicine, Vol. 41* (1999)
[11] M. Böhm, H. Thompson, A. Weir, A.M. Hasted, N.S. Maxwell, M.E. Herrtage "Serum antibody titres to canine parvovirus, adenovirus and distemper virus in dogs in the UK which had not been vaccinated for at least three years", *The Veterinary Record, April 10, 2004*
[12] B.J. Tennant, R.M. Gaskell, R.C. Jones, and C.J. Gaskell "Prevalence of antibodies to four major canine viral diseases in dogs in a Liverpool hospital population", *Journal of Small Animal Practice (1991) 32, 175-179*
[13] Dr Ronald D. Schultz, in Carin A. Smith "Are we vaccinating too much?", *JAVMA, Vol 207, NO. 4, August 15, 1995*

WHY would the WSAVA **endorse, advocate and promote** the **commercial, unscientific protocols** in the **consumer guidelines,** when, at the same time, it stresses in the **professional guidelines** that:

> **...the principles of 'evidenced-based veterinary medicine' would dictate that testing for antibody status (for either pups or adult dogs) is better practice than simply administering a vaccine booster...** (my emphasis)

Academia and industry seem to agree that CPV-2 is a disease of young puppies (<6 months old) which have not developed active immunity against this pathogen:

> *"The findings reported here generally supported the concept that CPV enteritis tends to be a disease of young and unvaccinated dogs…That CPV enteritis is a disease primarily of young dogs is not too surprising. More than 15 years have passed since CPV was first recognised as a cause of enteritis in dogs, and most adult dogs now are thought to be immune to CPV via vaccination or prior infection, with subclinical infection more common than clinical disease in dogs >6 months of age. Clinical disease tends to be a problem almost exclusively of pups between weaning age and about 6 months."*
>
> (Houston, Ribble & Head *Risk factors associated with parvovirus enteritis in dogs: 283 cases (1982-1991),* JAVMA, Vol. 208, No. 4, February 15, 1996)
>
> *"In populations in which the viruses are endemic, new cases occur mainly in young animals that become infected after maternal antibodies wane…"*
>
> (Hoelzer & Parrish, *Parvoviruses of carnivores*, Vet. Res. (2010) 49:39)

Carmichael in his 2005 *Annotated Historical Account of Canine Parvovirus* (J.Vet.Med. B 52, 303-311) observed:

> *"CPV-2 cases declined during the 1980-1981 period as a consequence of the herd immunity resulting from natural infection and the widespread use of vaccines"* (my emphasis),

echoing Schultz's 1982 appraisal, in *Theoretical and practical aspects of an immunization program for dogs and cats* (JAVMA, Vol. 181, No. 10) that

> *"A combination of vaccination and subclinical and clinical infection has resulted in approximately 75% of the dogs having antibody to parvovirus"*,

and confirming Greene, Schultz + Ford's (2001)[15] finding that

> *"…canine distemper, canine parvovirus, and canine rabies are virtually nonexistent among vaccinates."*

In 2011, Schultz, in his presentation *"What every veterinarian needs to know about canine vaccines and vaccination programs"* at the AAHA/OVMA conference (March 2011), reiterated that

> *"To get the best "herd (population) immunity" - It is the percentage of dogs vaccinated with core vaccines – not how often they are vaccinated!"*

Nearly 2 decades ago, Schultz had postulated (in Carin A. Smith *"Are we vaccinating too much?"*, JAVMA, Vol 207, No. 4, Aug 15, 1995) that

> *"I don't think there is a need to vaccinate adult dogs, since early vaccination will be sufficient to stimulate memory cells."*

Day (2006), in *The Immunology of Vaccination*, presented at the 2006 AVMA Convention, agreed:

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[14] Richard Squires in Anne Fawcett "Fur flies over small animal vaccination", *The Veterinarian Magazine, September 2009*

[15] Craig E. Greene, DVM, MS, Ronald D. Schultz, PhD, and Richard B. Ford, DVM, MS "Canine Vaccination", *Veterinary Clinics of North America: Small Animal Practice, Vol 31, No. 3, May 2001*

> *"That memory cells are generated following companion animal vaccination is clearly demonstrated by experiments showing long-term duration of immunity (to experimental challenge) and persistent seroconversion for many years, even in animals that have not been regularly revaccinated…",*

and, at the 2010 WSAVA Congress in Geneva/Switzerland (*"How I Vaccinate an Animal with Previous History of Adverse Reaction"),* Day emphasized that:

> *"…a dog that is appropriately immunized as a pup probably never requires another core vaccine during its lifetime"*

The WSAVA VGG, quite illogically, puts the onus of maintaining 'herd immunity' on the vet-going and vaccinating part of the population, thus effectively soliciting these unsuspecting vet clients to facilitate the perpetuation of the arbitrary, unscientific vaccination protocols. Despite the acknowledged low-to-moderate overall uptake of vaccines, i.e. ≤50% of the canine population is vaccinated against infectious viral diseases, there seems to be consensus amongst academia and the profession that CAV-1 disease has not been diagnosed in several decades, and CDV disease 'clusters' are now only rarely encountered in situations of over-crowding, such as in shelters; this leaves CPV-2 as the viral disease of concern for the broader community. Yet, the widespread and repeated use of combination DHP (Distemper, Hepatitis, Parvovirus, in Australia designated C3) vaccines is promoted rather than monovalent products to target the infectious disease of interest.

> *"The demand among veterinarians that vaccines be simple to administer and timesaving has led to the long-term and widespread use of polyvalent vaccines…polyvalent vaccines are routinely administered…with seemingly little regard for the actual risk of infection."*
>
> (Greene, Schultz, and Ford: *Canine Vaccination*, Veterinary Clinics of North America: Small Animal Practice, Vol 31, No. 3, May 2001)

I query:

1. **the motivation of the WSAVA VGG for withholding from the consumer of veterinary services, any meaningful information on antibody titre testing as a useful and validated method of verifying the immune response in the individual dog following vaccination;**

2. **the scientific basis and validity of the consumer guidelines' central message that every adult dog needs to be re-vaccinated with the MLV core antigens at intervals not exceeding 3 years;**

3. **the material risk of infection in a dog that has responded to the core vaccine antigens and thus has circulating antibodies AND immunological memory.**

I demand that the VGG provide immunological and epidemiological justification for its recommendations to the consumer of veterinary services to revaccinate dogs at 3-yearly intervals.

The WSAVA VGG downplays what it calls the 'drivers for change' for the vaccination protocols. The **consumer guidelines** state that

> *"No single adverse event like FISS [Feline Injection Site Sarcoma] was the driver for the development of canine vaccination guidelines."*

Yet, VGG member Day, whose *"research interests cover experimental models of autoimmunity and a range of companion animal immune-mediated and infectious diseases"* and who "*has published widely in the field of immunopathology, is author of the textbooks Clinical Immunology of the Dog and Cat (in second edition) and Veterinary Immunology: Principles and Practice."*[16] recently confirmed:

[16] Michael J. Day, BSc BVMS(Hons) PhD DSc Dipl ECVP FASM FRCPath FRCVS – Summary Curriculum Vitae; http://www.bristol.ac.uk/vetpath/cpl/mjd.htm accessed 28.01.2012

- *"The recognition of feline injection site sarcomas over 20 years ago had provided 'one of the first inklings that vaccination may have some safety issues related to it'…An example in dogs was the triggering of a spectrum of immune-mediated disorders…*
  Analysis of data on the frequency of adverse reactions had been one driver for change in vaccination protocols…" (2011)[17]

- *Put simply, an increasingly wide spectrum of adverse reactions is now recognised following the vaccination of cats and dogs.* (2010)[18]

The **consumer guidelines** trivialise the adverse reaction potential of immunobiological products. On the one hand, the VGG admits that *"every type of vaccine can and does have the ability to trigger an immunological reaction in high risk animals"*; that *"(t)here can never be a guarantee…that a vaccine will be perfectly safe and without adverse consequences"*; and that *"(c)ertain adverse vaccine reactions are not observed until days, weeks or even months and years after vaccination or revaccination"*. On the other hand, the VGG claims that vaccines are "mistakenly blamed" when, for instance, "purely hereditary factors are the cause of the problem". **If we don't know which "hereditary factors" might be involved, why expose animals willy-nilly to the unnecessary risk of unnecessary repeat vaccination?**

According to Pfizer[19]: *"…adverse reactions, and other unexpected events are a reality with biological products".*

And VGG member Schultz, having gone on record in 2000[20], saying that *"Adverse reaction…risks are not well studied…rates are not well documented…",* cautioned his audience of vet practitioners in March 2011[21]

> *"…the risk of adverse reactions, no matter how low, from the administration of a medical product that is not required is an **unacceptable medical practice.**"* (my emphasis)

The **consumer guidelines** briefly mention the RABIES CHALLENGE[22] which is underway in the U.S.A. The project is referred to as "*studies…to determine if a [rabies] vaccine with a much longer minimum DOI (e.g. 5 – 7 years) can be found".* I am appalled that the WSAVA VGG should so blatantly misrepresent the project's declared objective, which is the investigation of **existing** (non-infectious/killed) products to assess/determine **"the long-term duration of immunity of the canine rabies vaccine, with the goal of extending the state-mandated interval for boosters".**

The RABIES CHALLENGE is a prime example for the collective inaction by those with a vested interest in perpetuating the unscientific vaccination protocols. Had it not been for the admirable initiative by dog owner Kris Christine in the U.S.A., and the generous contribution and support of the studies by Dr Jean Dodds and Professor Ron Schultz, these studies which are geared at improving animal health and welfare, would not be done.

In the attached tables, I compare the vaccination background and advice given to owners and breeders of dogs with information published by those with "scientific credibility". I quote directly from – fully referenced – papers and articles to demonstrate the discrepancies, contradictions and omissions; some emphasis has been added to highlight pertinent passages.

[17] Michael Day in *"Different perspectives on vaccination advice"*, Veterinary Record 2011, 168:395-396 http://www.wsava.org/PDF/2011/BSAVA/2011-04_BSAVA_VaccinationPerspectives.pdf
[18] Michael J. Day *"Vaccination in 2010: The Hot Topic of the Millennium"*, Proceedings of ASAVA Conference, Hobart/Australia, August 2010
[19] Serge Martinod, Pfizer Central Research, Groton/CT/USA "*Vaccination Practices in Veterinary Medicine: Standardization versus Tailored to Needs?"*, Advances in Veterinary Medicine, Vol. 41 (1999)
[20] R.D. Schultz "Considerations in Designing Effective and Safe Vaccination Programs for Dogs" (2000)
[21] Dr Ronald D. Schultz *"What every veterinarian needs to know about canine vaccines and vaccination programs"*, Presentation at AAHA/OVMA, March 24-27, 2011
[22] http://www.rabieschallengefund.org/about-the-rcf/behind-the-challenge

Summarizing, the scientific literature, delivered by, among others, the members of the WSAVA VGG, seems to confirm, beyond argument, that:

- **ONE appropriately timed vaccination, in the absence of interfering MDA levels, will render the great majority of puppies actively immune – FOR LIFE**
- **Revaccination does not enhance disease resistance in an actively immune dog, and consequently, the revaccination of actively immune dogs does not increase herd immunity levels.**
- **Revaccination of actively immune, adult dogs is MEDICALLY CONTENTIOUS.**
- **The periodic lifelong revaccination "mandate" of a fraction of the canine population is an exploitative practice which disadvantages consumers of veterinary services and, most importantly, needlessly endangers the well-being and quality of life of untold numbers of dogs.**

I close with a quote from Dr Dennis Macy (1995)[23]:

> ***"Veterinarians and the industry need to have the guts to be honest with ourselves and assess risk, and not be trapped in tradition",***

I echo Professor Horzinek's (2005)[24] reminder that

> ***"Sufficient measures are justifiable, unnecessary measures are ethically dubious",***

and **I challenge the WSAVA to abandon the polemics and to spear-head the long-overdue implementation of EVIDENCE-BASED VETERINARY MEDICINE**.

Sincerely,

Beate Mies
Advocate for the **Judicious** Use of Vaccines

Copy to: Elizabeth Hart, Adelaide/Australia,
whose tremendous support of my work and own lobbying on both the national and international fronts for judicious vaccine use is acknowledged.

Cc: Monika Peichl, Germany
Dr. W Jean Dodds, USA
Kris Christine, USA

Note: The dissemination of this Open Letter to the WSAVA dated 6 February 2012 is not limited to the recipients listed herein. The cross-posting by anyone receiving this communication is encouraged.

[23] Dr Dennis Macy in Carin A. Smith "Are we vaccinating too much?", *JAVMA, Vol 207, No. 4, Aug 15, 1995*
[24] M. Horzinek – Presentation at INTERVET SYMPOSIER – STOCKHOLM 2005-12-06 OCH GÖTEBORG 2005-12-07
http://kliniken.msd-animal-health.se/files/sv/symposium/files/F%C3%B6rel%C3%A4sn%20mtrl%20TOT.pdf
accessed 07-09-2011

Appendices to critique of WSAVA VGG Vaccination Guidelines for the Owners and Breeders of Dogs and Cats (2010)

Table 1 – Misinformation on 'duration of immunity' provided by "40-year-old products"

Table 2 – Omission of titre testing option to determine timing of vaccination and to verify immune responses in puppies

Table 3 – Misrepresentation of puppy vaccination timing, potentially resulting in oversensitisation, or lack of effect & clinical disease

Table 4 – Omission of scientific data/research findings which provide evidence of long DOI of MLV core vaccines for dogs

Table 5 - Misrepresentation of biological necessity for revaccination, WILFULLY ignoring the first principle of ethics: DO NO HARM

Table 6 – Misrepresentation of reasons for 'extended inter-vaccination intervals'

Table 7 – Misrepresentation of KNOWN and SUSPECTED immune system dysfunction due to unnecessary vaccination and unsubstantiated claims regarding adverse event rates

Table 8 - Distortion of state-of-the-art vaccine 'technology' and licensing criteria, misleading the consumer of veterinary services

Table 9 - Misinformation on safety and efficacy of non-core vaccines

References to Appendices

Note: While the list of references is quite comprehensive, this is but a small selection of papers and articles published in the veterinary press on the subject of canine vaccines and vaccination over the last 3 decades.

Appendices to critique of WSAVA VGG Vaccination Guidelines for the Owners and Breeders of Dogs and Cats (2010)

Table 1 – Misinformation on 'duration of immunity' provided by "40-year-old products" (Day, 2010)[25]

Owner & Breeder Guidelines (2010) ---**THE CENTRAL MESSAGE**---	Publications relating to the "**Duration of immunity" conferred by MLV core vaccines** Authored by WSAVA VGG/SAC members in 2010
A lifelong vaccination programme for an animal will include consideration of inducing protection in early life (by priming and boosting the immune response) and maintenance of protective immunity and immunological memory by periodical revaccination in adulthood (boosting). **...every adult dog needs to receive the core vaccines**, but they need not be given more often than every three years.	Although the licensed duration of immunity (DOI) for the core vaccine components (DHP) is three years, there is now evidence for a **minimum DOI of 9 years for CDV and CPV** and, in reality, **a dog that is appropriately immunized as a pup probably never requires another core vaccine during its lifetime**." (**Day**)[i] In general, adaptive immunity following vaccination with modified live virus (MLV) vaccines develops earliest and most effectively in that it is often complete (e.g. sterile immunity is induced) and duration of immunity (DOI) is often lifelong...**in actively immunized pups** (either following natural or vaccine-induced immunization) the actual titre of antibody is not of importance, as long as the titre is detectable...Actively immune dogs will develop an innate and a rapid anamnestic humoral and cell-mediated response, thus will be protected from infection and/or disease...Only **one dose of the modified-live canine 'core' vaccine** (against CDV, CAV-2 and CPV-2)...**when administered at 16 weeks** or older, will provide **long lasting (many years to a lifetime) immunity in a very high percentage of animals**... " (**Schultz et al**)[ii] There are scientific and societal reasons for the change in the immunization protocols. Scientific arguments include the long persistence of protective antibody titres (in dogs >7 years for CDV and CPV; in cats >4 years for FPV, FCV and FHV), **the longevity of memory B- and T-cell populations (life-long for some antigens)**, but also **vaccination-challenge data obtained by the industry** in preparation of the product registration (which **only established a minimum DOI**)." (**Horzinek**)[iii] Given that immune responses to naturally-occurring infections vary a lot, it seems highly improbable that protection provided by chalk-and-cheese vaccines should, in so many cases conveniently last for just over a year. In fact it's not just highly improbable, it's simply not the case. **Regardless of their labelling, we know that many companion animal vaccines protect** for far longer than a year...Modified live versions of the "core" vaccines...are almost universally accepted to provide very long lasting protection, **for well over 3 years, and possibly for life**." (**Squires**)[iv]

[25] *"...The vaccines that we use for dogs and cats - a lot of them are actually very old. They're 40 year old products. But they still work incredibly well."* Michael Day, from transcript of interview "Vets accused of unnecessary vaccinations", ABC Radio 18.08.2010 http://www.abc.net.au/worldtoday/content/2010/s2986400.htm in response to article on Pet Vaccination published in Choice Magazine, 17-08-2010 http://www.choice.com.au/reviews-and-tests/household/backyard/pets/pet-vaccination.aspx accessed 27.08.2011

Table 2 – Omission of titre testing option to determine timing of vaccination and to verify immune responses in puppies

Owner & Breeder Guidelines (2010) THE IMMUNE RESPONSE *[It is intriguing that, despite the emphasis on "antibody" (the word appears a staggering 72 times (!) throughout the document), there is no recommendation to titre-test puppies and thus approach vaccination in a more scientific manner – just to the contrary…]*	Publications relating to **The concept of serology and age/MDA determinants for the active <u>immunisation</u> of neonates**
The vaccination schedules…take into account this potential difference [in colostrum uptake and transfer of passive immunity from the dam]…<u>we do not routinely test dams for antibody levels or the level of MDA in an individual pup</u> or kitten, repeated vaccination is given…	…simple and universally agreed on answers [to the question "At what age should the vaccination program begin"?] are not available. (Schultz, 2002)[v] From what has been said about maternal antibody, it is clear that there can be **no single, universally applicable schedule for vaccination. (**Cornwell & Thompson, 1982)[vi] The difficulty in selecting an appropriate age or interval at which to vaccinate is not knowing when maternally derived antibody will no longer interfere… (Schultz, 1998)[vii] <u>Testing for antibody is</u> presently <u>the only practical way to ensure that a puppy's immune system has recognised the vaccinal antigen</u>. Vaccines may fail for various reasons: (1) MDA neutralises the vaccine virus…; (2) The vaccine is poorly immunogenic…;[26] (3) The animal is a poor responder… …**<u>the principles of 'evidenced-based veterinary medicine' would dictate that testing for antibody status (for either pups or adult dogs) is better practice than simply administering a vaccine booster</u>** on the basis that this should be 'safe and cost less'… Most vaccinated dogs will have a persistence of serum antibody (against core vaccine antigens) for many years. Immunologically, this antibody reflects the function of a distinct population of long-lived plasma cells (memory effector B cells). Induction of immunological memory is the primary objective of vaccination. For core vaccines there is excellent correlation between the presence of antibody and protective immunity and there is long DOI for these products… (WSAVA VGG (Day, Schultz, Horzinek), 2007)[viii]

[26] Example:1994/95 Finland distemper outbreak amongst vaccinated dogs <2 years of age (Rikula (et al 2000, 2007), 2008), which followed the documented CDV outbreaks amongst vaccinated dogs in Switzerland (Glardon + Stöckli, 1985), and Germany (Harder et al (1991) and Kölbl et al (1995)

Table 3 – Misrepresentation of puppy vaccination timing, potentially resulting in oversensitisation or lack of effect & clinical disease

"There is no magic formula for designing a rational vaccination strategy. Each animal and its environment is a unique combination..."
(Coyne et al, Pfizer Animal Health, 2001)[ix]

Owner & Breeder Guidelines (2010) THE PRINCIPLE OF VACCINATION	Publications relating to **Blanket puppy vaccination schedules**
The vaccination schedule consists of this initial 'priming' of the adaptive immune response (that might occur at either 8, 12 or 16 weeks in any one individual) but also **crucially includes revaccination at 12 months of age or at 12 months after administration of the 14-16 week vaccination**.	No single primary vaccination policy will (therefore) cover all possible situations…many vaccine data sheets recommend an initial course of two injections. Some products are also licensed with a '10 week finish' designed such that the second of two vaccinations is given at 10 weeks of age[27]…Where such protocols are adopted, great caution should still be maintained by the owner – allowing restricted exposure of the pup to controlled areas and only to other pups that are healthy and fully vaccinated… (WSAVA VGG (Day, Schultz, Horzinek), 2007)[x] Since passively acquired antibody declines below the level where it can interfere with the current core vaccines by 12 to 14 weeks of age, **modified live CPV-2, CDV and CAV vaccines given at this age will immunize a very high percentage of pups (>90%) and the immunity from that single dose of vaccine will last for** several years. Our research on duration of immunity for the CPV-2, CDV and CAV vaccines has demonstrated a **minimum** duration of immunity of **7 years**; the **maximum** duration of immunity may be **for the life of most (>80%) vaccinated** animals… (Schultz, 2000)[xi] In our studies, pups vaccinated annually with modified live CPV-2, CDV and CAV vaccines received no added benefit from annual revaccination throughout a period of 7 years when compared to dogs that were vaccinated as pups then challenged with virulent virus at 7 years of age… (Schultz, 1995)[xii] Dogs that have responded to vaccination with MLV core vaccines maintain a solid immunity (immunological memory) for many years in the absence of any repeat vaccination…I don't think there is a need to vaccinate adult dogs, since early vaccination will be sufficient to stimulate memory cells. **Dogs that developed parvo at 1 year of age were probably never immunized properly**… (Schultz, 1988)[xiii] If the [antibody titre] test is not positive shortly…after the final [puppy] vaccination, it suggests that the animal was not immunized. **If you waited until 1 year of age, as we do now [2003], the animal would potentially be susceptible during the most critical time in its life**, the time when the animal needs to have vaccinal immunity. Experience with the [antibody titre] **test demonstrates greater than 90% of the dogs tested after the puppy series** and up to 3 years after vaccination **are positive**, an indication they have **sterile immunity and don't need to be revaccinated with core vaccines** (AAHA Canine Vaccine Task Force, 2003)[xiv]

"…it is the advocacy of the early vaccination (a final dose at 10 weeks for puppies) by its [NOAH = National Office of Animal Health, United Kingdom] members that contributes to the problem [of an increase in the prevalence of CPV]". **(Thompson, 2006[xv])**

[27] ***"No combination core product currently available will immunise an acceptable percentage of puppies when the last dose is given at 10 weeks of age."*** **WSAVA 2007**

Table 4 – Omission of scientific data/research findings which provide evidence of long DOI of MLV core vaccines for dogs

Owner & Breeder Guidelines (2010)	Publications relating to **Best Vaccination Practice**
Every <u>adult</u> dog needs to receive the core vaccines, but they need not be given more often than <u>every three years</u>.	My own observations…show that dogs not only have CDV antibody but are completely protected from infection when challenged five to seven years after vaccination. (Schultz, 1998)[xvi] …DOI studies in both the cat and dog show "memory effector B cells" continue to produce antibody to the core vaccines in the absence of overt antigenic stimulation for many years…**The ability to detect antibody, regardless of titer, in a previously vaccinated and actively immune animal demonstrates that "memory effector B cells" are present and functional**…The presence of antibody also suggests that memory B cells (not producing antibody) are very likely present… (Schultz, 2006)[xvii] Immunologic memory is responsible for the duration of immunity that develops after recovery from natural infection/disease and after vaccination…An antibody titre no matter how low shows the animal has immunologic memory since memory effector B cells [long-lived plasma cells of the adaptive immune system] must be present to produce that antibody…**If a puppy is immunized with the three MLV vaccines used to prevent these diseases** [CDV, CAV-1, CPV-2] **<u>there is every reason to believe the vaccinated animal will have up to life-long immunity</u>**. (Schultz, 2007)[xviii] In our studies (Schultz 2006) we have examined the **persistence of antibodies** in vaccinated dogs kept in natural as well as virus-free environments. The longest period of time after initial vaccination that dogs were sampled and that antibody was found to persist was 14 years for CDV (vaccination with MLV), 14 years for CAV-1 (MLV against CAV-1 or CAV-2) and 10 years for CPV-2 (MLV)."In environments free from CDV and CPV-2, we have not been able to keep dogs for longer than 9 years, thus the minimum DOI as defined by antibody persistence **was 9 years for CDV (MLV), CAV-1 (MLV) and CPV-2 (MLV)**…Dogs maintained in a CDV and CPV-2 free environment were also shown to resist challenge at 9 years post-vaccination. **The serum antibody levels in these dogs had decreased over time, but not significantly. However, when challenged all animals were completely protected regardless of antibody titre pre-challenge**… (Schultz, 2010)[xix]

Table 5 - Misrepresentation of biological necessity[28] for revaccination, WILFULLY ignoring the first principle of ethics: DO NO HARM

"..vaccination is known to prevent reinfection..." **(Schultz, 1982)**

Owner & Breeder Guidelines (2010)	Publications relating to **The current practice of companion animal vaccination**
The design of a vaccination programme for an individual pet animal is a medical activity that is best undertaken by your veterinarian.	...many essential facts regarding vaccines are lacking and myths continue to flourish...answers to the questions [whether all vaccines are necessary, whether they are safe in young pups, what is the degree of efficacy in preventing disease, what is the onset of immunity/duration of immunity, etc.] often reflect individual experiences, **vested interests**, or a **disinclination** to state that true answers are not known." (Carmichael, 1999)[xx] The purpose of a vaccination program is to prevent the development of overt clinical disease, by preventing or limiting infection. If the program is planned properly, it can improve animal care by providing a convenient time for a routine health examination. This aspect of the vaccination program has been abandoned by many clinicians... (Schultz, 1982)[xxi] We have had the idea for years that vaccines, if they don't do any good, won't cause harm. I think that's another concept the veterinarian has to get away from because whether it be modified live or non-infectious, **there is the potential to cause harm**! We've seen a good example of that within the last couple of years with some non-infectious products that were causing a great deal of harm, i.e. hypersensitivity reactions both generalized and systemic, causing untoward diseases, namely immune mediated disease which we had never seen in that species prior to the introduction of a non-infectious vaccine. (Schultz, 1988)[xxii] Schultz agrees with Ford adding that he picked the three-year interval because he thought practitioners would be more likely to accept it ***"I thought if the veterinarian understood that if a killed rabies vaccine could work for three years that they could surely understand that a modified-live distemper, adeno or parvo (vaccine) could work for three years, minimum,"*** he says. "Modified-live vaccines have a much longer duration of immunity than killed vaccines." (Schultz (2003), quoted by Baumgardner)[xxiii] In 1978, "an ideal vaccination program" was recommended [Schultz & Scott; Ref. 1 of the original AAHA 2003 report]...Also, in 1998, recommendations from a group of canine vaccine experts were published [Schultz; Ref. 3 of the original AAHA 2003 report]. They recommended revaccination with canine core vaccines no more than once every 3 years following initial booster revaccination at 1 year of age...but misunderstandings,

[28] "We tend to make immunology black and white, but there is almost nothing black or white about it...I also place some blame on my colleagues in industry, especially those who market vaccines. They have done a much better job of educating practitioners to their way of selling vaccines than immunologists have done in teaching the facts about vaccine-induced immunity. (Schultz, 2002)

	misinformation, and the conservative nature of the profession have slowed adoption of these protocols advocating decreased frequency of revaccination… (American Animal Hospital Association (AAHA)/Canine Vaccine Task Force, 2003)[xxiv] For many veterinary practitioners canine vaccination programs have been 'practice management tools' rather than medical procedures. Thus, it is not surprising that attempts to change the vaccines and vaccination programs based on scientific information have created great controversy and unique methods of resistance to the proposed changes have been and are being developed…[one reason] for the reluctance to change current vaccination programs is many practitioners really don't understand the principles of vaccinal immunity……I have also been told by many practitioners that 'I believe the duration of immunity for some vaccines like distemper, parvovirus and hepatitis is many years, but **until I find another way to get the client into my office on a regular basis I'm going to keep recommending vaccines annually**." (Schultz, 2007)[xxv] Since the vaccines we inject are neither completely safe nor provided for free, I think we need to be convinced that each vaccine we administer can be expected to do something directly beneficial for the recipient and, by extension, for the client who is paying for it. Unfortunately [!] **there is strong and mounting evidence that most vaccinations administered to adult dogs and cats serve no beneficial 'immunological' purpose whatsoever**. (Squires, 2009)[xxvi] The emphasis from current recommendations is on the development of a new way of thinking about vaccination…All of these concepts are enshrined in the 'annual health check'. This approach encourages veterinarians to move away from promoting an 'annual vaccination booster' to an 'annual health check' that involves a more substantial consultation with the client…This change in emphasis does not mean a reduction in practice income – simply a different way of charging for professional services. (Day, 2010)[xxvii] Of all veterinary activities, vaccination probably stands alone in that its result is not systematically evaluated – certainly not by the vaccinating practitioner. The 'shoot-and-trust' principle reigns, and trust is based on the claims of producers and on the registration files…vaccination/challenge experiments have governed the DOI discussion… so there would be no need to change a cherished habit… (Horzinek + Thiry, 2009)[xxviii]

NOTE also the British regulator's explanation/justification of the term 'science' as it applies to commercial versus academic 'argument':
"When you compare the [regulator] *authorised information for use of an individual vaccine* [product label] *to the guidance on vaccination within clinical guidelines it is important to take into account…(B)oth sets of information are science based, however, the MOTIVATIONS THAT **GENERATE THE SCIENCE** BEHIND THOSE DOCUMENTS ARE DIFFERENT."* (Anna-Maria Brady, Veterinary Medicines Directorate U.K., response to Elizabeth Hart (Adelaide), May 2011) (My emphasis)
http://www.vmd.defra.gov.uk/pdf/vaccines_VMD_Letter_110511.pdf

Table 6 – Misrepresentation of reasons for 'extended inter-vaccination intervals'

Owner & Breeder Guidelines (2010) DRIVERS FOR CHANGE IN VACCINATION PROTOCOLS	Publications relating to **'Drivers for change'**
No single adverse event like FISS [Feline Injection Site Sarcoma] was the driver for the development of canine vaccination guidelines. Instead, it was growing awareness that many vaccines provide a long duration of immunity (DOI) and therefore did not need to be administered yearly.	**The recognition of feline injection site sarcomas over 20 years ago had provided 'one of the first inklings that vaccination may have some safety issues related to it'...An example in dogs was the triggering of a spectrum of immune-mediated disorders... analysis of data on the frequency of adverse reactions had been one driver for change in vaccination protocols...** (Day, 2011)[xxix] A series of events have however caused us to re-examine this practice [annual booster vaccination] and develop new vaccination recommendations for small companion animals… This re-evaluation was largely triggered by the first reports of feline injection site sarcoma (FISS) in the early 1990s coupled with **reports that vaccination might be a trigger for canine immune-mediated haemolytic anaemia (IMHA) from the mid 1990s**…***These events were the 'driver' for the changes in companion animal vaccination that have been introduced over the past 10 years.*** (Day, 2010)[xxx] We now recognize that vaccines (particularly multicomponent, modified live products) appear to be able to trigger a range of immune-mediated and autoimmune diseases. (Day, 2010)[xxxi] IMHA, or AIHA (autoimmune haemolytic anemia) belongs to a "clinically significant group of disorders" for which Duval & Giger (1996)[xxxii] demonstrated **"[*A*] *significant association between recent vaccination and the development of idiopathic IMHA...*"** (Day, 1999)[xxxiii] It is by no means a surprise that such an association might occur – a stimulus to the immune response of some sort is thought to be necessary to trigger this (IMHA) and other immune-mediated diseases. (BSAVA, 1997)[xxxiv] There is **real concern that vaccines may predispose certain genetically susceptible individuals to immune-mediated disease**…The more antigens we administer, the higher the potential for hypersensitivity… **hypersensitivities are natural parts of the immune response**, but they cause a certain amount of tissue damage…**In many cases it is impossible to show a direct connection between the damage and a vaccine, since it is the accumulation of many antigens over many years that results in clinically evident disease.** (Schultz, 1995)[xxxv] I believe that repeated injections of immunogenic proteins can be potentially harmful. I work on the internal medicine service in a busy referral teaching hospital. My colleagues and I are all concerned about the **inordinate number of cases we see of autoimmune disease like immune-mediated hemolytic anemia, thrombo-cytopenia, and polyarthritis** – more than ever before. (Ford, 2002)[xxxvi]

	I think we underestimate how many problems overvaccination may be causing…we think overvaccination probably causes immunologic problems or at least contributes to the immunologic problems. **I think there are a vast number of** other **diseases** – immunologic or degenerative diseases such as atopy, chronic allergies, asthma, and other airway diseases – **that are exaggerated by, caused by, or stimulated by overvaccination**. (Olson, 2002)[xxxvii] …there are a proportion of cases in which the **immune-mediated blood dyscrasia is clearly secondary to an underlying cause, particularly…Recent administration of a vaccine (polyvalent, modified-live, adjuvanted vaccines are generally incriminated)** (Day, 2004)[xxxviii] …**the number of disease syndromes that are recognised as having an autoimmune basis is growing**… (Day, 2004/2010)[xxxix] **The concept that vaccination might trigger autoimmunity in the dog is not new**. It was recognised in the **early 1970s that distemper virus infection and distemper vaccination could result in thrombocytopenia in dogs**, that at least in part likely had an immune-mediated basis. **The introduction of parvovirus vaccination in the late 1970s was associated with recognition that some vaccinated dogs developed IMHA and a link was proposed between these events.** (Day, 2006)[xl]

Table 7 – Misrepresentation of KNOWN and SUSPECTED immune system dysfunction due to unnecessary vaccination and unsubstantiated claims regarding adverse event rates

Owner & Breeder Guidelines (2010) ADVERSE REACTIONS	Publications relating to **Adverse Event Potential and Reporting**
Of course adverse reactions do occasionally occur following vaccination of dogs…While these reactions [(relatively mild allergic events)] are readily related to preceding vaccine administration, it is more difficult to define the adverse reactions that occur a day, a week or months after vaccination. Good scientific data on the prevalence of vaccine reactions in man and animals simply do not exist. Even when the adverse reaction occurs shortly after vaccination there are many who fail to recognize that the vaccine caused the reaction. Certain adverse vaccine reactions are not observed until days, weeks or even months and years after vaccination or revaccination. The autoimmune disorders…may not develop for years after being triggered by vaccines. …every type of vaccine can and does have the ability to trigger an immunological reaction in high risk animals. Unfortunately, at times vaccines and vaccinations are often mistakenly blamed for causing or triggering various diseases and disorders when the vaccines are not responsible…With many of the adverse reactions or disorders it is difficult or impossible to know if the vaccines and not something else caused the problem, because there are often multiple causes. …on rare occasions, vaccination…might lead to an unexpected clinical reaction.	A wide range of adverse consequences of vaccination has now been recognised in companion animal species…Some of these…are likely to directly relate to the activation of immune and inflammatory pathways by the process of parenteral vaccination…**Canine vaccines have** (also) **been shown to have a relatively high antigenic content of bovine serum albumin and bovine IgG*[1] --- many orders the magnitude greater than the level recommended by the World Health Organisation for human vaccines**..It has been suggested that these IgE responses might act as a risk factor for the subsequent development of atopic disease or dietary hyper-sensitivity… (Day, 2006)[xli] [see Note *[1] below] …we should not lose sight of the fact that at the same time **we are challenging a naïve and evolving immune system and the full impact of such challenge might not be appreciated**. Vaccination of adult animals does lead to alterations in immune parameters in the post-vaccinal period (Strasser et al., 2003) and **at least in a small proportion of neonatal animals, vaccination may potentially lead to one of a wide array of possible adverse consequences**. (Day, 2007)[xlii] The current [1998] perception among many practitioners is that adverse vaccine reactions in dogs and cats are more common now than they were 10 or more years ago, especially in cats…Vaccines are known to trigger autoimmune disease in genetically susceptible animals and people…Postvaccination neurologic disorders, immunosuppression and other problems have been demonstrated to occur after administration of canine and feline vaccines. These adverse reactions can range from mild, self-limiting illness to chronic disease and death… It is apparent that the USDA, U.S. Pharmacopoeia **reporting system, and the companies making the vaccines do not in general have a high number of adverse reactions reported to them. This is surprising** when you consider the total number of vaccine doses sold. (Schultz, 1998)[xliii] …**adverse reactions, and other unexpected events are a reality with biological products**. The major safety problems reported are injection site reactions, systemic reactions, allergic reactions, immunosuppression, inadequate inactivation, residual pathogenicity, genetic recombinations, and contaminations. (Martinod, **PFIZER** Central Research U.S.A. 1999)[xliv] I believe that repeated injections of immunogenic proteins can potentially be harmful. I work on the internal medicines service in a busy referral teaching hospital. My colleagues and I are all concerned about the **inordinate number of cases** we see **of autoimmune disease like immune-mediated haemolytic anemia,**

	thrombocytopenia, and polyarthritis – more than ever before. (Ford, 2002)[xlv] I think we underestimate how many problems overvaccination may be causing…we think overvaccination probably causes immunologic problems or at least contributes to immunologic problems. I think **there are a vast number of other diseases** – immunologic or degenerative diseases such as atopy, chronic allergies, asthma, and other airway diseases – **that are exaggerated by, caused by, or stimulated by overvaccination**. (Olsen, 2002)[xlvi] Incidence rates and relative risks for specific VAAEs [vaccine-associated adverse events] cannot be calculated because of the lack of information about the overall vaccinated population (denominator data or the population at risk of a VAAE). (Moore et al, 2005)[xlvii] [see Note *[2] extract from published paper below] …it is impossible to provide an accurate summary of the prevalence and nature of such [adverse] reactions due to the recognized limitations of the passive surveillance schemes that currently operate in most countries. (Day, 2007)[xlviii] **The VGG recognises that <u>there is gross under-reporting of vaccine-associated adverse events</u>[29] which impedes knowledge of the ongoing safety of these products.** (WSAVA VGG (Day, Schultz, Horzinek), 2007)[xlix]

NOTES:

*[1] Extract from
Safety Data Sheet for Virbac Canigen $DH_{A2}PPi$
http://www.virbac.co.nz/p-virbacnzpuben/pdf/MSDS/Canigen_DHA2PPi.pdf
accessed 7-5-2011

40% antigen + 60% culture media

Composition / Information on Ingredients

Product components:	Chemical Entity:	CAS Number:	Proportion:
	40% Volume		
	Canine adenovirus type 2 (attenuated	-	10^4TCID_{50}
	Canine distemper virus (attenuated)	-	10^3TCID_{50}
	Canine parainfluenze virus (attenuated)	-	10^5TCID_{50}
	Canine parvovirus (attenuated)	-	10^5TCID_{50}
	A culture medium determined to be non-hazardous	-	60%

[29] A sentiment shared by COBTA (2001), VPC (2001), and AAHA (2003)

*[2] The Guidelines propose a genetic link, and breed and/or familial susceptibility, however fail to shed any light, whatsoever, on the breeds known for their propensity to autoimmunity. The 2005 study (by Moore et al) alluded to in the Guidelines (but no reference provided) gives some insight of documented adverse reactions in different breeds of dogs within 3 days after vaccination:

> *"**Results**…The VAAE rate decreased significantly as body weight increased [121.7/10'000 in Dachshund; 30.2/10'000 in Golden Retriever; 13/10'000 in German Shepherd and Rottweiler]. Risk was 27% to 38% greater for neutered versus sexually intact dogs and 35% to 64% greater for dogs approximately 1 to 3 years old versus 2 to 9 months old. The risk of a VAAE significantly increased as the number of vaccine doses administered per office visit increased; each additional vaccine significantly increased risk of an adverse event by 27% in dogs ≤10 kg and 12% in dogs >10 kg."* (Moore et al, 2005)

Given the target audience of the WSAVA Guidelines, i.e. owners and **breeders** of dogs, the omission of such information is inexcusable.

Table 8 – Distortion of state-of-the-art vaccine 'technology' and licensing criteria, misleading the consumer of veterinary services

"…the reality with immune responses and the licensing process is that vaccines tend to work at levels that are considerably less than 100%" (Hustead, Fort Dodge, 2001)[l]

Owner & Breeder Guidelines (2010)	Published information in the veterinary press and in the public domain
…the introduction of higher potency vaccines has led to higher levels of MDA that takes longer to fully degrade to permit an endogenous immune response.	…The vaccines that we use for dogs and cats - a lot of them are actually very old. They're 40 year old products. But they still work incredibly well. (Day, 2010)[li] Conventional vaccines used in companion animal medicine for the past 50 years have consisted predominantly of killed or attenuated live (modified-live) bacteria or viruses. Ironically, the science behind these vaccines is not significantly different from that used by Jenner 200 years ago… (Day, 2006)[lii] The adjuvants currently used in our vaccines reflect very old technology… (Day, 2006)[liii] It's important to note that the recommendations of the AAHA Canine Vaccine Task Force for triennial booster administration are based on data derived from vaccines that were on the market 5 years ago. **Independent studies support the fact that extended durations of immunity (protection) against canine distemper, parvovirus, and adenovirus-2 are provided by all of the licensed (core) vaccines that were on the market between 2000 and 2003**. Any implication that a "3-year vaccine" must be used when adhering to current vaccination recommendations is wrong…and **misrepresents the intent of the 2006 AAHA Canine Vaccine Guidelines**…It is important to understand that **the triennial booster recommendations** in the 2006 Canine Vaccine Guidelines have been **made without regard for** a specific vaccine manufacturer, a specific vaccine, or **any product sold as a "3-year" vaccine. (**Ford, 2006)[liv] At present, it should be understood that rabies vaccines are the only products for which the USDA require minimum DOI studies for licensing purposes. Currently, USDA approval is not required for the recommendation of extended DOI vaccination programs for any other vaccine. Thus, a veterinarian or animal owner can administer any vaccines other than rabies as often or as infrequently as needed or desired regardless of whether minimum DOI studies have been performed or recognised by the USDA. Therefore, all USDA licensed canine and feline vaccines can legally be used to meet the extended interval guidelines recommended by AAHA, AAFP… (Schultz, 2006)[lv] Minimum duration of immunity studies are required for rabies vaccines and products containing "new product fractions". A "new product fraction" is an antigen that was not commercially available at the time the efficacy guidelines were published on May 12, 1995. **Duration of immunity studies are not required to support label**

	revaccination recommendations for all current and future vaccine products containing many commonly used canine and feline antigens, including rhinotracheitis/calicivirus/panleukopenia (FVRCP), chlamydia, and feline leukemia virus (FeLV) for cats and distemper, adenovirus (canine hepatitis), leptospira, parainfluenza, parvovirus, and coronavirus for dogs. (E. Kathryn Mayer/US Pharmacopoeia, 2001)[lvi] To overcome the period of maternal antibody blockade, manufacturers have raised the titres or lowered their serial passage. (Greene, Schultz & Ford, 2001)[lvii]

NOTES:
In Australia, the national regulator APVMA approved extended "DOI" for the existing Protech vaccines and subsequently registered Duramune Adult as a repack of Protech in 2005 (Fort Dodge Animal Health, now Pfizer but, in Australia, divested to Boehringer Ingelheim). The vaccine strains and titres for CDV and CPV-2, published in the APVMA Gazette in April and July 2005 respectively, were identical, as were the study documents (using a commercial, 1999 batch of MLV Duramune polyvalent vaccine) for both products, released separately under the Freedom of Information Act in 2007.

Similar 'developments' for Intervet vaccines containing CPV-2 strain 154 are documented:

- The patented Intervet CPV strain 154 has been included in commercial MLV vaccines since at least January 1994 (see extract from trademark documentation below), and the trading name of the MLV vaccine including this strain was Progard (see published references and paper (Hoskins et al) below)
- The label for the MLV polyvalent vaccine sold in The Philippines confirms: *"In the USA Nobivac DHPPi is sold as Progard 5 (Progard 7 in combination with Nobivac Lepto, and Progard 8 in combination with Nobivac LC)."* http://www.msd-animal-health.ph/products/131_118596/productdetails_131_118760.aspx accessed 7-Jan 2012
- After carrying out the 3-year DOI study of Progard, the vaccine was renamed to Continuum.
- In 2011, MSD (now owner of Intervet/Schering-Plough) announced the name change from Continuum to Nobivac.

Thus, it follows that, as far as the CPV-2 virus strain and titration is concerned, the product now known as Nobivac is the same as that previously marketed as Progard. The latter was a traditional "annual" vaccine for which a minimum 3-year study was carried out (refer pages 3/4 of cover letter)

According to two studies by Larson + Schultz, published in 1996[lviii] and 1997[lix], high-titre vaccines are those that contain a **minimum CPV antigen mass of $10^{6.7}$ $TCID_{50}$**. Such products, as the 1996 study confirms, have been on the market since the 1990s: *"High-titer canine parvovirus (CPV) vaccines, which were first used in Europe, have recently been introduced in North America. These vaccines are intended for use in the one segment of the canine population that continues to be vulnerable to clinical CPV enteritis – **puppies four to 18 weeks of age. Pups from immune bitches carry maternally derived antibodies that interfere with active immunization**..."* (emphasis added)

It stands to reason that, for a vaccine to be deemed protective, it needs to be immunogenic --- the dire consequences of using non-immunogenic vaccines were highlighted by the 1994/95 Finland CDV outbreak. Looking at the data submitted in support of the patent application for the CPV-2 strain 154, contained in the Intervet MLV core vaccines, the claimed "high titre" seems to be in fact the MINIMUM IMMUNISING DOSE which satisfied the manufacturer's claim that the vaccine is protective in 12-week-old puppies with MDA:

United States Patent [19]
Welsh

[11] **Patent Number:** **4,810,494**
[45] **Date of Patent:** **Mar. 7, 1989**

The present invention concerns a vaccine comprising a novel canine parvovirus strain and having the property of being able to break through the maternally derived antibody levels persistent in 9–12 week old pups, and even to immunize the majority of pups at the age of 6 weeks in the presence of maternally derived antibodies.

Downloaded from http://www.freepatentsonline.com/4810494.html last accessed 24.01.2012

dose/pup (in tcid/50)	dog no.	MDA at vaccination (HI titre)	response
GROUP I: Nobivac PC			
10/6	1	16	no
	2	32	no
	3	16	yes
10/7	4	16	yes
	5	8	yes
	6	32	yes
10/8	7	16	yes
	8	32	yes
	9	32	yes

2 out of 3 puppies failed to respond to vaccination

CPV-2/154 antigen level contained in Nobivac (and Canigen UK) vaccines, according to authorized product labels in the UK, Ireland, Australia, New Zealand, Japan, Asia, Austria, Switzerland and Germany.*

**** "Nobivac/Continuum canine vaccines are made at a limited number of Intervet manufacturing sites around the world...They are all made from the same seed material and to the same specification."*** **(Marketing Manager Intervet Australia, personal correspondence, Nov 2006)**

The 'efficacy claim' on the label is *"to reduce clinical signs of disease"* (note: not INFECTION); yet, Intervet's latest advertising campaign in Australia claims STERILISING IMMUNITY (advertisement in *The Veterinarian* magazine, November 2011, excerpt below):

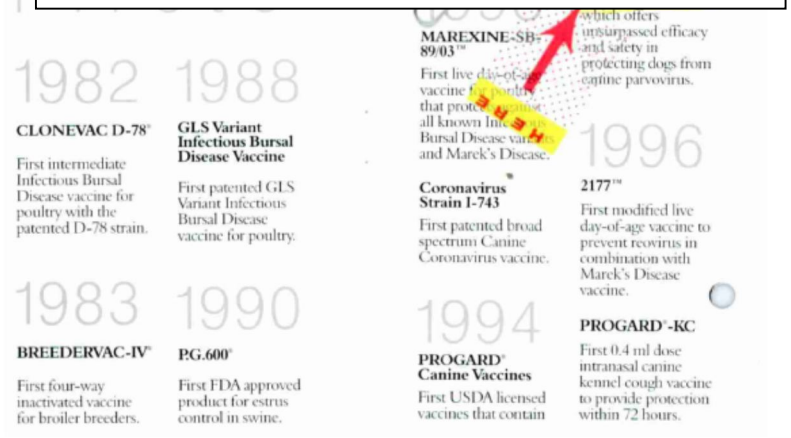
Unlike other canine parvovirus (CPV) vaccines, ONLY Nobivac offers published evidence of sterilising immunity to help create an uncontaminated environment for dogs.[1-5]

References: 1. Hoskins JD *et al* (1995) Challenge Trial of a New Attenuated Canine Parvovirus Vaccine. *Journal of Veterinary Internal Medicine* 9:197. 2. Greenwood NM *et al* (1995) Comparison of isolates of canine parvovirus by restriction enzyme analysis, and vaccine efficacy against field strains. *Veterinary Record* 136: 63-67. 3. Gore T *et al* (2005) Three-year Duration of Immunity in Dogs Following Vaccination Against Canine Adenovirus Type-1, Canine Parvovirus, and Canine Distemper Virus. *Veterinary Therapeutics* 6 (1): 5-14. 4. Spibey N *et al* (2007) Canine parvovirus type 2 vaccine protects against virulent challenge with type 2c virus. *Veterinary Microbiology* 128: 48-55. 5. Larson LJ and Schultz R (2008) Do two current canine parvovirus type 2 and 2b vaccines provide protection against the new type 2c variant? *Veterinary Therapeutics* 9 (2): 94-101.

Reference 1 = Hoskins et al: ABSTRACT in ACVIM, 1995
Note: The 1997 publication in *Canine Practice, Vol. 22, No. 4, July/August 1997 pp29-31*, by the same authors, reports on the testing of **Progard** in Rottweiler pups, a breed recognised for poorly responding to CPV vaccination.

Extracts from documents retrieved from US Patent and Trademark Office: http://tarr.uspto.gov/servlet/tarr?regser=serial&entry=75085863 accessed 5-Jan-2012

Extract from Intervet Product Guide, submitted in support of trademark application



Int. Cl.: 5

Prior U.S. Cls.: 6, 18, 44, 46, 51, and 52

Reg. No. 2,182,700

United States Patent and Trademark Office

Registered Aug. 18, 1998

TRADEMARK
PRINCIPAL REGISTER

CPV STRAIN 154

INTERVET, INC. (DELAWARE CORPORATION)
405 STATE STREET
MILLSBORO, DE 19966 INTERVET, INC. (DELAWARE CORPORATION)

405 STATE STREET
MILLSBORO, DE 19966

FOR: VETERINARY PREPARATIONS, NAMELY, A CANINE VACCINE, IN CLASS 5 (U.S. CLS. 6, 18, 44, 46, 51 AND 52).

FIRST USE 1-0-1994; IN COMMERCE 1-0-1994.

NO CLAIM IS MADE TO THE EXCLUSIVE RIGHT TO USE "CPV STRAIN", APART FROM THE MARK AS SHOWN.

SN 75-085,863, FILED 4-9-1996.

BALDEV SARAI, EXAMINING ATTORNEY

Intervet - Media Release 2005

Intervet Introduces Continuum™ DAP,
the First and Only Canine Vaccine Approved by the USDA
that Provides Three-Year Duration-of-Immunity

"Of course, the use of fewer vaccines decreases the risk of any vaccine-related reactions." (Karen Duncan, DVM, Intervet Inc.)

Baltimore, MD - March 20, 2005 – Intervet Inc., a leading manufacturer of animal health vaccines, introduced today Continuum™ DAP, the first and only canine vaccine approved by the United States Department of Agriculture (USDA) for three-year duration-of-immunity (DOI) against DAP (distemper, adenovirus, parvovirus).

The Continuum™ DAP vaccine contains three attenuated strains: high-titered Onderstepoort strain of CDV; Manhattan strain of CAV-2, which confers cross-protection against canine infectious hepatitis caused by CAV-1 without the adverse reactions associated with CAV-1; and the high-titered patented CPV STRAIN 154® of canine origin.

levels. At 36 months post-vaccination, the average titer for CAV-2 was found to be 1:357, for CDV was 1:193, and for CPV was 1:237. The findings established that the modified-live viruses in Continuum™ DAP protect against virulent CAV-1, CDV, and CPV challenges in dogs seven weeks of age or older for a minimum of three years following second vaccination.

Of interest also is that the median titres reported by Intervet appear to be well above the threshold correlated with protection, e.g. for CPV-2, a titre of 1:80 is deemed protective!

Table 9 - Misinformation on safety and efficacy of non-core vaccines (other than Rabies, as Australia is rabies-free)

Owner & Breeder Guidelines (2010)	Publications
It is...<u>INCUMBENT</u> ON THE OWNER to discuss the non-core (optional) vaccines with their veterinarian to determine the risks and benefits of all the non-core vaccines that are available.	Several **vaccines for dogs (and cats) have been licensed that have poor or questionable efficacy**; yet they continue to be produced and promoted, for example *Leptospira* bacterins, some coronavirus (CCV) vaccines...**New or "improved" vaccines are introduced almost yearly, yet <u>even perfunctory examination reveals a sparse amount of data that often overstates claims for a particular product</u>.** (Carmichael, 1999)[lx] ...allergic reactions may occur more commonly when inactivated coronaviral vaccines are combined with leptospiral bacterins...CCV [canine coronavirus] does not cause disease in adult dogs...The routine and frequent use of CCV vaccine in dogs is difficult to rationalize...CCV vaccine...has been identified...as a vaccine that, quite simply, is not needed. (Greene, Schultz & Ford, 2001)[lxi] ...modified-live vaccines do have limited ability to cause signs of infection...These signs...on occasion (such as...intranasal *Bordetella bronchispetica* vaccination) may actually cause significant clinical disease requiring treatment. (Day, 2006)[lxii] As inactivated bacterins, leptospiral vaccines have always had the tendency to cause allergenic reactions, especially when they have been combined with other adjuvanted agents. (Greene, 2006)[lxiii] Considering the **low efficacy [of leptospira vaccines], the adverse event rate and the minimal risk for leptospirosis**...; ...**kennel cough is not a vaccine preventable disease** because of the complex factors associated with this disease. Furthermore, this is often a mild to moderate self limiting disease. I refer to it as the 'Canine Cold.'... To date **no one has demonstrated a benefit for coronavirus vaccine**... (Schultz, 2007)[lxiv] Canine non-core vaccines should be used where there is proven geographical prevalence of a specific infection...In many countries, *Leptospira* vaccines are routinely administered to all dogs, often on the basis of little more than anecdotal evidence of local disease risk. Adjuvanted *Leptospira* vaccines are the most reactogenic of canine products and carry the highest risk of inducing hypersensitivity reactions in small breed dogs. (Day, 2010)[lxv] Intranasal Bb/CPiV/CAV-2 estimated efficacy 60 – 70%; Leptospira bacterins: one of the most reactogenic canine vaccines; estimated efficacy 60 to 90%, depending on serovar. (Schultz, 2011)[lxvi]

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