



ASSURING THE SAFETY, QUALITY AND EFFICACY  
OF VETERINARY MEDICINES

From the Chief Executive

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Dear Ms O'Driscoll

Thank you for your letter dated 21 December 2010. Our exchanges are now going over the same ground and therefore I have limited my response to critical areas rather than needlessly repeat information that has been already been provided. I must apologise for being slow in responding but you have graciously recognised the investment in resource that these exchanges require.

Your letter repeats your views on how the VMD should address what CHC regard as 'redundant, useless, one year MLV vaccines' and supports this with an argument claiming to address what CHC describes as the 'risk:benefit ratio'. Fundamentally, this superficial assessment is flawed for a number of reasons. The main benefit of any vaccine, whatever its duration of immunity (perceived or actual), is the induction of an immune response and this benefit can only be assessed taking into account the individual's immune status at the time of vaccination. Your risk:benefit evaluation focuses entirely on the revaccination of animals. However, all authorised vaccines have a value even if that value is perceived as being limited to a primary course of vaccinations an animal receives. I therefore repeat my previous comment - the most qualified person to assess what the animal needs is the veterinary surgeon, engaged by the owner. The veterinary surgeon and the owner should discuss the vaccination of a given animal and agree how to proceed. The VMD as a medicines regulatory body does not interfere in the relationship between the veterinary surgeon and their client.

In answer to your question on redundancy as a valid justification for a regulatory review of an authorised veterinary medicine, I can confirm there is a 'sunset clause' in the legislation that allows for the removal of medicines that have not been marketed for a significant period of time but this clearly does not apply to the case at hand. Other than this, redundancy in itself is not a justification for a regulatory review. The only reason for re-opening the benefit:risk assessment for a medicine (including vaccines) is evidence to suggest a change in the safety, quality or efficacy of the product. Such changes can be triggered as a result of modifications to the



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INVESTOR IN PEOPLE

manufacture of the product, a rising or atypical trend of a particular adverse reaction or evidence that the vaccine is failing to achieve its level of expected efficacy. As far as I am aware there is no evidence that the vaccines defined by the CHC as 'one year MLV vaccines' are responsible for any difference in suspected adverse reaction reporting when compared to other vaccines with longer durations of immunity recorded in their Summary of Product Characteristics. In the absence of evidence the VMD would not have a regulatory justification to act in the way you ask.

We have noted your comments on the JAVMA published report on Post-marketing Surveillance of Rabies Vaccines and have noted your comments based on a number of assumptions and extrapolations. In my opinion the extrapolations you have applied are overly simplistic to the extent the conclusions reached are unreliable. To illustrate this point, to extrapolate results for rabies vaccines to other vaccines is not scientifically valid, neither is the assumption that the same level of reporting applies to the USA and UK environment. In both cases the variables in the underlying factors would dramatically increase the risk of error in your conclusions. In addition, assuming that the claimed average level of 1% reporting of suspected adverse reactions can be equally applied to all types of reports and all products is also flawed. The more serious the reaction the more likely it is to be reported and some types of product are reported more frequently than others (e.g. Suspected Adverse Reactions (SARs) to canine medicines are more likely to be reported than for poultry medications). However, even if you were to rely upon your extrapolated figures to estimate the incidence rate of SARs in the UK it translates into an overall incidence rate of 0.8%. Given that the vast majority of SARs are transitory and do not lead to life threatening illness this confirms the VMD's assertion that serious adverse reactions to canine vaccines are very low.

I challenge your view that I have 'passed-off' under-reporting of SARs and in fact the VMD makes every effort to increase the level of reports we receive. Nevertheless, in focusing on the under-reporting of SARs, the fundamental point of pharmacovigilance is ignored, which I have tried and clearly failed to explain previously. Pharmacovigilance is an analysis of trends in the reports rather than the calculation of incidence rates. Having said this, a significant changing trend in incidence will act as a trigger for further assessment. Therefore, VMD can agree with the WSAVA Guidelines that under-reporting of SARs impedes knowledge of the ongoing safety of these products but this does not make the surveillance of the reports received valueless, nor does it invalidate the observation of trends in incidence rates as a measure. Incidence rates in themselves may also be used as trigger level for further investigation and the setting of a trigger level can take account of under-reporting. There is therefore no bias on either my own or the VMD's behalf and the external scrutiny we receive from the experts on the Veterinary Product's Committee helps ensure this is validated. Despite the drawbacks of the system, hard evidence is always preferable to anecdotal reports that do not allow the underlying facts to be subjected to detailed scrutiny.

I appreciate your confirmation that, despite your stated misgivings, the UK adverse reaction reporting scheme is recommended by the CHC, unfortunately your adverse comments in the past and perusal of your website gives no indication of this positive move. The underlying EU legislation requires the VMD to develop a database and our SAR reports are automatically transferred to the Eudravigilance (European) database held at the EMA. The VMD has recently introduced an on-line capability to report SARs.

In assessing the impact of any adverse event and given the overwhelming benefit vaccines provide for the pet animal, we must be very certain that any action to mitigate against known adverse reactions is proportionate and does not adversely compromise the future health of animals in general.

You persist in assuming the VMD can extend its regulatory role beyond the Veterinary Medicines Regulations. Let me state quite clearly:

- The cost of vaccination advice from a veterinary surgeon is a contract between the animal owner and the veterinary surgeon. The regulatory process takes no consideration of cost into account. It is not relevant to the regulation of veterinary medicines.
- The regulation of pet insurance, local dog clubs and boarding kennels are not included under the Veterinary Medicines legislation. I am sure you are aware of the publication of the Veterinary Medicine Regulations (2009) on the VMD website.
- Consent forms are a matter for the veterinary profession and are already used extensively where veterinary surgeons use medications associated with significant risks or in circumstances where the intended use is not part of the product authorisation. As this is a matter of legal indemnity for veterinary practices the VMD has no plans to become engaged in the production of consent forms.

CHC continues to misquote the science on MLV vaccines. In my view the WSAVA guideline published in 2010 is a document that provides good advice on vaccination but leaves the decision making to the veterinary surgeon. The extract below, from the WSAVA guidance, is provided for the casual reader of this correspondence and sets out the purpose of the guidance:

*In speaking to practitioner audiences about the 2007 guidelines it is clear that there is widespread confusion about their purpose. Many practitioners are initially alarmed that the recommendations appear contrary to those given on the product data sheet, and therefore feel that if they adopt guidelines recommendations, they are leaving themselves open to litigation. The distinct difference between a data sheet and guidelines document has been clearly discussed in a recent paper (Thiry and Horzinek, 2007). A data sheet (or 'summary of product characteristics'; SPC) is a legal document that forms part of the registration process for a vaccine. A data sheet will give details of the quality, safety and efficacy of*

*a product and in the case of vaccines will describe the legal DOI of the product. The legal DOI is based on experimental evidence, represents a minimum value and need not reflect the true DOI of a vaccine. Most companion animal vaccines, until recently, had a 1 year DOI and carried a recommendation for annual revaccination. The sensible response of industry to recent discussions about vaccine safety has been to increasingly license products with an 'extended' (generally 3 year) DOI. However, for most core vaccines (see below) the true DOI is likely to be considerably longer.*

*There are instances, where the guidelines may recommend a triennial vaccination with a product that still carries a 1 year licensed DOI. The simple reason for this is that the guidelines are based on **current** scientific knowledge and thinking, whereas the data sheet reflects the knowledge available at the time that the vaccine received its original license (which may be more than 20 years earlier). Consequently, guidelines advice will often differ from that given in the data sheet; however, any veterinarian may use a vaccine according to guidelines (and therefore current scientific thinking) by obtaining informed (and documented) owner consent for this deviation from legal recommendations ('off-label use'). Further confusion is often caused by company representatives who will advise, as they are legally obliged to do, that the veterinarian must adhere to the data sheet recommendation. A further point of confusion arises where veterinarians compare the recommendations given in different sets of guidelines. There are, for example, subtle differences in recommendations made in the USA and Europe that reflect differences in the opinions of local expert groups and in the perception of lifestyles of pet animals that may make them more or less exposed to infections. The VGG faces the difficult challenge of setting a middle-course through various national or regional guidelines. Its recommendations attempt to provide a balanced perspective to account for global differences in the keeping of small companion animals. In summary, veterinarians should feel comfortable about vaccinating according to the schedules given in these guidelines but should cross-reference these with local recommendations where available. Where the VGG recommendations differ from current legal requirements, the practitioner need only obtain informed client consent to provide that client, and the animal, with a current evidence-based vaccination schedule.*

In my view this adequately sets out the 'debate' CHC seeks to deny exists. I recommend to anybody interested in this subject to read the WSAVA guidance and will ensure this is made available on the VMD website. VMD will happily supply a printed copy to anybody on request.

Your criticism of the VMD leaflets is noted and will be considered when revisions are planned. One of the reasons we placed the leaflets on our website is to allow people to enlarge the print on screen to suit their needs. I can confirm these were commented upon by a consumer representative.

You raised the issue of the low level of viral contamination found in some vaccines. Quality controls on vaccines revealed the potential for contamination of some vaccines with retrovirus. New techniques allowed this to be investigated and the outcome was drawn to the attention of the European Medicines Agency (EMA). The EMA Executive Director requested a risk assessment by the Committee for Veterinary Medicinal Products. A copy of the public communication and the CVMP risk assessment is attached. This is an active, ongoing issue and the path towards a solution is not yet clear but, as you will see, the EU experts involved in the risk assessment believe the risk is low and outweighed by the benefit of vaccination. Extraneous agents in vaccines or any biologically derived material are a constant threat and this is why biologically derived materials used in the manufacture of medicines are closely monitored.

I thank you for confirming the central issue for you is 'how long the veterinary profession and vaccine industry can get away with over-vaccination'. I can therefore once more state that CHC's concern is a matter for discussion with the veterinary profession and industry. It is not a matter for the Veterinary Medicines Directorate. This does not mean the VMD is inactive in this area and the publication of our exchanges and the production of vaccination leaflets are both examples of how the Agency has sought to ensure the culture shift, that even WSAVA recognises is necessary to achieve its aims, can be progressed.

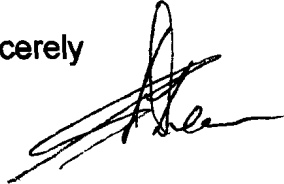
Once again I am disappointed that rather than retract your derogatory comments about myself and others you persist in stating unsupported allegations. I will repeat once again for the benefit of those who might read these exchanges I have not taken part in industry veterinary vaccine events, neither have I attended PR launches (whatever they may be) and have not assisted the promotion of any specific veterinary medicine. You are quite correct that any member of the public may question the impartiality of a Civil Servant but where allegations are made I believe it is my right to ask for justification of your assertions. To date you have not provided any evidence of inappropriate behaviour on the part of my staff or myself. I do not believe I have misunderstood your reasons for raising this issue and assure you this is not being taken personally. It is important for the public to be re-assured of Civil Servants' impartiality and anybody attempting to undermine this assurance in respect of the VMD deserves to be challenged by me to provide evidence. I am asking you to provide evidence or retract your allegations.

For the benefit of others who might be misled in reading your letter or this response I would make it clear there are requirements for the VMD to demonstrate impartiality and you are quite wrong to suggest this is not the case. Staff of the VMD and the independent members that make up the VPC declare any conflicts of interest or benefit received. In the case of VMD these declarations are minimal but anybody who has a conflict of interest does not take part in work where it would provide the potential for bias.

In responding to your latest letter I have ignored many of the rhetorical questions you have asked as they do not appear to be relevant to the question at hand on the safety of veterinary vaccines. However I have attempted to answer the specific questions you have asked.

In closing you ask how you might arrange a meeting with the Secretary of State. Normally this is done through your MP.

Yours sincerely

A handwritten signature in black ink, appearing to read 'S. Dean', with a stylized flourish extending to the right.

**Professor Steve Dean**