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Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON CONCURRENT ADMINISTRATION OF IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCTS IN VIEW OF DETERMINING DAY X TO BE 14 DAYS AND CONSEQUENT REVISION OF THE SUMMARY OF PRODUCT CHARACTERISTICS GUIDELINE FOR IMMUNOLOGICALS

AGREED BY IMMUNOLOGICAL WORKING PARTY	March 2006
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END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 July 2006

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1. INTRODUCTION

The concurrent administration of veterinary vaccines is a common practice for end users. It allows a reduction of costs for the owners and less stress for animals if the products are administered at the same time. In the context of food producing animals, especially for poultry, the administration of different vaccines at regular and sometimes short intervals is a current practice in the field.

2. PROBLEM STATEMENT

The CVMP has adopted in October 2003 the guideline on requirements for concurrent administration of immunological veterinary medicinal products (EMEA/CVMP/550/02) which came into effect on April 2004. This document outlines the requirements for demonstrating the compatibility for the concurrent administration of two or more IVMPs. The concurrent administration of two or more IVMPs was defined as the administration of the products at the same time but at separate application sites. The administration at different times (at the same or separate sites) was also included in the definition. In the case of administration at different times, section 4.8 of the SPC should indicate the minimum time between administrations for which data have been submitted by the applicant in compatibility studies. It is also stated that when adequate safety and efficacy data have been generated a compatibility statement can be included under section 4.8 of the SPC.

The Guideline SPC Immunologicals (DGENTR/F/2/AW D(2002)) states that :

- When no information has been provided on the safety and efficacy from use of the product with any other products, the following wording should be included in 4.8 of the SPC:

"*No information is available on the safety and efficacy from the concurrent use of this vaccine with any other. It is therefore recommended that no other vaccines should be administered within x days before or after vaccination with the product.*" The time period should be determined on a case by case basis.

- When adequate information has been provided on the safety and efficacy from use of the product with one or more other products, the following wording could be included :

"*No information is available on the safety and efficacy from the concurrent use of this vaccine with any other except <description of tested product(s)>. It is therefore recommended that no other vaccines than these should be administered within x days before or after vaccination with the product."*

During different mutual recognition procedures a lot of discussions have occurred between Member States on the interpretation of these Guidelines.
It seems that there is a lot of confusion and some disagreement over the exact meaning of the terms 'concurrent use', 'simultaneous use' and 'combined use'.
Furthermore, as the guideline on SPC for immunological products indicates the wording included in 4.8 when no information is available, x days before or after vaccination with the product has been arbitrarily set to 14 days without scientific justification. This point has also led to a lot of discussions during MRP and at the moment, the approach is not harmonised from one procedure to another.
These problems have been identified by the VMRFG which has sent a request to the CVMP for an interpretation of the guideline (CVMP/IWP/063/04).

The guideline on concurrent use provides the requirements on the quality, safety and efficacy data to support an application for concurrent administration and this part does not need to be revised.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

- The revised Annex I indicates that if there is a compatibility statement with other immunological products in the SPC the safety and/or the efficacy of the association shall be investigated**.**

- The NfG "Requirements for concurrent administration of immunological veterinary medicinal products" states that compatibility studies should be undertaken if the concurrent use is to be sought by the applicant for inclusion in the SPC.

- It is accepted that when adequate information has been provided on the safety and efficacy, a compatibility statement can be included under section 4.8 of the SPC. The wording from the SPC Guideline could be used:

"No information is available on the safety and efficacy from the concurrent use of this vaccine with any other except <description of tested product(s)>. It is therefore recommended that no other vaccines than these should be administered within x days before or after vaccination with the product". The x days have to be defined taking into account the compatibility studies provided by the applicant as requested by the NfG "Requirements for concurrent administration of immunological veterinary medicinal products". The products shall be administered at separate sites or at separate times at the interval between vaccinations to be mentioned in the SPC.

- However when no adequate information has been provided on the safety and efficacy, two kinds of wordings are possible:

- As indicated in the SPC guideline: "*No information is available on the safety and efficacy from the concurrent use of this vaccine with any other. It is therefore recommended that no other vaccines should be administered within x days before or after vaccination with the product"*. The x days should be determined on a case-by-case basis.

Or

- If no data are available to define the x days period *"No information is available on the safety and efficacy from the concurrent use of this vaccine with any other"*.

- The mention of a period of 14 days must be omitted as there is no scientific justification.

- There is a lot of confusion and some disagreement over the exact meaning of the terms 'concurrent use', 'simultaneous use' and 'combined use'. These terms have been defined in the recent Guideline on concurrent administration. However, the end user will not necessarily have the same interpretation as the Guideline's definition of 'concurrent'. For example, in English 'concurrent' is generally taken to mean 'simultaneous'.

- Bearing this in mind it has been suggested by some Member States that the SPC should state *"Safety and efficacy data are available which demonstrate that <vaccine X> can be administered within <Y number of> minutes/days/weeks following this vaccine"*.

It would be necessary for the applicant to propose and justify a time period based on information on the mechanism of action of the vaccine, existing safety and efficacy data for the IVMP when administered alone, supporting data, etc.

4. RECOMMENDATION

Revision of the NfG "Requirements for concurrent administration of immunological veterinary medicinal products (EMEA/CVMP/550/02) – FINAL to clarify the definitions of the terms "concurrent administration", "simultaneous administration" and make them understandable by the end user. It is suggested that this revision is made in parallel with the revision of the guideline on combined veterinary vaccines as the issues are the same.
Revision of Guideline, Summary of the Product Characteristics SPC-Immunologicals in order to harmonise the approach at the European level. The revision should clarify the wording used in the SPC section 4.8 in order to avoid any misinterpretation. It should also clarify the need to define a period before or after vaccination if no data are available.

5. PROPOSED TIMETABLE

Work on first draft Oct 2006
Draft Guideline March 2007
Adopted by CVMP for consultation in June 2007

6. RESOURCE REQUIREMENTS FOR PREPARATION

Appointment of Rapporteur
Adequate time for discussion at IWP
EMEA secretariat to manage the revision of the NfGs and consultation process
Discussions at CVMP

7. IMPACT ASSESSMENT (ANTICIPATED)

- **Impact for Industry and other Interested Parties**

The revised NfGs will have significant consequences for the industry and veterinarians. For industry, it will allow the designing of studies that would be acceptable for all Member states. If the claims in section 4.8 are clear and consistent, it is expected that there will be a benefit in performing elaborated compatibility studies. For the veterinarians, the wording should not be ambiguous and lead to misinterpretation. There is a need to clearly inform the end user of the data available in the MA dossier and which support the claims in the interaction section as he can have a practical use of the product with full knowledge of the facts.

- **Impact assessment for Regulatory Authorities**

The revised NfGs should be beneficial to regulatory authorities in terms of harmonisation at national and European levels. It should avoid confusion during decentralised and mutual recognition procedures and permit the acceptance of harmonised interaction statements.

8. REFERENCES TO LITERATURE, GUIDELINES ETC

Guideline on Requirements for concurrent administration of Immunological veterinary medicinal products EMEA/CVMP/550/02 –FINAL

Notice to Applicants – Guideline, Summary Of The Product Characteristics SPC-Immunologicals. Brussels DGENTR/F/2/AW D(2002)