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CHAPTER 3
COMMUNITY REFERRAL PROCEDURES
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CHAPTER 3 Community Referral Procedures

September 2007

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Legal Basis and purpose

Community pharmaceutical legislation has created a binding Community mechanism which may be invoked on the basis of the following articles:

1. Article 33 of Directive 2001/82/EC (“Mutual Recognition and Decentralised referral”)
2. Article 34 of Directive 2001/82/EC (“Divergent decision referral”)
3. Article 35 of Directive 2001/82/EC (“Community interest referral”)
4. Articles 39¹ and 40 of Directive 2001/82/EC (“Follow-up referrals”)

Whenever this binding mechanism is invoked, a scientific evaluation of the matter is undertaken by the Committee for Medicinal Products for Veterinary Use (CVMP) of the European Medicines Agency’s (EMA/Agency). These referrals lead to an opinion from which the Commission issues a single decision addressed to all Member States which is reported for information to the applicant(s) or marketing authorisation holder(s).

This chapter sets out the details for the above procedures.

¹ Referrals under Article 5(11), 6(12) or 6(13) of Regulation (EC) No 1084/2003.

REFERRALS UNDER ARTICLES 33, 34, 35, 39 AND 40 OF DIRECTIVE 2001/82/EC

1. Introduction

The specific conditions under which a referral procedure may be started and those entitled to trigger such referral differ in each of the cases and are specified in detail in sections 2 to 5.

Under certain, well-defined circumstances (where urgent action to protect human or animal health or the environment is necessary) Member States may take unilateral action whilst awaiting the outcome of a Community referral. These cases are illustrated in section 6.

The procedural elements of the referral procedure to the CVMP are laid down in Articles 36, 37 and 38 of Directive 2001/82/EC. These procedural elements are the same for all types of referrals to the CVMP and are described in section 7.

2. Article 33(4) of Directive 2001/82/EC ("Mutual Recognition and Decentralised referral")

2.1 Basic principles

If the Member States involved in a mutual recognition or decentralised procedure fail to reach an agreement within the 60-day period in the coordination group procedure of Article 33(1) to (3) of Directive 2001/82/EC, a referral according to Article 33(4) shall be triggered².

The referral shall be triggered by the reference Member State, on the grounds of potential serious risk to human or animal health or to the environment, where no agreement was reached during the coordination group procedure on the assessment report, the summary of product characteristics, or the labelling and the package leaflet, prepared by that reference Member State.

For a description of the coordination group procedure, see Chapter 2, section 5 of the Notice to Applicants. For the definition of potential serious risk to human or animal health or to the environment, the Commission has adopted a guideline, available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-6/a/vol6a_chap2_2005-11.pdf.

2.2 Can the application be withdrawn or the referral be stopped?

It is in the public interest and in the interest of the Community that questions raised on potential serious risks to human or animal health or to the environment are answered, and that all veterinary medicinal products authorised in the Community fulfil the requirements of quality, safety and efficacy.

An application for mutual recognition of a marketing authorisation or an application in the decentralised procedure may be withdrawn by the applicant(s)/marketing authorisation holder(s) at any time in any Member State.

After a potential serious risk to human or animal health or to the environment has been raised in accordance with Article 33(1) by a concerned Member State, a withdrawal of the

² Homeopathic veterinary medicinal products subject to a special simplified registration procedure foreseen in Article 17 of Directive 2001/82/EC may not be referred to the CVMP. If agreement within the veterinary coordination group procedure is not reached, national authorities are competent to decide on the registration.

application in some of the Member States will not stop the matter from being discussed within the Coordination Group (CMD(v)) and, eventually, from a referral procedure being triggered.

The referral can only be stopped if the applicant(s)/marketing authorisation holder(s) withdraws the application/authorisation in all EEA Member States.

2.3 Procedural steps leading to an Article 33 referral

If the Member States do not reach agreement in the coordination group procedure, the reference Member State will refer the matter to the Agency for the application of the procedure laid down in Articles 36, 37 and 38 of Directive 2001/82/EC.

In the referral, the reference Member State shall provide the Agency with a detailed statement of the matter(s) on which the Member States concerned have been unable to reach agreement and the reasons for their disagreement. The matter(s) referred to the Agency must be based on potential serious risk to human or animal health or to the environment and should be precise. A notification form for a referral to the CVMP/EMA is added in the Annex. The applicant/marketing authorisation holder is provided with a copy of this information. This detailed statement should focus on the following essential elements:

- i. description of the product: the latest available summary of product characteristics, labelling and package leaflet as achieved during the coordination group procedure;
- ii. description of the remaining areas of disagreement, giving a clear statement of the issues at referral, including in particular the reasons for disagreement and a proposal for question(s) to be addressed by the applicant.

In addition, the reference Member State should provide to the Agency a consolidated report addressing the following:

- i. description of the scientific discussion during the various stages of the mutual recognition/decentralised procedure between the reference Member State and concerned Member State(s), including a brief summary of the resolution of other major issues between day 0 and day 60 of the coordination group procedure and a summary of the discussions and outcomes of the coordination group procedure;
- ii. initial assessment report of the reference Member State and an updated assessment report following the coordination group procedure.

This report will be forwarded to the applicant(s)/marketing authorisation holder(s) at the start of the procedure.

As soon as the applicant(s)/marketing authorisation holder(s) is/are informed that the matter has been referred to the Agency, the applicant(s)/marketing authorisation holder(s) shall forward to the Agency a copy of the application he/they had submitted to the competent authorities of the Member States concerned, containing the information and documents referred to in Articles 12, 13, 13a, 13b, 13c or 13d and 14 of Directive 2001/82/EC.

2.4 Scope of the referral

The CVMP is called upon to issue an opinion on the concerns that, in accordance with the assessment report and product information proposed by the reference Member State, the authorisation of the veterinary medicinal product concerned might present a “potential serious risk to human or animal health or to the environment”.

The term ‘risk’ related to the use of veterinary medicinal products is defined in Directive 2001/82/EC, Article 1(19), as “any risks relating to the quality, safety or efficacy of the veterinary medicinal product as regards animal or human health” and “any risk of undesirable effects on the environment”. In addition, on the basis of Article 33(2) of Directive 2001/82/EC, the Commission has adopted a guideline to define a potential serious risk to human or animal health or to the environment, available at <http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev5.htm> .

If the CVMP is asked about “potential serious risk to human or animal health or to the environment” concerns, it may consider aspects subsequently arising during the assessment, necessary to draft the summary of product characteristics, labelling and package leaflet which will be annexed to the opinion of the CVMP and to the decision of the Commission as provided in Articles 36, 37 and 38 of Directive 2001/82/EC.

In the case of a positive outcome of the referral a summary of product characteristics, labelling and the package leaflet will be annexed to the CVMP opinion.

In cases where the assessment of the CVMP is restricted to limited parts of the summary of product characteristics, labelling and package leaflet it will be possible to have in the annex of the opinion only those parts which were subject to amendment during the referral, together with a statement that, for the remaining parts, the summary of product characteristics, labelling and package leaflet are the final versions achieved during the coordination group procedure. It is also possible that the assessment of the CVMP concludes that no modifications of the summary of product characteristics, labelling and package leaflet are needed. In such case, the annex of the opinion shall reflect that conclusion.

However, in situations where the matters referred demand intervention across several sections of the SPC a full summary of product characteristics, labelling and package leaflet will be annexed to the decision. Even in such cases, the invented names, the names of the marketing authorisation holders and the legal supply status may be different between Member States concerned.

2.5 Marketing authorisations before completion of the referral procedure

According to Article 33(6), when there is a failure to reach an agreement within the coordination group procedure, “Member States that have approved the assessment report, the draft summary of product characteristics and the labelling and package leaflet of the reference Member State may, at the request of the applicant, authorise the veterinary medicinal product without waiting for the outcome of the procedure laid down in Article 36. In that event, the authorisation granted shall be without prejudice to the outcome of that procedure.”

The summary of product characteristics, the labelling and the package leaflet to be covered by those marketing authorisations shall be the ones proposed by the reference Member State or, when these have been subject to amendments agreed within the coordination group procedure, the last version agreed therein.

3. Article 34 of Directive 2001/82/EC ("Divergent decision referral")

3.1 Basic principles

Any Member State, the Commission or the applicant/marketing authorisation holder of a particular veterinary medicinal product may trigger a referral if divergent decisions on the authorisation, suspension or revocation of a particular veterinary medicinal product have been taken by two or more Member States. The divergences are to be identified, in the notification form, in a sufficiently precise manner.

Article 34(1) of Directive 2001/82/EC may apply to all marketing authorisations which have been issued by Member States, both so-called "purely national" marketing authorisations (which have not been subject to any Community procedures) and national marketing authorisations which have been issued following a mutual recognition or decentralised procedure.

Article 34(1) may be invoked, for instance, in the following cases:

- Where a particular veterinary medicinal product has been nationally authorised in two or more Member States and the authorisations diverge;
- Where a particular veterinary medicinal product, with a national marketing authorisation in some or all the Member States, is suspended or revoked for quality, safety or efficacy reasons in some -but not all- Member States;
- Where a particular veterinary medicinal product is nationally authorised in some or all Member States and one of the authorisations is subsequently varied, introducing a divergence versus the other national authorisations.

3.2 Can the referral be stopped?

The referral can only be stopped if marketing authorisation holder(s) withdraw the concerned marketing authorisations from all EEA markets. This condition applies regardless of whether the procedure was triggered by the European Commission, a Member State or the marketing authorisation holder.

3.3 Procedural steps leading to an Article 34 referral

The referrer (Member State, applicant/marketing authorisation holder or the Commission) sends the question to the CVMP for consideration, together with a detailed explanation of the issue(s) raised. A notification form for a referral to the CVMP/EMA is provided in the Annex to this Chapter.

The divergences have to be presented and described to support the notification of the referral.

If the referrer is a Member State or the Commission, the applicant/marketing authorisation holder must be informed of the referral.

If the referrer is an applicant/marketing authorisation holder, in advance of making a referral under Article 34(1), he is recommended to have a pre-referral meeting with the EMA. Pre-referral meetings are also possible in cases where the referrer is a Member State or the Commission.

Following notification of the referral, the applicant(s)/marketing authorisation holder(s) and the Member States concerned forward to the Agency any information relevant to the referral. In particular, the applicant/ marketing authorisation holder is requested to forward copies of the relevant parts of the dossiers of the national marketing authorisations/applications in the Member States concerned.

3.4 Scope of the referral

The CVMP is called upon to issue an opinion on the area(s) of divergence amongst the national decisions, on the basis of the question referred to it relating to a particular veterinary medicinal product.

The scope of the referral is to resolve the divergences between the national decisions, and therefore this referral leads to a full harmonisation of the summary of product characteristics, labelling and package leaflet.

Certain differences may, however, remain, such as invented names, names of the marketing authorisation holders and legal supply status.

4. Article 35 of Directive 2001/82/EC ("Community interest referral")

4.1 Basic principles

Article 35 states that Member States, the Commission or the applicant(s)/marketing authorisation holder(s) of the concerned veterinary medicinal product shall trigger a referral whenever the interests of the Community are involved, before a decision is taken on a request for a marketing authorisation, or on the suspension, or revocation of a marketing authorisation or on any other variation to the terms of a marketing authorisation which appears necessary in particular to take into account pharmacovigilance information.

This referral is to be started in specific cases where the interests of the Community are involved. The expression "interest of the Community" refers particularly to the interests of human or animal health or of the environment related to veterinary medicinal products on the market in the Community in the light of quality, safety and efficacy data and to free movement of products within the Community.

Whenever a Member State or the Commission or applicant(s)/marketing authorisation holder(s) invokes Article 35, it should duly identify the relevant interests of the Community and set out how they are involved.

An Article 35 referral may concern only one veterinary medicinal product or a range or class of veterinary medicinal products (an active substance, which is present in several different veterinary medicinal products with different invented names and different marketing authorisation holders, or different active substances and veterinary medicinal products belonging to the same therapeutic class) - so-called 'class referral'.

When the referral concerns a range of veterinary medicinal products or a therapeutic class the specific provisions of Article 35(2) will apply. In this case, the legislation expressly states that the Agency/CVMP may limit the procedure to certain specific parts of the authorisation.

4.2 Can the referral be stopped?

Once the referral is triggered, the referral can only be stopped if applicant(s)/marketing authorisation holder(s) withdraw the concerned applications/authorisations from all EEA

markets. This condition applies regardless of whether the procedure was triggered by the European Commission, a Member State or the marketing authorisation holder.

4.3 Procedural steps leading to an Article 35 referral

The referrer (Member State(s), applicant(s)/marketing authorisation holder(s) or the Commission) clearly identifies the question which is referred to the CVMP for consideration together with a detailed explanation of the issue(s) raised and how the Community interests are involved. A notification form for a referral to the CVMP/EMA is provided in the Annex to this Chapter.

If the referrer is a Member State or the Commission, the applicant(s)/marketing authorisation holder(s) must be informed on the issues raised in the referral.

If the referrer is an applicant/marketing authorisation holder, in advance of making a referral under this Article, he is recommended to have a pre-referral meeting with the EMA. Pre-referral meetings between the applicant/marketing authorisation holder and the EMA are also possible in cases where the referrer is a Member State or the Commission.

Following the start of the referral procedure, the Member States and the applicant(s)/marketing authorisation holder(s) shall forward to the Committee all relevant information relating to the veterinary medicinal product(s).

4.4 Scope of the referral

4.4.1 Referral relating to a specific veterinary medicinal product

The CVMP is called upon to issue an opinion on a matter involving Community interests, on the basis of a question referred to it. However, the CVMP may consider aspects other than those explicitly mentioned in the referral which are necessary to evaluate quality, safety and efficacy of the veterinary medicinal product under consideration, and which are necessary to produce a fully harmonised summary of product characteristics, labelling and package leaflet to be annexed to its opinion.

Certain differences may, however, remain, such as invented names, names of the marketing authorisation holders and legal supply status.

4.4.2 Class referral

Where the referral to the Committee concerns a range of veterinary medicinal products or a therapeutic class, the Agency may limit the procedure to certain specific parts of the authorisation. If the Agency decides to limit the procedure in this way, only specific sections, or parts of them, of the summary of product characteristics will be harmonised with the corresponding changes to the relevant package leaflet section and labelling.

This has consequences, in that an Article 39 referral may only apply to those veterinary medicinal products if they were covered by the authorisation procedures referred to in Chapter 4 of Directive 2001/82/EC (i.e. mutual recognition and decentralised procedures) or when, having been granted purely national marketing authorisations, they have been subject to a referral³. Where a Community interest referral procedure related to so-called “purely

³ With the exception of a partial harmonisation within the meaning of paragraphs 48 and 49 of the judgement of the European Court of Justice in case C-39/03 P “Artegoda” (national marketing authorisations granted on a purely national basis outside mutual recognition subject to a harmonisation limited to the clinical particulars of the summary of product characteristics).

national” marketing authorisations has been limited to specific parts of the authorisations, Member States may continue to vary them using national procedures.

Centrally authorised veterinary medicinal products belonging to a class subject to an Article 35 referral may not be part of the referral procedure itself but may be handled where necessary via a parallel procedure according to Article 45 of Regulation (EC) No 726/2004 triggered by the Commission.

5. Articles 39 and 40 of Directive 2001/82/EC (“Follow-up referrals”)

5.1 Basic principles

These referrals, known as “follow-up” referrals, may be triggered by a Member State or the marketing authorisation holder in the respect of veterinary medicinal products which have been granted a marketing authorisation via the mutual recognition or decentralised procedures or which have been the subject of harmonisation as a result of a referral procedure.

Products which have been granted purely national marketing authorisations and which were subject to a subsequent partial harmonisation limited only to the clinical particulars of the summary of product characteristics (within the meaning of paragraphs 48 and 49 of the judgement of the European Court of Justice in case C-39/03) may not be subject to “follow-up referrals”.

A Member State may trigger a “follow-up referral” in the following situations:

- Upon rejection of a Type IB variation, by reference to Article 39 of Directive 2001/82/EC and Article 5(11) of Regulation (EC) No 1084/2003;
- When mutual recognition by one or more national competent authorities of the draft decision of the Reference Member State on a Type II variation is not possible, by reference to Article 39 of Directive 2001/82/EC and Article 6(12) of Regulation (EC) No 1084/2003;
- When it considers a variation, suspension or revocation of a harmonised marketing authorisation necessary for the protection of human or animal health or the environment, by reference to Article 40 of Directive 2001/82/EC.

The marketing authorisation holder may trigger a “follow-up referral” in the following situations:

- Upon rejection of a Type IB variation, by reference to Article 39 of Directive 2001/82/EC and Article 5(11) of Regulation (EC) No 1084/2003;
- When the competent authorities of the Member States concerned by the application are of the opinion that the Type II variation can not be accepted, by reference to Article 39 of Directive 2001/82/EC and 6(13) of Regulation (EC) No 1084/2003.

Article 41 of Directive 2001/82/EC extends the scope of Articles 39 and 40 referrals to veterinary medicinal products authorised by Member States following an opinion of the CVMP given in accordance with Article 4 of Directive 87/22/EEC before 1 January 1995 (ex-concertation veterinary medicinal products).

5.2 Can the referral be stopped?

Once the referral is triggered, the referral can only be stopped if marketing authorisation holder(s) withdraw the concerned marketing authorisations from all EEA markets. The same condition applies if the procedure was triggered by the marketing authorisation holder.

5.3 Procedural steps leading to Articles 39 and 40 referrals

For Article 39 and Article 40 referrals the procedural steps of Article 33 and Article 35 referrals apply in a similar manner, respectively.

5.4 Scope of the referral

In accordance with the general principle that achieved harmonisation must be maintained, Community pharmaceutical legislation has created an arbitration mechanism which aims to resolve divergences arising between Member States AFTER harmonisation has been achieved.

As provided for in Article 6(12) of Regulation (EC) No 1084/2003, the procedure referred to in Article 39(2) of Directive 2001/82/EC (i.e. the procedure for referral to CVMP) shall apply where it has not been possible to achieve agreement under the mutual recognition procedure for a variation.

Article 40 applies where a Member State considers that the variation of a marketing authorisation which has been granted in accordance with the provision of Chapter 4 of Directive 2001/82/EC (mutual recognition or decentralised procedures) or its suspension or withdrawal is necessary for protection of human or animal health or of the environment.

The CVMP is called upon to issue an opinion on the matter of variation of the terms of a marketing authorisation, its suspension or revocation, framed on a question referred to it.

The CVMP should limit its opinion to the question referred, since harmonisation has already been achieved.

However, the CVMP may consider aspects others than those explicitly mentioned in the referral, in those cases where the referral was initiated for the protection of human or animal health or for the environment, in so far it appears necessary to guarantee such protection.

6. Unilateral Action by Member States in urgent cases

When concerns about a veterinary medicinal product have a European dimension (i.e. the product is authorised in more than one Member State) or are of Community interest, divergence between the Member States on the need to vary, suspend or revoke the marketing authorisation shall be resolved at European level, within the Community arbitration mechanisms described above. Unilateral national action is thus not acceptable.

However, Community pharmaceutical legislation does recognise the need for unilateral measures by Member States where, in exceptional cases, urgent action is essential to protect human or animal health or the environment and until a definitive action is adopted. In accordance with Article 40 (2) of Directive 2001/82/EC, in these specific cases, the Member States may temporarily adopt national measures suspending the marketing and use of a veterinary medicinal product. They must inform the Commission, the Agency and the other Member States no later than the following working day not only of the urgent measure adopted but also of the reasons for such measure.

In addition it should be noted that Article 78(1) of Directive 2001/82/EC places an obligation on each Member State to inform the Agency, the other Member States and the marketing authorisation holder of the need of a variation, to restrict an indication or the availability, to amend the posology, or to add a contraindication or a new precautionary measure or the suspension or revocation of a marketing authorisation for any veterinary medicinal product – even purely nationally authorised products – resulting from the evaluation of pharmacovigilance data.

Article 78(2) of Directive 2001/82/EC also allows Member States, “where urgent action to protect human or animal health is necessary”, to suspend the marketing authorisation of a specific veterinary medicinal product. In the event this action is taken, the Member State shall inform the Agency, the Commission and the other Member States no later than the following working day.

When the Agency is informed, on the basis of Article 78(3), that a Member State is considering a variation in accordance with the specification above or a suspension or revocation of a marketing authorisation, or that urgent action was undertaken by a Member State, by suspending a marketing authorisation, the Agency shall prepare an opinion to address the issue. On the basis of such opinion, the Commission may request the Member States where the product is authorised to take temporary measures immediately, while waiting for the adoption of final measures, which shall follow the procedure foreseen in Article 89(3).

7. Procedural elements

Notwithstanding the legal provisions described above (Articles 36, 37 and 38 of Directive 2001/82/EC as amended), it is recommended to take a number of preliminary procedural steps in order to streamline the operation of the Community referral procedure.

In advance of making a referral, it is strongly encouraged that a notification is sent to the Agency by the applicant/marketing authorisation holder or Member State, including:

- The intention to submit a referral;
- Clear and concise identification of the question to be referred to the CVMP, indicating the veterinary medicinal product concerned, pharmaceutical forms and/or strengths, route of administration, target species, applicant(s)/ marketing authorisation holder(s);
- Proposal on documentation to be provided in support of the referral;
- Where appropriate, request for a meeting with the Agency to discuss regulatory and procedural issues linked to the referral.

When an issue is referred to the CVMP, each Member State is asked to make available to the Agency before the end of the first CVMP meeting following the referral a list of the names of the veterinary medicinal product(s) affected by the referral (including pending applications), together with information on the respective applicant(s)/marketing authorisation holder(s), strength(s), pharmaceutical form(s), target species and route(s) of administration.

In the case of Article 33 referrals triggered in the frame of a repeat use mutual recognition procedure, the list of the names of the veterinary medicinal product affected by the referral shall also include those authorised by the first mutual recognition procedure.

A Member State triggering a referral should submit all available information relating to the veterinary medicinal product and depending on the type of referral to the matter in question to the CVMP. In cases where the referral follows the revocation or the suspension of the marketing of a veterinary medicinal product in a Member State, that Member State should immediately forward all information relating to this action to the CVMP members, the competent authorities of the other Member States and the Agency.

In the case of referrals initiated by (an) applicant(s)/marketing authorisation holder(s), the referral should be accompanied by expert reports/overviews which take into account legislation in force and which have been updated to include data supporting the reasons for referral. In addition the applicant(s)/marketing authorisation holder(s) should ensure that all available information relating to the matter in question is forwarded to the CVMP members, the competent authorities of the Member States and the Agency.

To ensure a smooth implementation of the above-mentioned requirements, the Agency will inform the applicant(s)/marketing authorisation holder(s) for each referral on the documentation needed as well as on the number of copies to be sent to the Rapporteur, the Co-Rapporteur and other CVMP members.

For Article 34(1) and Article 35 referrals initiated by the applicant(s)/marketing authorisation holder(s), the Agency will inform the applicant(s)/marketing authorisation holder(s) about the fees to be paid in accordance with Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency, as amended by Council Regulation (EC) No 1905/2005⁴.

7.1 Organisation of work within the CVMP/EMEA

The CVMP appoints one of its members to act as Rapporteur. The appointment of a Rapporteur and, if appropriate, of a Co-Rapporteur is made by the CVMP on a case-by-case basis.

In cases of a 'class referral', according to Article 35(2), it is not necessary to appoint a (Co-) Rapporteur for each veterinary medicinal product. One lead Rapporteur and more than one Co-Rapporteur(s) may be appointed for a class of products.

Once the appointment of the (Co-) Rapporteur(s) has been made, the Agency informs the applicant(s)/marketing authorisation holder(s) and communicates also the name of the Agency Product Team Leader in charge.

The CVMP may also appoint individual experts to advise it on specific questions. When it does so, the Committee defines their tasks and specifies the time limit for the completion of these tasks.

For referrals triggered by a Member State or by the Commission, at the first CVMP meeting following the initiation of the referral, the CVMP formulates the question(s) to be addressed to the applicant(s)/marketing authorisation holder(s) and discusses, on the basis of the proposal from the party notifying the referral, the scope of the documentation actually requested or needed.

For referrals triggered by the applicant(s)/marketing authorisation holder(s), at the first CVMP meeting following the initiation of the referral, the CVMP starts its assessment of the issues referred. A list of questions may be adopted at day 30 of the procedure.

⁴ OJ L 304 of 23. 11. 2005, p. 1.

The CVMP may also take into account any other information at its disposal which concerns the quality, safety and efficacy of the veterinary medicinal product(s) concerned and which may help in arriving at its opinion.

It should be stressed that all members of the CVMP are equally concerned by the question submitted to the CVMP. They take part in the evaluation procedure and the adoption of opinion independently of the Member State, which has designated the CVMP member, and of the situation of the veterinary medicinal product in the Member States.

7.2 Hearing of the applicant/marketing authorisation holder

Before issuing its opinion, the CVMP provides the applicant(s)/marketing authorisation holder(s) with an opportunity to present written or oral explanations.

7.3 Timetable and clockstop provisions

After notification of the referral, the CVMP considers the matter and issues a reasoned opinion within 60 days of the date of the referral.

For Article 34 and Article 35 referrals, the CVMP may extend that period to 150 days, taking into account the views of the applicant(s)/marketing authorisation holder(s).

For all referrals, in case of urgency, on a proposal from its Chairperson, the CVMP may agree on a shorter deadline.

The timepoints provided within the referral timetable below are given as the key steps in the referral procedure. They can be altered in order to reflect the particularities of a referral or to accommodate the interest of the company when needed. The timepoints refer to active days, i.e. correspond to the real time the CVMP takes to assess the data provided. The CVMP will not exceed the overall timeframe provided in the legislation.

The CVMP may, however, suspend the time limit of 60/150 days (clock-stop) in order to allow the applicant(s)/marketing authorisation holder(s) to prepare the responses to a CVMP List of Questions, List of Outstanding Issues or an oral explanation (as appropriate).

Referral triggered by a Member State or the Commission - **Timetable for the procedure**

Day 0	Notification of a referral to the CVMP/EMA Secretariat
Day 1	First meeting of the CVMP following notification of referral. The CVMP discusses the question(s) referred during the plenary meeting. Rapporteur/(Co)-Rapporteur appointed/confirmed, as applicable
	Adoption of CVMP List of questions to be addressed by the MAHs/ applicant(s) and timetable
Clock stop	For the MAHs/applicant(s) to answer CVMP List of questions
Clock re-start (day 2)	Following submission of responses (in accordance with published submission dates) (and if applicable including English SPC, Labelling and PL)
	Adoption of CVMP timetable for the rest of the procedure
Day 20	Rapporteur and Co-Rapporteur(s) circulate a report on the written responses from the applicant(s)/Marketing Authorisation Holder(s)

	together, if applicable, with the draft SPC/Labelling/PL to be annexed to the opinion
Day 25	Comments from CVMP members on the (Co-)Rapporteur(s) assessment report(s) and draft SPC/Labelling/PL (if applicable)
Day 30	Discussion at the CVMP: Adoption of the CVMP Opinion, or Adoption of CVMP List of outstanding issues to be answered in writing and/or in oral explanation
Clock stop	If necessary, for the preparation and submission of written and/or oral explanations
Clock re-start	If necessary, following the submission of written explanations (in accordance with the published submission dates) and/or at the time of oral explanations
Day 60	Adoption of the CVMP opinion (with annexes as provided in Article 36 of Directive 2001/82/EC)

Referral triggered by the applicant(s)/marketing authorisation holder(s) - **Timetable for the procedure**

As in principle there is no “list of questions” at day 1 of the procedure, the timetable is as follows:

Day 0	Notification of a referral to the CVMP/EMA Secretariat
Day 1	CVMP meeting following notification of referral and provided relevant documentation has been submitted by the MAH/Applicant in advance of the start of the procedure. The CVMP discusses the question(s) referred during the plenary meeting. Rapporteur/(Co)-Rapporteur appointed/confirmed. Adoption of the CVMP timetable. No adoption of List of questions.
Day 20	Rapporteur and Co-Rapporteur(s) circulate assessment reports on the submission from the MAH(s)/applicant(s) and, if applicable, comments on the proposed SPC/Labelling/PL
Day 25	Comments from CVMP members on the (Co-)Rapporteur(s) assessment reports and draft SPC/Labelling/PL (if applicable)
Day 30	Discussion at the CVMP: Adoption of the CVMP Opinion, or Adoption of CVMP List of questions to be answered in writing and/or in oral explanation
Clock stop	If necessary, for the preparation and submission of oral explanations
Clock re-start	If necessary, following the submission of written explanations (in accordance with the published submission dates) and/or at the time of oral explanations
Day 60	Adoption of the CVMP opinion (with annexes as provided in Article 36 of Directive 2001/82/EC)

7.4 CVMP opinion and re-examination mechanism

The opinion of the CVMP may have implications for the applicant(s)/marketing authorisation holder(s), i.e., where the CVMP finds that:

- The application does not satisfy the criteria for authorisation, or
- The summary of the product characteristics proposed by the applicant(s)/ marketing authorisation holder(s) in accordance with Article 14 of Directive 2001/82/EC should be amended, or
- The authorisation should be granted subject to conditions, considered essential for the safe and effective use of the veterinary medicinal product including pharmacovigilance, or
- The marketing authorisation should be suspended, varied or revoked.

Once the opinion of the CVMP is adopted, the Agency immediately informs the applicant(s)/marketing authorisation holder(s).

Within 15 days of the receipt of the opinion, the applicant(s)/marketing authorisation holder(s) may notify Agency in writing of his/their intention to request a re-examination of the opinion. In that case, he/they forward the detailed grounds for the request to the Agency within 60 days after receipt of the opinion.

Within 60 days from receipt of the detailed grounds for the request, the CVMP shall re-examine its opinion. In order to do so, it will appoint a new Rapporteur and, where necessary, a new Co-Rapporteur different from those appointed for the initial opinion. The Rapporteur (and Co-Rapporteur where appropriate) is responsible for making an assessment of the detailed grounds for re-examination. Each of the grounds for re-examination should be dealt with separately and a reasoned conclusion on all relevant points must be included in the assessment report.

If no request for re-examination is notified in writing to the Agency within 15 days of receipt of the opinion by the applicant(s)/marketing authorisation holder(s), the opinion automatically becomes a final opinion.

7.5 Final opinion

Within 15 days of the adoption of the final opinion of the CVMP, the Agency forwards it to the Member States, the Commission and the applicant(s)/marketing authorisation holder(s) together with a report describing the assessment of the referral concerning the veterinary medicinal product(s) and stating the reasons for its conclusions.

The conclusions of the re-examination are an integral part of the evaluation and should therefore be integrated within the final assessment report appended to the opinion and be reflected in scientific conclusions.

In the event of an opinion in favour of granting, maintaining or varying a marketing authorisation for the veterinary medicinal product concerned, in accordance with Article 36(5) of Directive 2001/82/EC, the following documents are annexed to the opinion:

- i. List of the veterinary medicinal products and marketing authorisation holders concerned by the procedure;

- ii. Draft summary of the product characteristics;
- iii. Any conditions affecting the authorisation considered essential for the safe and effective use of the veterinary medicinal product including pharmacovigilance, if applicable;
- iv. Details of any recommended conditions or restrictions with regard to the safe and effective use of the veterinary medicinal product, if applicable;
- v. The proposed text of the labelling and package leaflet;
- vi. Scientific conclusions justifying the outcome of the referral.

In the cases of an Article 33 or Article 35(2) referral where only parts of the summary of products characteristics and the corresponding parts of the labelling and package leaflet are harmonised only these will be annexed to the opinion. The same may apply in case of follow-up referrals.

Furthermore, in those situations where no amendments to the summary of products characteristics, labelling or package leaflet are foreseen, the annex shall include a statement to that effect.

In the event of an opinion recommending the suspension or revocation of the marketing authorisation(s) for the veterinary medicinal product concerned, the 'scientific conclusions and grounds for suspension or revocation of the marketing authorisation' are annexed to the opinion, as well as the conditions for the lifting of the suspension.

7.5.1 Conditions and restrictions with regard to the safe and effective use of the veterinary medicinal product addressed to the applicant/marketing authorisation holder according to Article 36(4)(third indent) and (5)(b) and (c) of Directive 2001/82/EC

In the cases foreseen in Article 36(4)(third indent) and (5)(b) and (c) of Directive 2001/82/EC the authorisation should be granted subject to certain conditions, in view of conditions considered essential for the safe and effective use of the veterinary medicinal product including pharmacovigilance or other recommended conditions or restrictions with regard to the safe and effective use of the veterinary medicinal product.

The opinion/assessment report of the CVMP should thus include justification for the conditions proposed, i.e. timelines to be kept and details of the reports, including the details for the pharmacovigilance reports to be presented to guarantee a sufficient follow-up of the marketing authorisation. The follow-up to the conditions will normally be monitored by the Member States and only in exceptional cases by the CVMP.

8. Decision making procedure at Community level

After the reception of the final opinion of the CVMP, the Commission starts the Community decision-making procedure. For a detailed description of this procedure, see chapter 6.

The decision will be reported for information to the applicant(s)/marketing authorisation holder(s). The Member States are required to either grant, maintain, suspend, or withdraw/revoke the marketing authorisation, or vary the terms of the marketing authorisation as necessary to comply with the decision within 30 days of its notification and are required to inform the Commission and the Agency of the measures taken.

When the decision provides for granting or maintaining a marketing authorisation, the documents annexed to the decision are: the list of the names, pharmaceutical forms, strengths and routes of administration of the veterinary medicinal product and its applicants/marketing authorisation holders in the Member States, the summary of product characteristics, the text of the labelling and package leaflet, the scientific conclusions and, as the case may be, any condition affecting the authorisation considered essential for the safe and effective use of the veterinary medicinal product including pharmacovigilance, and any conditions or restrictions with regard to the safe and effective use of the veterinary medicinal product.

When the decision provides for the suspension of the marketing authorisation, the conditions for the lifting of the suspension will also be annexed.

9. Consequences of a commission decision following a referral to the CVMP

Member States national requirements for the implementation of a referral decision, as well as details on the national procedure(s) to be followed to the Commission decision are included in Chapter 7, section 6.

9.1 Actions to be taken by the Member States after a referral

Commission decisions following a Community referral procedure are addressed to all Member States.

Commission decisions taken following a Community referral request Member States directly concerned by the referral procedure to comply with the Community decision within 30 days of its notification and to inform the Commission and the Agency.

The marketing authorisation holder is urged to take appropriate steps necessary to allow the Member States to comply with the Community decision within 30 days after its notification, for instance by timely providing any necessary translations.

After a referral procedure with a positive opinion concerning granting or the maintenance of a marketing authorisation, Member States concerned by the procedure must vary the terms of the marketing authorisation, as necessary, to comply with the decision of the Commission within 30 days after its notification.

When the opinion is that a marketing authorisation must be suspended or withdrawn/revoked, Member States where the veterinary medicinal product is authorised shall suspend or withdraw/ revoke the marketing authorisation. The same applies when the opinion of the Committee is that a marketing authorisation must be refused.

In those Member States not directly concerned by the procedure, no immediate action is necessary since there are no pending applications or marketing authorisations for the veterinary medicinal product(s) in question. These Member States, however, as addressees of the decision, should consider whether any action is appropriate as regards products authorised by them, and should take the decision into account in any future regulatory action.

Member States should also consider appropriate action in case the referred veterinary medicinal product has been subject to multiple applications for marketing authorisation.

In the case of a subsequent application for the same veterinary medicinal product, the evaluation must take into account the Commission decision and Member States should grant or refuse the national marketing authorisations according to the terms of the Commission

decision unless there are potential serious risks to human or animal health or to the environment or issues which have not been previously considered. Any Member State or the Commission would as appropriate refer the new scientific issue to the CVMP in order to start a new referral procedure.

The same applies in case where a marketing authorisation is pending for the veterinary medicinal product, which was the subject of the referral. The Member States must grant or refuse national marketing authorisations in accordance with the Commission decision.

9.2 Independent applications for marketing authorisation submitted during a referral procedure

While a referral procedure is ongoing, independent applications for marketing authorisation concerning veterinary medicinal products with the same active substance(s) can be submitted. For instance, if an Article 34 referral concerns the “originator” veterinary medicinal product, applications for “generic” veterinary medicinal products of this “originator” veterinary medicinal product may be submitted.

However, where independent applications for products with the same active substance are submitted once a referral is ongoing, Member States should consider the outcome of the referral as far as it may be relevant for the assessment of such applications.

The same occurs in the frame of Article 35 “class” referrals, if applications for marketing authorisations of veterinary medicinal products of the same class or range are submitted.

Applications for variations can be submitted and ongoing procedures can be finalised, even if the veterinary medicinal product is involved in a referral. However, when a referral procedure based on Article 33 is ongoing it is recommended that no new variation procedure is started for the veterinary medicinal product concerned, unless it relates to human or animal health or environmental matters.

9.3 Subsequent applications occurring after finalisation of the referral

Subsequent applications for a specific veterinary medicinal product which has been the subject of a referral must use the harmonisation achieved following the referral. After Articles 33, 34 and 35 referrals subsequent applications for the same veterinary medicinal product must be submitted through the mutual recognition or decentralised procedure and must be mutually recognised in accordance with the relevant Commission decisions unless a new referral is triggered with respect to a new potential serious risk to human or animal health or the environment. In accordance with Articles 12(3)(n) and 22 of Directive 2001/82/EC and Commission Communication C98/229/03, the mutual recognition procedure will also apply if the same company, or a company from the same group of companies, applies for a separate marketing authorisation for the product, regardless of whether the product has been the subject of full harmonisation.

However with regard to the Article 34 and Article 35 referrals there are some particularities that should be noted.

Where the referral leads to harmonisation (with the exception of partial harmonisation, as explained in section 4.4.2), the mutual recognition procedure has to be followed afterwards, in order to maintain the achieved harmonisation.

Where the procedure is limited to certain specific parts of the authorisation, the obligation to follow a mutual recognition procedure only applies if the marketing authorisations were granted initially by the decentralised or mutual recognition procedure. In this case, the

marketing authorisations granted through “purely” national procedures stay national. Nevertheless it is the responsibility of the marketing authorisation holder and the Member State to keep the level of harmonisation reached by the referral procedure.

In case of an Article 35(2) referral, there may be a large number of products. In this case, different Reference Member States can be chosen for different veterinary medicinal products but the harmonisation should be maintained.

In the case of Article 34 or Article 35 referrals and where there is no reference Member State, the applicant(s)/marketing authorisation holder(s) must choose the reference Member State for the follow up of the procedure.

9.4 Follow-up of European Commission referral decisions

As a general rule, the follow-up of a Commission decision following a referral procedure will be undertaken by the Member States. The adoption of the referral decision concludes the referral procedure. It will normally be for the authorising national competent authorities to implement any conditions imposed on the marketing authorisation and to perform any subsequent assessments that may be necessary. If this eventually leads to divergences amongst Member States, a new referral procedure would have to be initiated.

Exceptionally, however, a referral decision may explicitly foresee further action to be taken by the Agency and the Commission.

**NOTIFICATION TO THE CVMP/EMEA SECRETARIAT OF A
REFERRAL UNDER ARTICLE 34 OF DIRECTIVE 2001/82/EC
FAX NUMBER – 44 207 418 8447**

This notification is an official referral under Article 34 of Directive 2001/82/EC to the CVMP made by the following

<Member State (MS) >:-----

<Applicant(s)> <Marketing Authorisation Holder(s) (MAH(s)) >:-----

THIS NOTIFICATION IS TO BE COPIED BY THE REFERRING PARTY TO APPLICANT/ MARKETING AUTHORISATION HOLDER AND ALL CVMP MEMBERS

Name(s) of particular veterinary medicinal product <in the Referring Member State>*	
<Active substance(s)>	
Pharmaceutical form(s) <in the Referring Member State>	
Strength(s) <in the Referring Member State>	
Target species	
Route of administration(s) <in the Referring Member State>	
Presentations <in the Referring Member State>	
Marketing Authorisation Holder(s) <in the Referring Member State>	

Harmonisation of SPC for {name of veterinary medicinal product} (and associated names):
Rationale for the notification of the Article 34 referral

The above-mentioned veterinary medicinal product {NAME} and its associated names, does not have the same Summary of Product Characteristics (SPC) across all EU Member States, Iceland and Norway with respect to e.g. <indications>, <posology>, <contra-indications>, <undesirable effects> <and sections dealing with the recommendations for use>. The following examples constitute a non-exhaustive list.

<4.1 Indications>

[please provide a detailed overview of the divergencies]

<4.2 Posology>

[please provide a detailed overview of the divergencies]

etc

<Discrepancies also exist between MS regarding sections {other SPC sections with divergencies but for which no detailed overview is provided above}>.

Due to the divergent national decisions taken by Member States concerning the authorisation of the above-mentioned product, {Member State}{Applicant} {Marketing Authorisation Holder} <the European Commission> notifies the EMEA of an official referral under Article 34 of Directive 2001/82/EC in order to resolve divergences amongst the nationally authorised SPCs for the above-mentioned product and thus to harmonise its divergent SPCs across the EU.

.....Signed
.....Date

* When triggered by the MAH the whole range of names, pharmaceutical forms, strengths, routes of administration, target species and presentations of the veterinary medicinal product in all EU Member States (Iceland and Norway, if appropriate) should be mentioned

**NOTIFICATION TO THE CVMP/EMEA SECRETARIAT OF A
REFERRAL UNDER ARTICLE 5(11) OF COMMISSION
REGULATION (EC) No 1084/2003
FAX NUMBER –44 207 418 8447**

This notification is an official referral under Article 5(11) of Commission Regulation (EC) No 1084/2003 to the CVMP made by the following

<Concerned Member State (CMS)>:-----

<Marketing Authorisation Holder(s) (MAH(s))>: -----

Reference Member State:-----

Concerned Member State(s):-----

THIS NOTIFICATION IS TO BE COPIED BY THE REFERRING PARTY TO APPLICANT(S)/MARKETING AUTHORISATION HOLDER(S) AND ALL CVMP MEMBERS

Product Name<in the RMS>, if appropriate, Strength, Target Species and Pharmaceutical Form	
Marketing Authorisation Holder(s)	
Mutual Recognition variation procedure No.	
<p>(please provide a summary of background information and clearly precise the question that triggers the referral) (if this space is not sufficient, please summarise and add annex):</p>	
Signed	Date

**NOTIFICATION TO THE CVMP/EMEA SECRETARIAT OF A
REFERRAL UNDER ARTICLE 6(12) OF COMMISSION
REGULATION (EC) No 1084/2003
FAX NUMBER –44 207 418 8447**

This notification is an official referral under Article 6(12) of Commission Regulation (EC) No 1084/2003 to the CVMP made by the following:

Concerned Member State(s):

Reference Member State:-----

Concerned Member State(s):-----

THIS NOTIFICATION IS TO BE COPIED BY THE REFERRING PARTY TO APPLICANT(S)/MARKETING AUTHORISATION HOLDER(S) AND ALL CVMP MEMBERS

Product Name<in the RMS>, if appropriate, Strength, Target Species and Pharmaceutical Form	
Marketing Authorisation Holder(s)	
Mutual Recognition variation procedure No.	
<p>(please provide a summary of background information and clearly precise the question that triggers the referral, together with the latest version of the SPC, labelling and package leaflet as achieved during the coordination group procedure) (if this space is not sufficient, please summarise and add annex):</p>	
Signed	Date

**NOTIFICATION TO THE CVMP/EMEA SECRETARIAT OF A
REFERRAL UNDER ARTICLE 6(13) OF COMMISSION
REGULATION (EC) No 1084/2003
FAX NUMBER –44 207 418 8447**

This notification is an official referral under Article 6(13) of Commission Regulation (EC) No 1084/2003 to the CVMP made by the following

Marketing Authorisation Holder: -----

Reference Member State: -----

Concerned Member State(s): -----

THIS NOTIFICATION IS TO BE COPIED BY THE REFERRING PARTY TO ALL CVMP MEMBERS

Product Name<in the RMS>, if appropriate, Strength, Target Species and Pharmaceutical Form	
Marketing Authorisation Holder(s)	
Mutual Recognition variation procedure No.	
<p>(please provide a summary of background information and clearly precise the question that triggers the referral) (if this space is not sufficient, please summarise and add annex):</p> <p>Signed _____</p> <p style="text-align: right;">Date _____</p>	

**NOTIFICATION TO THE CVMP/EMEA SECRETARIAT OF A
REFERRAL UNDER ARTICLE 40 OF DIRECTIVE 2001/82/EC
FAX NUMBER –44 207 418 8447**

This notification is an official referral under Article 40 of Directive 2001/82/EC to the CVMP
made by the following Member State -----

Reference Member State, if applicable-----

Concerned Member State(s), if applicable: -----

<Product Name<in the RMS>, if appropriate, Strength, Target Species and Pharmaceutical Form> <Active Substance(s)>	
Mutual recognition Procedure No, when applicable	
Marketing Authorisation Holder(s)	
<p>The above mentioned Member State, considers that it is necessary for the protection of human or animal health or of the environment to refer the above-mentioned <veterinary medicinal product(s)> <active substance(s)> to the CVMP/EMEA Secretariat.</p> <p>(please provide a summary of background information and clearly precise the question that triggers the referral) (if this space is not sufficient, please summarise and add annex):</p> <p>Signed _____</p> <p style="text-align: right;">Date _____</p>	