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Veterinary Medicines Division

Guidance for applicants requesting scientific advice

Introduction

The Scientific Advice Working Party (SAWP-V) of the Committee for Medicinal Products for Veterinary Use (CVMP) has been set up in accordance with the requirements of the legislation, with the remit of providing scientific advice on any requests forwarded to it.

Scientific advice is available to applicants including commercial enterprises, research organisations and academics to support veterinary medicinal product development. The guidance document provides an overview of the procedure to obtain scientific advice and gives guidance to applicants in preparing their request. It will enable applicants to submit requests which are in conformity with the SAWP-V requirements.

If you seek further information on any of the included topics and/or want to apply for a scientific advice pre-submission meeting please contact: VetScientificAdvice@ema.europa.eu

It should be highlighted that this document has been produced for guidance only and should be read in conjunction with applicable policies and legislation.

References and useful links

- Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004;
- Directive 2001/82/EC of the European Parliament and of the Council of November 2001;
- Mandate, objectives and rules of procedure for the CVMP Scientific Advice Working Party (SAWP-V) (EMA/CVMP/SAWP/676117/2010);
- Standard operating procedure on Scientific advice to be given by the CVMP for veterinary medicinal products (SOP/V/4016);
- Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the Agency, as amended by Council Regulation (EC) No 2743/98 as amended;
- Commission Regulation (EC) No 2049/2005 of 15 December 2005;

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Send a question via our website www.ema.europa.eu/contact

- Explanatory note on fees payable to the European Medicines Agency http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000327.jsp&mid=WC0b01ac0580024596

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1. What is the legal basis/scope for the provision of scientific advice?

According to Regulation (EC) No 726/2004 one of the tasks of the Agency is, where necessary, advising applicants on the conduct of various tests and trials necessary to demonstrate the quality, safety and efficacy of medicinal products. Article 56(3) of Regulation (EC) No 726/2004 provides that CVMP shall establish a standing working party with the sole remit of providing scientific advice to undertakings.

CVMP is responsible to give scientific advice to industry by answering specific questions based on the documentation provided by the applicant in the light of the current scientific knowledge.

CVMP gives scientific advice based on the report and recommendations of the SAWP-V on questions concerning specific issues relating to the establishment of MRLs, the quality, the safety and clinical development of veterinary medicines.

Scientific advice is restricted to purely scientific issues. It covers the whole development process and can be used to provide advice on protocols for clinical trials. National authorities throughout the EU however retain the competence to review trials on their territory and it should be remembered that there may be additional national requirements.

Regulatory aspects should be the matter of a separate request. The regulatory and administrative questions will be answered by the Agency secretariat directly (see pre-submission guidance for users of the centralised procedure http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000171.jsp&mid=WC0b01ac058002d9ab).

Scientific advice received from the Agency is valid throughout the EU, for all veterinary medicinal products irrespective of the route of authorisation (centralized or decentralized).

Applicants seeking advice under Article 56 of Council Regulation (EC) 726/2004, as amended, must note that any advice given is not binding on the Agency with regard to any future marketing authorisation application of the product concerned but will be taken into account in the evaluation of marketing authorisation application.

Advice is also provided in the form of scientific guidelines which are published on the Agency website.

2. Is my medicinal product eligible for receiving scientific advice?

Scientific advice may be requested for all veterinary medicinal products, as defined in Directive 2001/82/EC, irrespective of eligibility for the centralised procedure.

It may also be requested regarding the establishment of maximum residue limits (MRLs) for pharmacologically active substances in accordance with Regulation (EC) No 470/2009, or even in respect to the question whether a substance included in the veterinary medicinal product would be pharmacologically active or not and therefore requiring or not an MRL evaluation (in case of veterinary medicinal products intended for food-producing animals).

If applicants are established outside the European Economic Area (EEA), it is advisable to nominate a contact point within the EEA to facilitate communication between the Agency and such applicants.

3. When can an applicant request scientific advice?

Scientific advice can be requested during the initial development of the veterinary medicinal product (usually before submission of the marketing authorisation application or an application for the establishment of MRLs) or during the post authorisation phase, where guidance is needed in selection and design of tests for product development and for general advice on the design of clinical trials.

Scientific advice may be requested where a prospective applicant asks for interpretation of a scientific aspect of an existing guideline. Following the provision of scientific advice the CVMP may consider whether adjustments/modifications to existing guidelines are advisable.

In cases where an applicant chooses to deviate in their development plan from existing guidance available (whether in the form of guidelines or Ph. Eur. monographs), it is also possible to seek scientific advice from the SAWP-V, provided that a justification for such a deviation is forwarded.

4. What is the content of a scientific advice request?

The question(s) posed by the applicant should be as precise and clear as possible. Question(s) should address specific scientific issues concerning:

- quality aspects (e.g. specific issues concerning tests to be performed during the development of chemical or biotechnological products);
- safety aspects (e.g. establishment of MRLs and other safety related areas including consumer, environmental and user safety);
- clinical aspects (specific issues concerning the clinical development programme, e.g. endpoints, trial duration, target population, choice of comparator).

The questions should be prospective and concern the future development of a medicinal product. Each question should be formulated in such a way that it would be readily comprehensible when read in isolation. The applicant should indicate their intended path, along with the justification for this, taking into account guidance where available. SAWP-V will then, in the response, provide a justification for their position also whether in agreement or not with the applicants position. Questions should not ask for general advice, for example how to design a study but should show how the applicant intends to design the study and their justification for the choices made. Scientific advice is not a pre-assessment of studies already conducted to be included in a proposed marketing authorisation.

The scientific advice is restricted to scientific issues and purely regulatory aspects will therefore be dealt with separately (see pre-submission guidance for users of the centralised procedure http://www.ema.europa.eu). It is understood that scientific issues and regulatory aspects may be linked and consequently responses may be provided at the same time.

5. What is the structure of a scientific advice request?

The request (one electronic copy) should be presented as follows:

- Letter of intent (template published on the Agency website, to be submitted in Word format);
- Scientific advice request including questions and the applicant's position (template published on the Agency website, to be submitted in Word format);
- Annexes (references or other supporting data), as applicable.

The questions are ordered to address specific scientific issues (quality/safety/ MRL/ clinical development).

Each question is followed by the applicant's position and justification(s). Relevant concise justification should be provided. However, extensive amount of information from reference documents (e.g. draft study protocols or study reports) should not be included in the request, but to be provided as annexes.

The annexes can include (as applicable):

- Contract agreement when the request is submitted by a consultant on behalf of the applicant (mandatory);
- Background information (product profile, investigators' brochure);
- Information relating to the questions (e.g. relevant study protocols – as detailed as possible)
- Bibliographical data (references);
- Content of previous scientific advice received (national EU authorities, other relevant international authorities);
- Relevant guidelines (other than CVMP guidance documents).

6. When and how shall I ask for a scientific advice pre-submission meeting?

The SAWP-V emphasises the importance of meetings with applicants, especially in case of a first request for scientific advice. Scientific advice pre-submission meetings are a vital opportunity for applicants to introduce their proposed requests and to discuss the possibility of asking for scientific advice in different areas. Advice can be obtained on how to identify and present the questions to be included in the request for scientific advice with a view to obtaining satisfactory answers.

More detailed information can be provided on e.g.:

- content of the request for scientific advice (scope of questions);
- structure of the request (separating regulatory and scientific issues);
- all questions concerning the procedure for obtaining scientific advice.

Scientific advice pre-submission meetings can take place at any time during the development, but should take place at least 1-2 months prior to the anticipated date of submission.

There are no fees for these meetings.

Applicants are requested to send a meeting request together with relevant background information (issues to be discussed, draft product profile, overview of the development plan, proposed attendees etc.) to the following contact point: vetscientificadvice@ema.europa.eu

7. What are the fees for scientific advice?

Full details on all fees and fee reductions are published on the Agency website (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000327.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac0580024596

The ranges and classification that shall apply for fees for scientific advice related to veterinary medicinal products are published on the Agency's website. Fees can change and applicants are advised to check the website for current fee levels. Fees for scientific advice will be invoiced by the Agency to the applicant, at the address detailed in the letter of intent as received, once the application is started. No fees are requested prior to validation of the request.

Scientific advice fees - MUMS/limited markets and SME applicants

Free scientific advice may be granted in respect of supporting the research and development of veterinary medicinal products destined for MUMS/limited markets. Products that are classified by CVMP as intended for MUMS/limited markets with the financial incentives announced are given free scientific advice. Financial incentives are given to support products for food producing species where no alternative product is authorised for that specific indication in a particular species and the market is considered to be limited. Requests for classification may be submitted to CVMP by completing the template on the Agency website where full details of the policy and further guidance are also published. http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000175.jsp&mid=WC0b01ac058002d89f

Financial support is available to applicants with assigned SME status by EMA according to Commission Regulation (EC) No 2049/2005 of 15 December 2005, including fee reduction for scientific advice. Where an applicant could, in respect of the same fee, benefit from both reductions from MUMS and SME incentives the provisions which are most favorable to the applicant will apply. Cumulative fee reductions for a given fee and a given applicant will not be accepted. Further guidance on requesting SME registration and related incentives is available in the Agency webpage. http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000059.jsp&mid=WC0b01ac05800240cc

MUMS or SME status must be in place at the time of validation of the request for the fee incentives to apply. They cannot be applied retrospectively.

8. How and when shall I submit my scientific advice request?

If no scientific advice pre-submission meeting was requested, the SAWP-V secretariat should be notified about the intent to submit a scientific advice at least one month before the anticipated date of submission.

The deadline for receiving the complete request (structure and content according to SAWP-V requirements) at the Agency is **22 working days** before the start of the SAWP-V meeting. The date should be confirmed in advance with the SAWP-V secretariat. The SAWP-V meets on the first day of the CVMP meeting each month apart from August.

However, applicants are invited to submit, if possible, their request at an earlier stage. This enables a possible revision of the request, which might be necessary following the validation performed by the SAWP-V secretariat, before the deadline has expired.

The complete request should be forwarded to SAWP-V secretariat in the Agency electronically via email or Eudralink to the mailbox: Vetscientificadvice@ema.europa.eu

The SAWP-V secretariat will be the contact point for the applicant for any discussion concerning the validation of a request and other questions concerning the procedure for obtaining scientific advice.

9. What is the procedure for requesting parallel scientific advice with the FDA?

The applicant may request parallel scientific advice from the Agency and FDA. Requests should be made at the time of initial submission and the applicant is responsible for liaising with both authorities in relation to their individual submission dates in order that the final scientific advice may be finalised in a similar timeframe. The SAWP-V will make every effort to ensure that its timetable is followed and that the advice is given within a maximum of 90 days.

For these requests please contact the SAWP-V secretariat (Vetscientificadvice@ema.europa.eu) directly giving an overview of the request to be submitted along with the status in the other regulatory authority. The Agency will then liaise with the other regulatory authority to propose a suitable timeframe for the request. Separate reports will be provided by each regulatory authority clearly indicating where agreement has been reached and where differences remain due to regulatory/legal/other requirements in a region.

10. How shall my request be validated?

The secretariat of the SAWP-V will be in charge of validation and processing of the request. The request for scientific advice is validated with regard to:

- SAWP-V receipt of the complete request within the required deadline (see also "How and when should I submit my dossier");
- structure and content of the request (according to SAWP-V requirements).

If one of these criteria is not according to requirements set out in this guidance, the request will not be validated and shall be postponed to the next SAWP-V meeting after positive validation.

11. What is the procedure for appointment of a co-ordinator and the role of the co-ordinator?

At the start of the procedure (Day 0), SAWP-V appoints a co-ordinator. Appointments are based solely on availability of appropriate expertise and equal opportunity. Preferences regarding coordinatorship expressed by applicants cannot be taken into consideration.

The Agency has a policy on the handling of competing interests for its scientific experts**,** including committee and working parties members. Experts can only be involved in the Agency's activities if they have signed a declaration of interests form and the Agency has assessed his or her interests. All proposed members for its scientific committees have their declarations of interests screened before their formal nomination.

The appointment of rapporteurs/co-rapporteurs for subsequent centralised marketing authorisation or MRL applications is decided separately from any previous appointment of scientific advice co-ordinators. Rapporteurs are appointed by CVMP based on available expertise and experience and may or may not be the same person as the co-ordinator for the scientific advice.

Following the SAWP-V meeting, the applicant will receive a letter indicating the name of the appointed co-ordinator and the responsible secretariat contact point for correspondence.

The SAWP-V secretariat is the contact person for the applicant in all matters related to the procedure and should be informed about any direct interaction, or correspondence between the applicant and the co-ordinator.

Additional experts may be nominated by the co-ordinator and (in some cases) or by other SAWP-V members. A network of experts ensures that the adequate experts are available to participate in the scientific advice procedure, including attendance at oral explanations.

The co-ordinator is responsible for preparing the draft reports in response to the scientific advice requests taking into account the timetable for evaluation of such requests. These reports are considered working documents only and will not be released to applicants.

The co-ordinator will compile questions and comments from the SAWP-V and other CVMP Working Parties where appropriate.

The co-ordinator will propose to the SAWP-V to hold an oral explanation with the applicant if applicable and will draft the list of issues. The oral explanation will be chaired by the co-ordinator.

12. What is the procedure and timetable for providing applicants with scientific advice?

The scientific advice provided to applicants is the result of a collegial work from the co-ordinator, the SAWP-V experts, and the CVMP. The draft report is prepared by the co-ordinator and may then be submitted to relevant CVMP working parties for comments, if appropriate, and finally to the CVMP for adoption.

At the end of the validation of the request for scientific advice by the SAWP-V secretariat, the validated scientific advice request is forwarded by the SAWP-V secretariat to the SAWP-V members. The SAWP-V formally accepts the scientific advice request in the following meeting and appoints a co-ordinator from among the members of the group. The co-ordinator may appoint other experts to assist in the procedure. The timetable is agreed and the applicant will be informed of the appointment of the co-ordinator and the timetable for the procedure following the SAWP-V meeting.

Scientific advice will usually be given on a 60 days procedure. The timetable is agreed at the start of the procedure based on the complexity of the questions asked and the need to involve other working parties/experts and may be extended to 90 days. Where the applicant has requested parallel scientific advice with the FDA/other regulatory authorities, this will be taken into account in the timetable for the procedure and is more likely to be extended to 90 days.

When the draft report of the co-ordinator is discussed in the SAWP-V, the SAWP-V decides whether it is necessary to invite the applicant to provide further clarification in the form of written responses to a list of questions or in an oral explanation. In some cases SAWP-V may also decide to extend the procedure after initial discussion in the working party if further reflections on questions are needed. The secretariat will advise the applicant for the updated timetable and the procedure for an oral explanation.

After final discussion (either at day 60 or day 90 the SAWP-V adopts the scientific advice report that is the forwarded to CVMP for adoption (usually in the ongoing CVMP meeting).

The SAWP-V secretariat will forward the final scientific advice report electronically to the applicant following the CVMP meeting.

13. How do I prepare for an oral explanation?

At day 30 or day 60 of the scientific advice procedure the SAWP-V will discuss the co-ordinator's draft report. It will be decided at this stage, whether it is necessary to invite the applicant for an oral explanation.

The applicant may request an oral explanation in the initial request for scientific advice. In general such requests will be granted. However, the decision to invite the applicant will be made by the SAWP-V on a case by case basis following the identification of outstanding issues which need to be clarified by the applicant.

SAWP-V will adopt a detailed list of issues (including pertinent background information reflecting the SAWP-V discussion) to be clarified by the applicant during the oral explanation and it is sent to the applicant following the SAWP-V meeting, together with the invitation and the draft meeting agenda.

The list of questions is divided in two categories:

- issues to be dealt with as a priority during the oral explanation;
- points for clarification to be answered in writing by the applicant prior to the oral explanation.

The oral explanation will always take place at the Agency, usually at Day 61, during the SAWP-V meetings. The applicant will be informed of the exact timing 15 days before the oral explanation.

Applicants should ensure at the beginning of the scientific advice procedure, that, in case they are invited for an oral explanation, their relevant experts will be available in order to participate in such meetings. The applicant will be asked to provide a list of participants 10 days prior to the oral explanation and inform the secretariat about the technical requirements for the presentation. Applicants are requested to send to the secretariat electric versions of all relevant visual materials they intend to present no later than five working days before the meeting.

In most cases, there will be a 30-40 minute discussion with the applicant (including the presentation given by the applicant). This is usually preceded by an internal SAWP-V discussion. The presentation should focus exclusively on the outstanding issues. Applicants are advised to restrict their presentation to a maximum of 20 minutes in order to allow sufficient time for discussion with the group. Following the meeting with the applicant, the SAWP-V will further discuss the responses to draw conclusions.

The applicant will be asked to remain available in the Agency premises until the end of SAWP-V discussion in case further points (mainly procedural) have to be clarified or agreed.

14. Is the scientific advice given binding?

Applicants seeking scientific advice under Article 56(3) of Council Regulation (EEC) No 726/04 must note that any scientific advice given is not legally binding with regard to any future clinical trial approval or marketing authorisation application of the product concerned, neither to the Agency/CVMP nor to the applicant.

The answer given by the CVMP is based on the questions and documentation submitted without prejudice to evolution and state of the art developments and the subsequent opinion of the CVMP.

Furthermore, applicants should note that the advice provided is without prejudice to applicable legislation relating to the particulars and documents, which must be submitted in support of a marketing authorisation application or an application for the establishment of MRLs. It is also without prejudice to any intellectual property rights of third parties.

When providing scientific advice, the CVMP does not pre-empt the outcome of the evaluation of any subsequent marketing authorisation application or application for establishment of MRLs. However, recommendations given by the CVMP in a scientific advice procedure will be taken into account in the assessment of any future applications. Details of any scientific advice given are included in the dossier for submission of a marketing authorisation.

Advice will be given in good faith but circumstances could change especially in the case of early advice or subsequent scientific developments. In some cases, e.g. as a result of scientific developments, an alternative approach to that advised may be appropriate.

In this case applicants are recommended to request a follow up to the initial scientific advice given.

However where applicants choose not to apply the advice, they are requested to clearly justify their position in the expert report of any subsequent marketing authorisation application or application for establishment of MRLs.

Likewise, the CVMP will provide argumentation during the evaluation of the marketing authorisation application or application for establishment of MRLs when diverging from its position following the provision of scientific advice.

15. Is a clarification or a follow up to scientific advice possible?

Request for a clarification

The quality and extent of advice given will be dependent in part on the detail and clarity of the questions submitted in the original application. However, in the event that applicants feel that part of the advice provided is not readily comprehensible without further explanation, it is possible to ask for clarification. This also applies in case the applicant feels that the advice given does not reflect the request put forward by the applicant initially. This should be done in writing within 6 months after the receipt of the final scientific advice report, addressed to the secretariat. The co-ordinator will draft a reply to be endorsed by the SAWP-V and also by CVMP prior to sending the response to the applicant. The secretariat will keep a record on clarification request. There is no fee involved in this request.

Request for follow up

Applicants may ask for a "follow up" to the initial request for scientific advice.

A follow up to the initial request is any subsequent request falling within the same therapeutic indication and initial area(s) as the initial request, (area meaning quality, preclinical and/or clinical development including pharmacovigilance/risk management aspects).

Applicants may ask for a "follow up" to the initial request for scientific advice to reconsider the scientific advice or part of the scientific advice already given in the light of new information available to the applicant following completion of studies also after a marketing authorisation has been granted.

When submitting a follow up to the initial request for scientific advice, the applicant should make reference to the previous scientific advice received and highlight the issues to be considered.

The applicant will be asked to forward new information and all supporting documents in accordance with the SAWP-V requirements regarding structure and content of the scientific advice request (documents already submitted at the time of the initial request do not have to be included in the follow up request).

The applicant should submit the request for a follow up within the required deadline: receipt of request at the Agency at day 22 (three weeks before start of the SAWP-V meeting). The date should be confirmed with the SAWP-V secretariat.

The fees for follow up requests are published on the Agency website. Fees will be invoiced once the procedure has started.

The procedure (timetable) in place for provision of a follow up scientific advice follows the same as the procedure for the initial request. If necessary, the applicant will be invited for an oral explanation. The appointment of the co-ordinator for the follow up request is made independently from the appointment of the co-ordinator for the original request and therefore the co-ordinator may not be the same as for the initial request.

16. Will scientific advice be published?

Scientific advice given by the CVMP for a veterinary medicinal product is considered confidential and will not be made public. However, following each CVMP meeting, a reference to any scientific advice adopted by the Committee is published in general terms in the CVMP press release. Once a marketing authorisation has been issued by the European Commission for any veterinary medicinal product assessed under the centralised procedure an European Public Assessment Report (EPAR) is published which may contain reference to areas where scientific advice has been given and an indication of whether this advice has been followed or not.