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NOTICE TO APPLICANTS
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Procedures for marketing authorisation

CHAPTER 2
MUTUAL RECOGNITION PROCEDURE AND DECENTRALISED PROCEDURE

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The Notice to Applicants Volume 6A Procedures for marketing authorisation for veterinary medicinal products

Rue de la Loi 200, B-1049 Bruxelles/Wetstraat 200, B-1049 Brussel - Belgium - Office: BREY 10/073.
Telephone: direct line (+32-2)299.15.11, switchboard 299.11.11. Fax: (+32-2)299.80.46.
Karin.Krauss@cec.eu.int

CHAPTER 2 Mutual recognition procedure and decentralised procedure

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1. LEGAL BASIS AND PURPOSE

The legal provisions covering the mutual recognition procedure and the decentralised procedure for veterinary medicinal products are contained in Directive 2001/82/EC.

Both the mutual recognition procedure and the decentralised procedure aim at facilitating access to a single market by relying upon the principle of mutual recognition. Thus with the exception of those veterinary medicinal products which are subject to the centralised procedure (see Chapter 4), a marketing authorisation or the assessment in one Member State (the so-called reference Member State) ought in principle to be recognised by the competent authorities of the other Member States (the so-called concerned Member States), unless there are grounds for supposing that the authorisation of the veterinary medicinal product concerned may present a potential serious risk to human or animal health or for the environment.

If a concerned Member State is requested to recognise a marketing authorisation granted or an application assessed by the reference Member State it can raise grounds that the veterinary medicinal product presents a potential serious risk to human or animal health or for the environment. Such grounds would have to be fully **justified** in order to ensure that they do not act as an indirect and artificial hindrance to the free movement of goods within the European Economic Area.

2. SCOPE

2.1 Applications eligible for the mutual recognition procedure and decentralised procedure

The mutual recognition procedure and decentralised procedure must be used for applications for marketing authorisation for veterinary medicinal products in more than one Member State[1]. The requirements of submitting an application are described in sections 3 and 4. Once the procedure has been used, all **variations** to these medicinal products must use the procedure foreseen in the Variations Regulation[2].

In addition, variations to "ex-concertation" veterinary medicinal products authorised by Member States following an opinion of the Committee for Medicinal Products for Veterinary Use (CVMP) given before 1st January 1995 are required to use the mutual recognition procedure. These applications are converted to the mutual recognition procedure (see Commission Communication of 19.3.94, OJ C82 Vol. 37). Furthermore, variations of veterinary medicinal products that have been subject to referral procedures under Articles 34 and 35 of Directive 2001/82/EC made *after* 1st January 1995 are required to use the mutual recognition procedure. However, an

[1] See Chapter 1 section 3.1 scope of the centralised procedure
[2] See Articles 4(1), 5(1) and 6(1) of Regulation (EC) No 1084/2003

exception is provided under Article 35(2) of Directive 2001/82/EC: when the referral procedure concerns a range of veterinary medicinal products or a therapeutic class and the EMEA may limit the procedure to certain parts of the authorisation (see Chapter 1of the Notice to Applicants).

The mutual recognition procedure or the decentralised procedure is also applicable for **extensions**[3] of existing national marketing authorisations (cf. Chapter 1 of the Notice to Applicants). Before the applicant can use the mutual recognition or decentralised procedure, he has to ensure that the submitted dossiers are identical. This requires harmonising the already approved national summary of product characteristics, package leaflet and labelling by using either national variations, a mutual recognition procedure, or a referral procedure under Article 34 of Directive 2001/82/EC. After a harmonised marketing authorisation in a mutual recognition procedure or decentralised procedure has been achieved, no national extension is possible.

The mutual recognition/decentralised procedure is required for applications referring to **well-established veterinary use** intended for authorisation in more than one Member State and for which the use of the centralised procedure is neither mandatory nor chosen by the applicant.

2.2 Repeat use

It is possible to use the mutual recognition procedure more than once for subsequent applications to other Member States in relation to the same veterinary medicinal product (so-called repeat use). It is recommended that, wherever feasible, the marketing authorisation holder considers involving all Member States where the product is intended to be marketed, in the first use of mutual recognition procedure or decentralised procedure.

In case the applicant withdraws its application for marketing authorisation during a decentralised or mutual recognition procedure, this does not prevent the marketing authorisation holder to initiate a second procedure of mutual recognition for that/those Member State(s) at a later stage. Each subsequent procedure will be treated as a new mutual recognition procedure including the possibility of new concerned Member States to raise objections based on a potential serious risk to human or animal health or for the environment.

In the case of such a repeat use procedure, the subsequent application for mutual recognition will have to comprise the original dossier updated by any variation or renewal which had been approved and/or amended after authorisation; if necessary, additional data accepted by all Member States involved in the previous procedure and a proposal for a summary of product characteristics, package leaflet and labelling identical to the currently authorised. The reference Member State will send the original assessment report including the assessment of the updated dossier and variations as an Annex or as an updated assessment report to the concerned Member States.

In order to initiate a repeat use after 30 October 2005 of a previous mutual recognition procedure, the applicant is recommended to obtain harmonisation of the package leaflet and labelling of the veterinary medicinal product concerned. The proposed changes are to be submitted to the authority responsible for the marketing authorisation prior to start the repeat use[4].

[3] as defined in Annex II of Regulation (EC) No 1084/2003

[4] Changes to the labelling or the package leaflet not connected with the summary of product characteristics are not within the scope of the provisions of Commission Regulations (EC) No 1084/2003 and No 1085/2003 on variations.

Member States concerned in any repeated mutual recognition procedure shall normally recognise the authorisation granted in the previous procedure. In exceptional circumstances, where a concerned Member State considers that there are grounds for supposing that authorisation of the veterinary medicinal product concerned may present a potential serious risk to human or animal health or for the environment, the Member State shall refer the matter to the veterinary coordination group for mutual recognition and decentralised procedure (hereafter "the veterinary coordination group"). The applicant cannot stop this procedure by subsequently withdrawing the application in the referring Member State. If no agreement can be reached in this group the matter is referred for arbitration. Any matter dealt with by the veterinary coordination group in a previous mutual recognition procedure or decentralised procedure may not be raised again in any subsequent procedure except for justified reasons. Matters dealt with in an arbitration in a previous mutual recognition procedure or decentralised procedure may not be raised again in any subsequent procedure.

The veterinary coordination group has released a Best Practice Guide of Repeat Use of The Mutual Recognition Procedure to clarify dossier requirements and the divided responsibility prior and during the procedure for the marketing authorisation holder and the involved Member States.

2.3 Exclusions

The mutual recognition procedure and decentralised procedure will not be used for applications for:

- products falling under the compulsory scope of the centralised procedure as set out in the Annex to Regulation (EC) 726/2004 i.e.
  a) products developed by certain biotechnological processes,
  b) medicinal products for veterinary use intended primarily for use as performance enhancers

- products where the company has selected to submit through the centralised procedure according to Article 3(2) and 3(3) of Regulation (EC) 726/2004, irrespective of whether the marketing authorisation was granted, was rejected (negative opinion), or the applicant withdrew his application after an assessment by the EMEA of the submitted data;

  However, if the dossier for a withdrawn veterinary medicinal product or a veterinary medicinal product which has had a negative opinion in the centralised procedure is supplemented with new data based on new pre-clinical studies and tests and clinical trials, the application is considered to be based on a new dossier. For those applications, the applicant **can apply** again through centralised, mutual recognition or decentralised procedure where applicable, in those cases where a centralised procedure is not compulsory.

- veterinary homeopathic products authorised according to Article 19(2) of Directive 2001/82/EC cf. Article 43(2) of that Directive.

- products falling within the transitional arrangements for Lithuania and Poland upon their accession to the EU, cf. the Act of Accession[5] (see Chapter 1 of the Notice to Applicants for further details).

Extensions

- introducing in a veterinary medicinal product a proteinaceous component obtained through a biotechnology process listed in the Annex to Regulation (EC) 726/2004
- of original veterinary medicinal products which have not been
    a) harmonised via national procedures,
    b) referred in accordance with Article 34 or 35 of Directive 2001/82/EC or
    c) authorised by Member States following Directive 87/22/EEC ("Ex-concertation" procedure)

Variations

- introducing in a veterinary medicinal product a proteinaceous component obtained through a biotechnology process listed in Annex to Regulation (EC) 726/2004

  However, if the variation to a veterinary medicinal product not containing a proteinaceous constituent, concerns for instance a reagent like an enzyme prepared by rDNA technology, the veterinary medicinal product **remains in the procedure foreseen in the Variations Regulation** as this enzyme does not appear in the final composition and can therefore not be considered as an introduction of a proteinaceous component[6]. Likewise, for a change in the manufacturing process of a non-proteinaceous component due to the introduction of a biotechnology step, the product remains in the procedure foreseen in the Variations Regulation[7].

- of veterinary medicinal products which have not been considered through
  a) mutual recognition procedure or decentralised procedure
  b) “ex-concertation” procedures
  c) referral in accordance with Articles 34 or 35 of Directive 2001/82/EC.

2.4 Coordination group for mutual recognition and decentralised procedure for veterinary medicinal products – CMD(v)

The Veterinary Mutual Recognition Facilitation Group started its work in 1997 as an informal group. With the adoption of Directive 2004/28/EC the Veterinary Mutual Recognition Facilitation Group has an official status and is renamed as veterinary coordination group. According to Article 31 of Directive 2004/28/EC the group consists of one representative per Member State. An observer from the Commission and EMEA may participate at the meetings. The EMEA provides a secretariat to the veterinary coordination group. The group is responsible for the smooth

[5] The Treaty of Accession 2003 of Lithuania and Poland; Signed in Athens on 16 April, 2003 http://europa.eu.int/comm/enlargement/negotiations/treaty_of_accession_2003/treaty_accession_16.htm
[6] See Annex I, Introductory statements, 6th paragraph to Regulation (EC) No 1084/2003.
[7] See Annex I, Introductory statements, 6th paragraph to Regulation (EC) No 1084/2003.

functioning and good outcomes of mutual recognition and decentralised procedures with a mix of regulatory and scientific work.

The main tasks of the veterinary coordination group are:

- To address procedural and scientific issues arising from the mutual recognition and decentralised procedures.

- To consider points of disagreement raised by a Member State in relation to the assessment report, summary of product characteristics, package leaflet and labelling of a veterinary medicinal product on the grounds of a "potential serious risk to human or animal health or for the environment" within a mutual recognition or decentralised procedure. In the case of unsolved disagreement, the veterinary coordination group will refer the matter to the EMEA/Committee for Medicinal Products for Veterinary Use for arbitration with a detailed reasoning for the disagreement.

- To facilitate the establishment of dialogue between Member States, through meetings and oral explanations and to provide a forum to discuss any difficulties in dialogue and seek to overcome such difficulties.

- In order to promote harmonisation of marketing authorisations across the Community, to lay down a list of products where the summary of product characteristics needs to be harmonised taking into account proposals from Member States.

- To facilitate the resolution of procedural, regulatory and scientific issues arising from variation and renewal procedures, with a view to maintaining harmonisation of a marketing authorisation following mutual recognition or the completion of a decentralised procedure or following a referral.

- To identify issues which will be referred to the Committee for Medicinal Products for Veterinary Use, the Commission, the Veterinary Pharmaceutical Committee, Heads of Veterinary Medicines Agencies or other appropriate bodies.

- In close liaison with the Pharmacovigilance Working Party of the Committee for Medicinal Products for Veterinary Use, to ensure best practice for risk management of marketing authorisations granted through the mutual recognition/decentralised procedure.

- To undertake tasks concerning the overall management of the mutual recognition and decentralised procedures, maintaining close interaction with Heads of Medicines Agencies.

- To draw up its own Rules of Procedure for endorsement by Heads of Veterinary Medicines Agencies and for Commission approval.

The chairperson of the veterinary coordination group shall be elected by and from amongst its members for a period of three years, renewable once. The Vice-chairperson shall be appointed from among the members of the veterinary coordination group by the Member State which has the presidency of the Council of the European Union for the duration of the term of the presidency.

The veterinary coordination group meets normally once a month at the EMEA. In connection to the plenary meeting, there are breakout sessions relating to ongoing procedures when considered

necessary. Additional subgroup meetings are organised on specific topics. A press release is normally issued after each meeting.

All publicly available documents related to the work of the veterinary coordination group (e.g. recommendations, position papers, Best Practice Guides, Standard Operating Procedures) are published on the website for the Heads of European Veterinary Regulatory Authorities http://www.hevra.org/vmrfg/sop.asp).

2.5 Arbitration procedure

In the case of unsolved disagreement in the veterinary coordination group procedure, the veterinary coordination group will refer the matter to the EMEA/Committee for Medicinal products for Veterinary Use for arbitration with a detailed reasoning for the disagreement.

During the arbitration procedure all members of the Committee for Medicinal Products for Veterinary Use are involved in the evaluation and opinion taking process. The Commission decision following the arbitration procedure shall be addressed to all Member States. Those Member States where the veterinary medicinal product is authorised or where an authorisation is pending shall be required to take action following the Commission decision on arbitration within 30 days. Member States in which an application has not been submitted are bound by the decision in the event that an application is subsequently submitted. However, in such cases of repeat use of the mutual recognition procedure, Member States can raise issues which they consider grounds of a potential serious risk to human or animal health or for the environment provided these grounds were not already covered in the earlier arbitration. In case such grounds are raised in the repeat use procedure, they will lead to a new discussion in the veterinary coordination group and, possibly, to a new arbitration procedure.

Further details on the arbitration procedure are contained in Chapter 3 of the Notice to Applicants.

3. THE MUTUAL RECOGNITION PROCEDURE[8]

3.1 General principles

The mutual recognition procedure is to be used in order to obtain marketing authorisations in several Member States where the veterinary medicinal product in question has received a marketing authorisation in any Member State at the time of application.

The procedure to be followed will depend upon whether it is a Member State who triggers or the marketing authorisation holder who initiates the mutual recognition.

As set out in Directive 2001/82/EC Member States have to approve during the mutual recognition procedure the assessment report, the summary of product characteristics, the package leaflet and the labelling.

Specific national requirements, for example information on distribution, have to be presented in a so-called “blue box”.

[8] See Annex I – Flow Chart

See also the updated version of Chapter 7 of the Notice to Applicants section 10 “Blue-Box Requirements for the package leaflet and labelling in the mutual recognition or decentralised procedure”.

The mutual recognition procedure is divided in the following steps:

- National validation by the reference Member State (not further described here)
- Preparation or update of assessment report by reference Member State (90 days)
- Validation by the concerned Member States
- Approval by the concerned Member States (90 days)
- Discussion at the veterinary coordination group level, if needed
- National Marketing Authorisation step

3.2 Procedure leading to mutual recognition

After the first marketing authorisation in the Community is granted, the marketing authorisation holder may request one or more Member State(s) to recognise an authorisation granted by the reference Member State by submitting an application in accordance with Article 32 of Directive 2001/82/EC (for details see below “making the application”). Within 90 days of receipt of a valid application, the reference Member State will provide the assessment report together with the approved summary of product characteristics, package leaflet and labelling to the concerned Member States and to the marketing authorisation holder (Article 32(2) of Directive 2001/82/EC).

Within 90 days of receipt of these documents, the concerned Member States shall recognise the decision of the reference Member State and the approved summary of product characteristics, package leaflet and labelling by granting a marketing authorisation with a harmonised summary of product characteristics, package leaflet and labelling (Article 32(4) of Directive 2001/82/EC). However, if there are grounds for supposing that the authorisation of the veterinary medicinal product concerned may present a potential serious risk to human or animal health or for the environment, the procedure according to Article 33(3) has to be followed and, if Member States fail to reach agreement, an arbitration shall be initiated.

Differences between the summary of product characteristics, package leaflet and labelling approved in one Member State and the summary of product characteristics, package leaflet and labelling submitted in another Member State, do not automatically prevent the latter from a mutual recognition procedure. If these differences have no therapeutic implications (no difference in the efficacy and safety profile) e.g. both products have the same qualitative and quantitative (strength) composition in active substance and the same pharmaceutical form, they have to be considered as being the same and a mutual recognition procedure has to be followed (cf. Chapter 1 of the Notice to Applicants). In respect of veterinary medicinal products, different animal spe-

cies for which the veterinary medicinal product is indicated may prevent the triggering of a mutual recognition procedure.[9]

It is not possible for the same applicant (e.g. company belonging to the same mother company or group of companies or exercising concerted practices) to apply for a further national application referring to the identical marketing authorisation in the reference Member State. Therefore, an application for a "duplicate" (multiple applications) would have to be submitted to the reference Member State followed by mutual recognition of this second authorisation in other concerned Member States. In this context, the fact that one company sells the right to use parts of its dossier to another company (allows an "informed consent" application) does not necessarily imply that these two companies must be considered as the same company. Pharmaceutical companies which are independent from the marketing authorisation holder of the first authorisation would be allowed to ask for subsequent marketing authorisations, "national duplicates", of nationally authorised veterinary medicinal products in any Member State (the concerned Member State or the reference Member State), if the applicant company is independent from the marketing authorisation holder of the first authorisation.

3.2.1 Triggering by a Member State

According to Article 22 of Directive 2001/82/EC, where a Member State is informed in accordance with Article 12(3)(n) that another Member State has authorised a veterinary medicinal product which is the subject of a marketing authorisation application in the Member State concerned, it shall reject the application unless it was submitted in compliance with Articles 31 to 43, i.e. under the mutual recognition procedure.

In the context of Article 12(3)(n) of Directive 2001/82/EC (which obliges the applicant to submit copies of any authorisation granted for the veterinary medicinal product in question), Member States have to consider applicants belonging to the same mother company or group of companies as one company. The same principle applies to applicants, which, without belonging to the same mother company or group of companies, have concluded agreements (e.g. "licensees") or which exercise concerted practices concerning the placing on the market of the relevant medicinal product in different Member States.

The veterinary medicinal product in question encompasses any veterinary medicinal product which has the same qualitative and quantitative composition in active substance and same pharmaceutical form.

3.2.2 Initiation by the marketing authorisation holder

According to Article 32(1) of Directive 2001/82/EC with a view to the granting of a marketing authorisation for a veterinary medicinal product in more than one Member State, an applicant shall submit an application based on an identical dossier in these Member States, designating one Member State to act as reference Member State (for details see below under "making the application"). In the mutual recognition procedure Article 32(2) applies.

[9] Note: This is different to the human version (no species!) and stemming from the previous version; the veterinary coordination group wants to keep it because of the problem concerning the availability of veterinary medicinal products

3.2.2.1 Discussion with the reference Member State

Before submitting an application under the mutual recognition procedure the marketing authorisation holder must inform the reference Member State that such an application is to be made.

The marketing authorisation holder is in any case advised to discuss, in advance, the proposed mutual recognition application with the reference Member State. Such discussion would include whether the dossier and detailed and critical summaries should be updated to ensure that all relevant information is supplied according to current requirements, legal and technical aspects. The reference Member State may require the marketing authorisation holder to provide reassurance that the dossier submitted in other Member States is identical to that upon which it took its own decision.

Generic medicinal products: see also Chapter 1 of the Notice to Applicants.

For a generic application, the applicant will need to carefully consider the choice of the reference veterinary product for his product and should discuss this choice with the reference Member State. The applicant has to demonstrate that his product is bioequivalent with the reference veterinary medicinal product. Member States shall accept the demonstration of bioequivalence, independent of whether or not the reference veterinary medicinal product has been authorised in all Member States concerned.

The competent authority of the Member State in which the reference veterinary medicinal product has or has had a marketing authorisation, shall transmit upon request of the reference Member State within a period of one month, a confirmation that the reference veterinary medicinal product is or has been authorised together with the full composition of the reference veterinary medicinal product and if necessary other relevant documentation like the summary of product characteristics and information on the date of authorisation.

Information about the reference veterinary medicinal product used in the bioavailability/bioequivalence study will be given in the assessment report of the reference Member State in a **confidential attachment** stating the full qualitative and quantitative composition and finished product specification. In case of doubt, a concerned Member State may request additional information from the reference Member State. (see guidelines on Investigation of bioavailability and bioequivalence on the web-site of the EMEA: http://www.emea.eu.int/pdfs/vet/ewp/001600en.pdf)

The reference Member State will allocate a procedure number to this application (according to the numbering system described in section 7 of this Chapter) and will inform the applicant accordingly.

3.2.2.2 Updating the dossier and the detailed and critical summaries (if necessary)

Necessity to update

Article 27 of Directive 2001/82/EC requires the marketing authorisation holder to continuously update the dossier to take account of technical and scientific progress and to introduce any change that may be required for the manufacture and control of the veterinary medicinal product.

Updating the dossier should be taken up through the variations procedure, and reflected in the dossier and/or detailed and critical summaries, as appropriate. Furthermore, it may be necessary to *consolidate* the dossier in order to reflect the changes made by variations since the first authorisation was granted. However, Part II (Module 3 if accepted by Member States) does not need to be supplemented; a discussion in the quality summary is sufficient.

In case new guidelines were issued since the veterinary medicinal product has been placed on the market, they should be reflected in the detailed and critical summaries in relation to the data presented in the dossier. If the applicant believes that, in addition, modifications are necessary in the summary of product characteristics, package leaflet and the labelling then such changes should be approved by the reference Member State.

Procedure for updating prior to starting the mutual recognition procedure

As stated previously, it is preferable for the marketing authorisation holder to give the reference Member State in advance notice of the intention to use the marketing authorisation in the mutual recognition procedure. In case the marketing authorisation holder needs to update the dossier involving a large volume of data prior to initiating a procedure, it is necessary that the marketing authorisation holder and reference Member State will agree on a timetable.

Furthermore, the applicant is recommended to discuss with the reference Member State if the product has already been marketed for a long time as much of the pre-clinical data are unlikely to be still relevant in light of clinical data and experience accumulated since marketing authorisation.

In addition, a more extensive discussion may be required in the detailed and critical summaries as to changes in veterinary medical practice and the development of the product in the intervening years. Even though the dossier is continuously updated and there is one renewal after 5 years after the authorisation is granted, there could be a need for a comprehensive review in both the pre-clinical and the clinical detailed and critical summaries.

In any event, after the marketing authorisation holder has updated the dossier and the detailed and critical summaries and has included all variations, he must submit his formal application and thereby request the reference Member State in writing to supply an assessment report or an updated assessment report to the concerned Member States.

3.2.2.3 Before submission of the application to the concerned Member State(s)

Dialogue with the applicant, in particular on summary of product characteristics, package leaflet and labelling

In accordance with Article 32(4) of Directive 2001/82/EC, all Member States concerned shall approve the assessment report, the summary of product characteristics, the package leaflet and the labelling submitted for mutual recognition.

In order to ensure a smooth procedure for this recognition, Member States have agreed to use the following procedure intended for clarification and dialogue:

Before initiation of the mutual recognition procedure, the reference Member State is requested to achieve and to agree on a summary of product characteristics, package leaflet and labelling through discussion with the applicant, which would take into account all existing national summary of product characteristics, package leaflets and labelling for the veterinary medicinal product and for veterinary medicinal products with the same active substance which have been approved in earlier mutual recognition procedures and decentralised procedures.

Especially for applications according to Article 13(1) of Directive 2001/82/EC (generic veterinary medicinal products), the applicant will be requested to present to the reference Member State an overview of the sections: Indications, Posology, Contraindications, Special Warnings, Precautions for Use, Target Species and Withdrawal period of the summary of product characteristics, package leaflet and labelling of the corresponding reference products of the intended concerned Member State(s) for this application. The reference Member State will discuss with the applicant to what extent a summary of product characteristics, package leaflet and labelling can be achieved on which a successful mutual recognition procedure can be based.

Both the reference Member State and the applicant are expected to react in a flexible manner.
The marketing authorisation holder should ensure that:

i) the product will be regarded as a veterinary medicinal product in all concerned Member States and that it will not be regarded, for example, as a cosmetic, a feed additive, a medical device or a biocide;

ii) the product is falling under the scope of the mutual recognition procedure;

iii) the application including the three detailed and critical summaries on Parts II (Module 3 if accepted by Member States), III and IV is updated appropriately (i.e. in accordance with relevant legislation);

iv) either the clinical indications sought have been previously authorised for a veterinary medicinal product containing the same active substance in the concerned Member State(s)

or,

adequate clinical data is available to support the claimed indications in the summary of product characteristics, package leaflet and labelling;

or

it is an application according to Article 17 of Directive 2001/82/EC (registration procedure for the homoeopathic veterinary medicinal products)

v) in the case of generic applications the requirements of Article 13(1) of Directive 2001/82/EC have been met, i.e. that there is a veterinary medicinal product which is or has been authorised in a Member State for the following period:

- for more than 6 or 10 years (i.e. the period of protection of Directive 2001/82/EC before amendment by Directive 2004/28/EC) in case the application for authorisation of the reference product had been submitted **before** Directive 2004/28/EC started to apply;

- for not less than 8 years in case the application for authorisation of the reference product had been submitted **after** the date of transposition of Directive 2004/28/EC;

vi) the dossiers in the reference Member State and concerned Member States are the same;

vii) variations and renewals to the original authorisation have been authorised by the reference Member State in advance of the initiation of the procedure;

and

viii) the final text of the approved summary of product characteristics, and that of the package leaflet and labelling, for information, in the national language of the reference Member State should be available, with appropriate translations and taking into account relevant guidelines.

3.2.2.4 Making the application

The marketing authorisation holder must submit an application to the competent authorities of each of the Member States where a marketing authorisation is to be sought. The application shall be submitted together with the information and particulars referred to in Articles 12, 13, 13a, 13b, 13c, 13d and 14 of Directive 2001/82/EC.

The application shall include a list of all concerned Member States. The Member State who has already granted a marketing authorisation shall act as “reference Member State” and prepare an assessment report on the veterinary medicinal product.

The marketing authorisation holder must confirm (usually in the covering letter accompanying the application) that the dossier as well as the summary of product characteristics, package leaflet and labelling are identical to

a) the ones accepted by the reference Member State, and

b) the ones submitted to all other concerned Member States.

The dossier must include the EU Application Format Part IA.

The following information on the requirements on the application in the concerned Member States can be found in Chapter 7:

- The numbers of copies of the dossier and required languages for submissions to the Member States.
- Copies of the summary of product characteristics, label and package leaflet texts in the language(s) as set out for each Member State
- Requirements for samples of the active substance and finished product are set out for each Member State.
- How the appropriate national fees have to be paid
- In some Member States, there may be different addresses for submission of the dossier and for correspondence in connection with an application.
- It is not part of the responsibility of the competent authorities to arrange customs clearance of applications. It is the responsibility of the marketing authorisation holder to deliver the application to the officially designated address, free of any charges to the addressee.

- A copy of the application should be available to be sent to the reference Member State on request, and also, **only** in the event of an arbitration, to the EMEA.
- Additional national requirements, if applicable.
- Submission of electronic dossiers

3.3 Action following the submission of the application

3.3.1 Preparation or update of assessment report by reference Member State

In accordance with Article 32(2) of Directive 2001/82/EC, the reference Member State shall prepare or update the assessment report within 90 days[10] of receipt of a valid application.

Normally, the assessment report prepared during the initial assessment of the veterinary medicinal product will be available. However, the reference Member State needs to update it in order to maintain consistency between the dossier and the assessment report. The assessment report would include all variations and any additional information bearing upon quality, safety and efficacy reported since the initial marketing authorisation had been granted.

The reference Member State will notify the marketing authorisation holder when the assessment report is/will be available.

According to Article 32(2) of Directive 2001/82/EC, this assessment report together with the approved summary of product characteristics, labelling and package leaflet shall be sent to the concerned Member States and to the applicant.

However, if an Active Substance Master File (ASMF) was submitted, the section of the assessment report referring to the closed part of the Active Substance Master File as well as any other confidential information will not be made available to the applicant (see Guideline on Active Substance Master File Procedure http://www.emea.eu.int/pdfs/human/qwp/022702en.pdf). Where it is made available to the marketing authorisation holder, the other concerned Member States will be informed. For the information provided in the Active Substance Master File the letter of access should be included.

It also might be necessary that the assessment report needs to be translated. Arrangements for translation of the assessment report will be made by the reference Member State, but the costs of translation are borne by the marketing authorisation holder.

3.3.2 Procedure for validation of the application by the concerned Member State

The procedure for validation of the application by the concerned Member States starts when the marketing authorisation holder confirms to both the reference Member State and concerned Member States the dates of dispatch of the dossier to all concerned Member States and when the reference Member State has sent the assessment report to all concerned Member States.

[10] It should be noted that the timelines imposed in Directive 2001/82/EC on Member States or the EMEA are maximum timelines, which do not prevent then from acting within a shorter timeframe.

The application is validated by the concerned Member States within 14 days[11] using the check-in procedure described in Chapter 7 of Notice to Applicants. Notably, it will be verified that all necessary documentation and translations are available and that the fees have been paid. Any problems are notified immediately by the Communication and Tracking System[12] (CTS) to the reference Member State and the other concerned Member States and by e-mail, fax or telephone to the marketing authorisation holder.

If a concerned Member State informs the reference Member State that the application is invalid, the clock will only start when that concerned Member State informs the reference Member State that the application has become valid or that the application has been withdrawn. The concerned Member State must inform the reference Member State that the application has become valid within 5 days of the missing information being supplied.

In case of minor problems, the marketing authorisation holder will be given the opportunity to rectify the application within two weeks after he has been notified of the problems.

In case of major problems or if the marketing authorisation holder failed to rectify minor problems, the application is deemed invalid and the applicant will be advised to withdraw the application. In the case of possible different views among Member States on the legal basis for the application, the matter can be discussed in the meeting of the veterinary coordination group.

In order to facilitate the check-in procedures in national competent authorities, the veterinary coordination group has published a document “Procedure for automatic validation of applications in the mutual recognition procedures”.

3.3.3 Start of the 90-day period for approval by the concerned Member States

In accordance with Article 32(4) of Directive 2001/82/EC, all concerned Member States have 90 days to approve the assessment report, the summary of product characteristics, the package leaflet and the labelling.

The reference Member State will normally start this 90-day period on the first agreed start date after it has sent the notification for validation to the concerned Member States (automatic validation procedure), unless it has been informed by a concerned Member State that the application is not valid (see 3.3.2).

The reference Member State notifies all concerned Member States and the marketing authorisation holder of the start of the 90-day period referred to in Article 32(4) of Directive 2001/82/EC.

Starting dates

The veterinary coordination group publishes on annual basis the start dates for mutual recognition procedure on the Heads of Veterinary Medicines Agencies website. These start dates will coincide with the meeting of the veterinary coordination group on day 77/78 of the procedure.

[11] Days are considered as calendar days

[12] The Communication and Tracking System is used by the reference Member State and all concerned Member States to exchange information in all steps of the procedure such as validation and start of the procedure.

3.3.4 Clarification and dialogue - Operating procedure

Response of concerned Member States

During the operation of the mutual recognition procedure, the reference Member State will act as the central point between the concerned Member States and the marketing authorisation holder. All dialogue between the parties involved should be channelled through the reference Member State.

If a concerned Member State considers that there are grounds for supposing that the authorisation of the veterinary medicinal product may present a potential serious risk to animal or human health or for the environment, it is recommended to notify this concern as soon as possible to the reference Member State, the other concerned Member States and the applicant at latest on day 54 of the 90-day period. All objections, reasons for objections to grounds of potential serious risk to human or animal health or for the environment and any issues for clarification are carefully screened within the national agencies.

Member States have agreed to distinguish in their day 54 letter their concerns in potential serious risks to human or animal health or for the environment which, unresolved, could lead to the procedure within the veterinary coordination group according to Article 33(3) of Directive 2001/82/EC and if failed to an arbitration procedure.

The reference Member State will compile a consolidated list of questions and circulate it to the concerned Member States and the applicant. The list of questions will be written in accordance with the veterinary coordination group template published on the Heads of Veterinary Medicines Agencies website (http://www.hevra.org/vmrfg/sop.asp).

If the situation could be solved, the reference Member State will inform the co-ordination group accordingly, so that all Member States can benefit from the information and, if relevant, adopt common positions.

Discussion on the summary of product characteristics, package leaflet and labelling

At the end of the 90-day period for approval by the concerned Member States, agreement must be reached on the summary of product characteristics, package leaflet and labelling.

In the period from day 54 - 90 discussions would mainly concentrate on:

- indications
- posology and method of administration
- contra-indications
- special warnings and precautions for use
- shelf-life and storage requirements
- withdrawal periods

Response from the applicant

It is recommended that the applicant should provide answers to the questions raised by the concerned Member States in electronic format directly into the consolidated list prepared by the ref-

erence Member State. The answers from the applicant together with all supporting documentation should be sent to all concerned Member States by electronic means and/or courier mail. The veterinary coordination group has published a document to help document management during the mutual recognition procedure "Guidance for e-mail use during Mutual Recognition Procedure ".

Additional information from the applicant should always be sent to all concerned Member States and reference Member State **but** it should be noted that the applicant does not have the possibility of addressing questions/objections by providing additional studies during the procedure.

However, supplementary data from studies included in the submission can be provided.

In this response document the applicant will provide, if requested, a new proposed summary of product characteristics, package leaflet and labelling with track changes together with the answers to the questions raised by the concerned Member State on the different sections of the summary of product characteristics, package leaflet and labelling.

The applicant should answer questions (if any) on Part II (Module 3), III, IV and V (Part V for immunological veterinary medicinal products only). Cross-references could be useful from one response to another.

Clarification of concerns and deficiencies will be carried out by dialogue between the reference Member State and the concerned Member States as appropriate. It may be necessary for the applicant to discuss issues directly with concerned Member States but the reference Member State must be kept informed.

The reference Member State will provide an assessment of the responses of the applicant to the document with concerned Member States comments and applicant response, which will permit the concerned Member States a period of one week in which to consult their experts before the discussion at the veterinary coordination group meeting.

The reference Member State will inform Member States of actions (i.e. modifications to the summary of products characteristics, package leaflet and labelling) suggested by other Member States in order to allow a consensus to be reached. During this 90-day period it is recommended that a person within the applicant company always be available to resolve any issues which may arise.

Break-out sessions

The meetings of the veterinary coordination group have been identified as occasions where all Member States can meet. Alongside these meetings, break-out sessions may be organised under responsibility of the reference Member State to discuss applications or to resolve outstanding questions. The reference Member State will inform the marketing authorisation holder if it is considered that representatives from the applicant might be available at the relevant meeting to aid in the resolution of these issues.

Although applicants should be aware that they may not be required to participate in the session they may be asked to agree amendments to the summary of product characteristics, package leaflet and labelling or to answer questions from the Member States. Applicants should ensure that their representatives are able to take decisions on amendments to summary of product characteristics, package leaflet and labelling being proposed by Member States.

The same procedure applies to the decentralised procedure.

After the veterinary coordination group meeting the reference Member State will immediately inform the applicant of the outcome of the discussion.

Finalisation of the procedure

Further updated drafts of the summary of product characteristics, labelling and package leaflet will be circulated immediately after the veterinary coordination group meeting (day 82 at the latest) and again at day 85, if necessary to take account of final modifications, so that all are aware of the text to be approved. These drafts should be prepared by the applicant.

At certain critical times during the 90-day period, it is essential that a responsible contact person from the applicant company be available to resolve any issues which may arise.

All concerned Member States should give their final opinion at latest day 88. On occasion further discussion may be needed around day 85 to avoid a procedure in the veterinary coordination group or an arbitration (alternatively a telephone conference or videoconference may be used). Any further changes in the summary of product characteristics, package leaflet and labelling should be agreed on by reference Member State and all other concerned Member States.

No agreement could be reached during the mutual recognition procedure

See section 5 ‘Veterinary Coordination Group procedure on disagreement on potential serious risk to human or animal health or for the environment’.

Withdrawal

Where an applicant withdraws an application regarding a veterinary medicinal product in one concerned Member State during a mutual recognition procedure, it is not allowed to submit a national application subsequently. Any such an application will be rejected.

An application for a marketing authorisation may be withdrawn by the applicant at any time during the mutual recognition procedure. However, once a potential serious risk to human or animal health or for the environment has been raised in accordance with Article 33(1), to be dealt with by the veterinary coordination group (see section 5) and if failed by the Committee for Medicinal products for Veterinary Use in an arbitration procedure (see Chapter 3 of the Notice to Applicants), the opinion of the veterinary coordination group and of the Committee for Medicinal Products for Veterinary Use will be given unless all applications and existing marketing authorisations for the product are withdrawn. In the latter case, the Committee for Medicinal Products for Veterinary Use may decide either to close or to continue the referral procedure, if there still is a concern for human or animal health or for the environment.

3.3.5 Recognition of the marketing authorisation (mutual recognition) and granting of national authorisations

In accordance with Article 32(4) of Directive 2001/82/EC, each concerned Member State will recognise the marketing authorisation and the summary of product characteristics, package leaflet and labelling granted by the reference Member State within the 90-day period.

According to Article 32(5) of Directive 2001/82/EC competent authorities shall adopt a decision within 30 days after acknowledgement of their agreement to the assessment report, the summary of product characteristics and the labelling and package leaflet as approved by the reference Member State. The applicant should therefore in their own interest provide the requisite documentation (adequate translation of the agreed summary of product characteristics, package leaflet and labelling) not later than 5 calendar days after the end of the procedure.

When mutual recognition occurs, the Member State which recognises a marketing authorisation informs the reference Member State, the other concerned Member States, the EMEA via the Communication and Tracking System as well as the marketing authorisation holder.

Further information can be found in the "Best practice guide for mutual recognition procedure" published and updated in a regular manner by the veterinary coordination group.

Granting of national marketing authorisation during an on-going arbitration procedure

According to Article 33(6) of Directive 2001/82/EC, even if there is no agreement among all Member States, those Member State(s) which have approved the summary of product characteristics, package leaflet and labelling may, on request of the applicant, grant a marketing authorisation while the arbitration procedure is ongoing. This authorisation shall be without prejudice to the outcome of the arbitration procedure.

4. DECENTRALISED PROCEDURE[13]

In order to facilitate the check-in procedure, the veterinary coordination group has published a Best Practice Guide: 'Procedure for the veterinary decentralised procedure'.

4.1 General principles

The decentralised procedure is to be used in order to obtain marketing authorisations in several Member States where the veterinary medicinal product in question has not yet received a marketing authorisation in any Member State at the time of application.

The procedure to be followed will depend upon whether it is a Member State or the marketing authorisation holder which initiates the decentralised procedure.

[13] See Annex II – Flow Chart

As set out in Directive 2001/82/EC Member States have to approve during the decentralised procedure the assessment report, the summary of product characteristics, the package leaflet and the label.

Specific national requirements have to be presented in a so-called ‘blue box’.

See also the updated version on the Chapter 7 of the Notice to Applicants section 10. ‘Blue-Box Requirements for the package leaflet and labelling in the decentralised or mutual recognition procedure’.

The decentralised procedure is divided in five steps:

- Validation step
- Assessment step I
- Assessment step II
- Discussion at the veterinary coordination group level, if needed
- National Marketing Authorisation

4.2 Procedure leading to decentralised procedure

4.2.1 Triggering by a Member State

According to Article 21(2) of Directive 2001/82/EC where a Member State receives an application for marketing authorisation and notes that another marketing authorisation application for the same veterinary medicinal product is being examined in another Member State, the Member State concerned shall decline to assess the application and shall remind the applicant that the decentralised procedure (Articles 31 to 43 of Directive 2001/82/EC) applies.

The Member State which already has started the examination will normally be the future reference Member State.

In the cases mentioned above the start of the decentralised procedure will be counted from the date when the reference Member State has been agreed and all concerned Member States have validated the application.

By day 120 of the procedure the reference Member State will prepare a draft assessment report, a draft summary of product characteristics, a draft package leaflet and a draft labelling. These documents will be forwarded to the concerned Member States and to the applicant.

4.2.2 Initiation by the applicant

According to Article 32(1) of Directive 2001/82/EC with a view to the granting of a marketing authorisation for a veterinary medicinal product in more than one Member State, and where no marketing authorisation has been granted in the Community for that medicinal product, an applicant shall submit an application based on an identical dossier in these Member States, designat-

ing one Member State to act as reference Member State (for details see below under “making the application”). Article 32(3) applies.

4.2.2.1 Discussion with the reference Member State

Before submitting an application under the decentralised procedure, the applicant must inform the reference Member State that such an application is to be made.

The applicant is in any case **advised** to discuss, in advance, the proposed application with the reference Member State. The reference Member State may require the applicant to provide reassurance that the dossier submitted in other Member States is identical to that upon which it takes its own decision.

When an application is submitted in a Member State with the intention to request a decentralised procedure a timely notification to the reference Member State is advantageous as to provide advice. This would also facilitate the availability of the assessment report within the period of time as stated in Article 32(3) of Directive 2001/82/EC.

The reference Member State will allocate a procedure number to this application, according to the numbering system described in section 7 of this Chapter and will inform the applicant accordingly.

In the case of possible different views among Member States on the legal basis of the application, the matter can be discussed either at the meeting of the veterinary coordination group prior to the application or during the validation phase.

For a submission of a **generic application** see above under 3.2.2.1.

4.2.2.2 Before submitting the application to the reference and concerned Member State(s)

Dialogue with the applicant, especially on summary of product characteristics, package leaflet and labelling

In accordance with Article 32(4) of Directive 2001/82/EC, “all Member States concerned shall approve the assessment report, the summary of product characteristics, package leaflet and labelling submitted.” Therefore, in order to maximise the efficiency of this clarification and dialogue stage, Member States have agreed to use the following procedure:

For applications according to Article 13(1) of Directive 2001/82/EC (generic veterinary medicinal products), the applicant will be requested to present to the reference Member State an overview of the sections: Indications, Posology, Contraindications and Special Warnings and Precautions for Use of the summary of product characteristics, package leaflet and labelling, species and withdrawal period of the corresponding innovator products of the intended concerned Member State(s) for this application. The reference Member State will discuss with the applicant to what extent a summary of product characteristics, package leaflet and labelling can be achieved on which a successful decentralised procedure can be based.

Both the reference Member State and the applicant are expected to react in a flexible manner.

The applicant **should** ensure that all requirements as set out in section 3.2.2.3(i) to (vi) are fulfilled accordingly.

4.2.3 Making the application

The applicant must submit an application to the competent authorities of each of the Member States where a marketing authorisation is to be sought. The application shall be submitted together with the information and particulars referred to in Articles 12, 13, 13a, 13b, 13c, 13d and 14 of Directive 2001/82/EC.

The application shall include a list of all concerned Member States and the applicant shall designate one Member State to act as "reference Member State" and to prepare an assessment report on the veterinary medicinal product.

The applicant must confirm (usually in the covering letter accompanying the application) that the dossier as well as the summary of product characteristics, package leaflet and labelling are identical in all Member States involved in the decentralised procedure.

Information on the requirements on the application in the reference Member State and the concerned Member States can be found in Chapter 7 of the Notice to Applicants (see section 3.2.24).

4.3 Action following the submission of the application

4.3.1 Validation Phase

The procedure for validation of the application starts when the applicant confirms both to the reference Member State and concerned Member States the dates of dispatch of the dossier to all Member States.

The application should be validated by all concerned Member States and the reference Member State. The validation can be made according to the check-in procedure described in Chapter 7 of the Notice to Applicants or using any appropriate form.

Any validation issues are notified immediately by the Communication and Tracking System (CTS) to the reference Member State or at latest within 14 days following the receipt of the notification of dispatch dates, to the applicant and the reference Member State.

In case of problems, the applicant will be given the opportunity to rectify the application within a given timeframe after he has been notified of the problems.

4.3.2 Start of the decentralised procedure: assessment step I[14]

In accordance with Article 32(3) of Directive 2001/82/EC, the reference Member State has 120 days to prepare a draft assessment report, a draft summary of product characteristics and a draft of the labelling and package leaflet.

[14] Assessment step I corresponding to the national assessment phase (Article 32(3) of Directive 2001/82/EC)

The reference Member State will start the assessment step I after the applications have been validated by all concerned Member States and the reference Member State.

In order to prepare the draft assessment report, the reference Member State forwards a preliminary assessment report on the dossier to the concerned Member States within 70 days after the start of assessment step I.

The concerned Member States should communicate their comments on the dossier, the preliminary assessment report and the summary of product characteristics to the reference Member State within the timeframe set by the reference Member State.

If a concerned Member State can already identify at this early stage that there are grounds for supposing that the authorisation of the veterinary medicinal product may present a potential serious risk to human or animal health or for the environment, it should notify its concerns as soon as possible to the reference Member State and the other concerned Member States. All objections, reasons for objections to grounds of potential serious risk to human or animal health and for the environment and any issues for clarification are carefully screened within the national agencies.

The reference Member State will compile the list of questions (loq). It is up to the reference Member State to decide if some comments should be left out and the reference Member State should combine similar questions in order to not lengthen the list of questions unnecessarily.

The reference Member State will send the consolidated list of questions to the applicant and if necessary stop the clock in order to allow the applicant to prepare a response document.

This clock-stop period will be determined in agreement with the applicant, depending on the complexity of the questions raised but will not exceed a recommended period of 3 months unless duly justified.

The applicant must submit the response document to the competent authorities of all concerned Member States and the reference Member State within the time-frame determined. He also must notify to the reference Member State and concerned Member States the dates of dispatch of the response document (for details see Chapter 7 of the Notice to Applicants and the veterinary coordination group guidance document).

The procedure restarts when the applicant provides the requested data.

The reference Member State shall supply the draft assessment report, draft summary of product characteristics, package leaflet and labelling to the concerned Member States and the applicant not later than 120 days after validation of the application (cf. Article 32(4) of Directive 2001/82/EC). The draft assessment report would include an appropriate evaluation of any information available upon quality, safety and efficacy. The reference Member State will notify the applicant when the draft report is/will be available.

Normally, the reference Member State makes the draft assessment report available to the applicant. However, if an Active Substance Master File (ASMF) was submitted, the section of the assessment report referring to the closed part of the Active Substance Master File as well as any other confidential information will not be made available to the applicant (see Guideline on Active Substance Master File Procedure http://www.emea.eu.int/pdfs/human/qwp/022702en.pdf). Where it is made available to the marketing authorisation holder, the other concerned Member

States will be informed. For the information provided in the Active Substance Master File the letter of access should be included.

4.3.3 Assessment step II: 90-day period for approval by Member States

In accordance with Article 32(4) of Directive 201/82/EC, all concerned Member States have 90 days to approve the (draft) assessment report, the summary of product characteristics and the labelling and package leaflet.

For further details for the starting days see under 3.3.3 above.

4.3.4 Clarification and dialogue - Operating procedure

Day 0 of the 90-days assessment step II corresponds with day 120 of the decentralised procedure. This date corresponds to start dates as published on the HEVRA website. The reference Member State will update the Communication and Tracking System database with the date of sending of those documents on day 0.

Each concerned Member State should send its comments on the draft assessment report, draft summary of product characteristics, package leaflet and labelling to the reference Member State and fill in the Communication and Tracking System database by day 25 at the latest. The reference Member State will forward the comments to the applicant immediately.

The reference Member State will compile the list of questions in accordance with the veterinary coordination group template and circulate it according to the timeframe agreed.

The applicant will send his response to the list of questions to the reference Member State, who will forward the document to concerned Member States immediately.

The reference Member State should evaluate the response document and communicate the result of this assessment in writing to all concerned Member States and the applicant. The concerned Member States should send by return their outstanding issues and confirm if there is a need for a break-out session.

If potential serious risks to human or animal health or for the environment are not resolved at this stage, a break-out session will be organised at the EMEA in connection with the veterinary coordination group meeting, upon request from the reference Member State.

If solved, the reference Member State will inform the veterinary coordination group at the plenary meeting of the discussion’s conclusion, in order all Member States can benefit from the information and, if relevant, adopt common positions.

Following the meeting the reference Member State will inform the applicant of the result of the discussion.

The applicant will circulate the updated drafts of summary of product characteristics, package leaflet and labelling to the reference Member State who will forward them to the concerned Member States immediately.

The final assessment report together with final versions of the summary of product characteristics, package leaflet and labelling will be sent by the reference Member State to the concerned Member States and the applicant.

The concerned Member States send their final comment to the reference Member State and the applicant.

On day 90 the reference Member State closes the procedure by sending the agreed on summary of product characteristics, labelling and package leaflet to the concerned Member States and the applicant.

If no agreement could be reached within the 90-day period, and if potential serious risks to human or animal health or for the environment remain for one or more Member States, which, if unresolved would necessitate a call for arbitration under Article 33 of Directive 2001/82/EC, the reference Member State shall inform the veterinary coordination group by forwarding the detailed reasoning from the complaining Member States for discussion at the forthcoming meeting of the veterinary coordination group.

The points of disagreement should be referred to the veterinary coordination group by the reference Member State on day 90 at the latest.

Response of concerned Member States

In the operation of the decentralised procedure, the reference Member State will act as the central point between the concerned Member States and the applicant. All dialogue between the parties involved should be channelled through the reference Member State.

If a concerned Member State considers that there are grounds for supposing that the authorisation of the veterinary medicinal product may present a potential serious risk to human or animal health or for the environment it will notify this concern as soon as possible to the reference Member State, the other concerned Member States and the applicant. Only objections which present a potential serious risk to human or animal health or for the environment, as defined in the guideline of the Commission, shall be presented to the reference Member State, the other concerned Member States and the applicant.

In any event these will be communicated within the 90-day period for mutual recognition in order to allow time to resolve the issue. Member States have agreed to distinguish in their letter their concerns based on potential serious risks to human or animal health or for the environment which, unsolved, could lead to the procedure within the veterinary coordination group according to Article 33(3) of Directive 2001/82/EC and if failed to an arbitration procedure.

Discussion on the summary of product characteristics, package leaflet and labelling

At the end of the 90-day period for approval by the concerned Member States, agreement must be reached on the summary of product characteristics, package leaflet and labelling.

Response from the applicant

The applicant should provide answers to the questions raised by the concerned Member States in electronic format directly into the consolidated list prepared by the reference Member State. The answers from the applicant together with all supporting documentation should be sent to all concerned Member States by electronic means and/or courier mail. The veterinary coordination group has published a document to help document management during the mutual recognition and decentralised procedure "Guidance for e-mail use during mutual recognition and decentralised Procedure".

In response to the objections or questions communicated to the applicant by the concerned Member States, the applicant will provide, if requested, a new proposed summary of product characteristics, package leaflet and labelling. Any amendments compared to the 120-day draft summary of product characteristics, package leaflet and labelling from the reference Member State and concerned Member States should be outlined in track changes.

For further details see the relevant section under 3.3.4 above.

Finalisation of the procedure

All concerned Member States should give their final opinion on day 85 (day 205) at the latest. On occasion further discussion may be needed around day 85 to avoid a procedure in the veterinary coordination group or an arbitration (alternatively a telephone conference or videoconference may be used). Any further changes of the summary of product characteristics, package leaflet and labelling should be agreed on by the reference Member State and all other concerned Member States.

No agreement could be reached during the decentralised procedure

See section 5 'Veterinary Coordination Group procedure on disagreement on potential serious risk to human or animal health or for the environment'.

Withdrawal

Where an applicant withdraws an application regarding a veterinary medicinal product in one concerned Member State during a decentralised procedure, it is not allowed to subsequently submit a national application. Any such application has to be rejected.

In principle, an application for a marketing authorisation may be withdrawn by the applicant at any time during the decentralised procedure. . However, during the assessment step II, once a potential serious risk to human or animal health or for the environment has been raised in accordance with Article 33(1), to be dealt with by the veterinary coordination group (see section 5) and if failed by the Committee for Medicinal Products for Veterinary Use in an arbitration procedure (see Chapter 3 of the Notice to Applicants), the opinion of the veterinary coordination group and of the Committee for Medicinal Products for Veterinary Use will be given unless all applications and existing marketing authorisations for the product are withdrawn. In such a case, the Committee for Medicinal Products for Veterinary Use may decide either to close or to con-

tinue the referral procedure, if there is still is concern for human or animal health or for the environment.

4.4 Granting of national marketing authorisations

According to Article 32(5) of Directive 2001/82/EC competent authorities of the concerned Member State(s) and the reference Member State shall adopt a decision within 30 days after acknowledgement of their agreement to the assessment report, the summary of product characteristics, the package leaflet and labelling.

The applicant should therefore, in his own interest, provide the requisite documentation (adequate translation of the agreed summary of product characteristics, package leaflet and labelling) not later than 5 calendar days after the end of the procedure.

The Member State which will grant a marketing authorisation informs the reference Member State, the other concerned Member States, the EMEA via Communication and Tracking System and the marketing authorisation holder.

Granting of national marketing authorisation during an on-going arbitration procedure

According to Article 33(6) of Directive 2001/82/EC, even if there is no agreement among all Member States, those Member State(s) which have approved the summary of product characteristics, package leaflet and labelling may, on request of the applicant, grant a marketing authorisation while the arbitration procedure is ongoing. This authorisation shall be without prejudice to the outcome of the arbitration procedure.

4.5 Choosing an EU Birth date/Periodic Safety Update Report submission circle

If an international birth date is already known before the end of the decentralised procedure, the applicant may use the international birth date as the EU Birth Date (according to EUDRALEX Volume 9 - Pharmacovigilance). In that case this should be communicated to the reference Member State so to include the Periodic Safety Update Report Submission Cycle and the first renewal date in the day 90 closure letter.

If the applicant does not choose the international birth date as EU Birth Date, he should be reminded to inform as soon as possible the reference Member State and concerned Member States of the date of granting the first marketing authorisation in the EU (which will be the EU Birth Date), the Periodic Safety Update Report submission cycle and the common renewal Birth Date.

5. VETERINARY COORDINATION GROUP PROCEDURE ON DISAGREEMENT ON POTENTIAL SERIOUS RISK TO HUMAN OR ANIMAL HEALTH OR FOR THE ENVIRONMENT

According to Article 33(3) of Directive2001/82/EC, all involved Member States shall use their best endeavours to reach agreement on the action to be taken within 60 days following the communication of disagreements at the level of the veterinary coordination group. During the 60-days procedure no clock-stop is foreseen. The veterinary coordination group guideline/standard operation procedure on the 60-days procedure within the veterinary coordination group should be followed.

During the 60-day procedure, the applicants shall be allowed by the veterinary coordination group to make their point of view known, orally or in writing. Whether a written procedure or a hearing is the most appropriate way to reach an agreement has to be decided in consultation with the applicant.

Written procedure

A written procedure should be restricted to measures deemed urgent by the chairperson, to the adoption of draft statements previously discussed by the veterinary coordination group and to measures for the implementation of practices adopted earlier by the veterinary coordination group. A full report on the outcome of the written procedure should be made at the following meeting.

Draft statements are addressed to members of the veterinary coordination group, who may raise objections within 10 calendar days following transmission. In case of serious objections, the chairperson decides whether the written procedure should be suspended and the adoption of the draft statement be postponed to the next meeting of the veterinary coordination group.

Hearing

The procedure to be followed in case of a request for a hearing by the applicant will be defined in a Standard Operating Procedure to be adopted by the veterinary coordination group

Hearings shall be indicated clearly in the draft agenda of the meeting during which it is deemed to take place. The scientific and/or regulatory argumentation on which a presentation will be based shall be sent to the members of the veterinary coordination group in advance. The veterinary coordination group shall not express any final positions during these presentations.

End of coordination procedure

If, within 60 days of the communication of the points of disagreement, Member States reach an agreement, the reference Member State shall record the agreement, close the procedure and inform the applicant accordingly.

If Member States fail to reach an agreement within the 60-day period, the EMEA shall be immediately informed, with a view to the application of the procedure under Articles 36, 37 and 38 of Directive 2001/82/EC. The EMEA shall be provided with a detailed statement of the matters on which the Member States have been unable to reach agreement and the reasons for their dis-

agreement. A copy shall be forwarded to the applicant. The procedure described in Chapter 3 of the Notice to Applicants should be followed using the appropriate form to notify the EMEA.

Member States that have approved the assessment report, the draft summary of product characteristics, 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 of Directive 2001/82/EC. In that case, the authorisation granted shall be without prejudice to the outcome of that procedure.

The reference Member State should fill in the Communication and Tracking System database according to the outcome of the procedure.

6. PROCEDURE AFTER THE FINALISATION OF A MUTUAL RECOGNITION PROCEDURE OR A DECENTRALISED PROCEDURE

6.1 Changes to the marketing authorisation in the reference Member State after finalisation of the mutual recognition procedure

Where, in the course of the mutual recognition procedure, the reference Member State and concerned Member States agree that changes to the current authorisation in the reference Member State are necessary in order for mutual recognition to take place, the marketing authorisation holder/applicant and reference Member State will introduce these using the appropriate (national) procedures. These changes can relate to the summary of product characteristics, package leaflet and labelling and Parts II, III or IV of the dossier.

6.2 Maintenance of identical dossiers

Having the benefit of mutual recognition of the marketing authorisation or a decentralised procedure also carries through the life of the veterinary medicinal product. Thus, variations to a veterinary medicinal product which has benefited from mutual recognition or a referral in accordance with Articles 34 or 35 of Directive 2001/82/EC[15], benefit from the procedure foreseen in the Variations Regulation[16] which provides that notifications for variations have to be submitted simultaneously to all Member States where the veterinary medicinal product has been authorised. In this way, the summary of product characteristics, package leaflet and labelling of the marketing authorisation, which has been harmonised, continues to be consistent and identical in all Member States where the veterinary medicinal product is authorised.

6.3 Renewals

In accordance with Article 28 of Directive 2001/82/EC the marketing authorisation may be renewed after 5 years on the basis of a re-evaluation of the risk/benefit balance by the competent authority of the authorising Member State. Once renewed, the marketing authorisation shall be

[15] See NTA Chapter 1 section 4 Community Referrals
[16] See Articles 4(1), 5(1) and 6(1) of Regulation (EC) No 1084/2003.

valid for an unlimited period unless the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal.

6.3.1 Timing of submission

The application for renewal has to be submitted at least 6 months before the marketing authorisation ceases to be valid. The basic principle is that the application can be submitted earlier but not later than this time. For mutual recognition products it is recommended to reach an agreement and a common renewal date for all Member States concerned by the mutual recognition procedure or decentralised procedure at time of granting the marketing authorisation to keep the harmonisation reached.

6.3.2 Documentation to be submitted

The marketing authorisation holder is responsible for ensuring that the dossier is kept up to date throughout the life of the product by way of the variation process (see Chapter 5 of the Notice to Applicants). A consolidated list of documents should be submitted. The competent authority may require the applicant to submit the listed documents at any time.

The renewal application should be submitted in EU format.

6.3.3 Further renewal

In principle, after one renewal, the marketing authorisation is valid indefinitely. In some circumstances, however, the competent authority may decide that an additional 5-year renewal is required based on pharmacovigilance grounds.

Guidelines on processing of Renewals in the Mutual Recognition and Centralised procedures (NtA Volume 6C) should also be consulted where appropriate.

6.4 Extension of application

Extensions to marketing authorisations can be made, provided that the conditions reflected in Annex II of Regulation (EC) No 1084/2003 are met.

After receiving a marketing authorisation either in the mutual recognition procedure or in the decentralised procedure all follow-ups have to be handled according to the Regulation (EC) No 1084/2003 on variations. See also Chapter 1 of the Notice to Applicants.

6.5 Product index and assessment report

The mutual recognition and decentralised procedures are based on the principle that veterinary medicinal products are approved or assessed by the reference Member State followed by a 90-days period where the concerned Member State(s) consider the reference Member State assessment report. This assessment report has to be publicly available according to Article 25(4) of Directive 2001/82/EC.

In order to manage the 90-days procedure Members States operate a Communication and Tracking System (CTS) where the reference Member State updates the product information. The reference Member State and concerned Member States update all events during the 90-days period.

The veterinary coordination group created a European Product Index including all veterinary medicinal products undergoing the mutual recognition procedure and decentralised procedure. The index was launched in 1999 and the particulars (product name, name of marketing authorisation holder, pharmaceutical form, species, strength, active substance, reference Member State, concerned Member States and type of application) are transferred from the Communication and Tracking System. The maintenance of the index is a decentralised responsibility, which means that the competent authority acting as reference Member State or concerned Member State is responsible for keeping the product index up to date.

The product index and the assessment report are located on the Heads of Veterinary Medicines Agencies web-site (http://www.hevra.org/).

6.6 Multiple applications

The application for multiple marketing authorisations for an identical veterinary medicinal product with a different name by the same or a different marketing authorisation holder is possible.

7. NUMBERING SYSTEM FOR THE PROCEDURES FOR MUTUAL RECOGNITION AND DECENTRALISED PROCEDURE

Each veterinary medicinal product authorised through the mutual recognition or the decentralised procedure is characterised by a unique and specific number for unambiguous identification. (called procedure number in this document). The principle of the system is as follows:

The reference Member State is responsible for allocating the number for all mutual recognition procedures i.e. new and post-marketing applications.

The number for a specific procedure is a unique combination of six sections:

CC/D/nnnn/sss/Y/vvv

The information in the sections are:

C: the initials (2 digits) of the Reference Member State

AT:	Austria	IT:	Italy
BE:	Belgium	LV:	Latvia
CY:	Cyprus	LI:	Liechtenstein
CZ:	Czech Republic	LT:	Lithuania
DE:	Germany	LU:	Luxemburg
DK:	Denmark	MT:	Malta
EE:	Estonia	PL:	Poland
EL:	Greece	NL:	The Netherlands

ES:	Spain	NO:	Norway
FI:	Finland	PT:	Portugal
FR:	France	SK:	Slovakia
HU:	Hungary	SI:	Slovenia
IE:	Ireland	SE:	Sweden
IS:	Iceland	UK:	United Kingdom

D: 'H' for medicinal products for human use or 'V' for medicinal products for veterinary use

nnnn: the 'Medicinal Product Number' characterising the medicinal product, related to an active principle and to an applicant.

sss: is the 'Speciality Number' characterising the strength and/or pharmaceutical form of a medicinal product, in relation with the strength and/or pharmaceutical form and/or target species.

Y: is the type of application to the veterinary medicinal product:

- MR for Mutual recognition Procedure
- DC for Decentralised Procedure
- IA for Type IA Notifications
- IB for Type IB Notifications
- II for Type II Variations
- R for Renewals
- E for Repeat-use Procedures
- X for line extensions procedures

vvv: is the chronological number for notifications/variations, renewals, repeat use or line extensions procedures.

Requirements

1. The numbering system should comply with the variation Regulation (Commission Regulation (EC) No 1084/2003).

2. The numbering system should not limit the possibility for an applicant to vary a marketing authorisation.

3. The number for the section sss is "001" or "1" and not "000" or "0" for the first application for a new product even if only one pharmaceutical form/strength is applied for.

Annex I

FLOW CHART for the MUTUAL RECOGNITION PROCEDURE	
Before day -14	Applicant discusses the application with RMS RMS will • Update the AR • Allocate procedure number • Create procedure in CTS • Inform CMS of proposed start date Submission of the dossier to the CMS (and RMS if necessary) Circulation of the AR to CMS
-14 Days	Automatic validation of the application
Day 0	Start of the procedure
Day 54	CMS send comments to RMS and applicant (via RMS)
Day 57	RMS circulates LOQ to the applicant and CMS
Day 65	Applicant sends response to LOQ to RMS RMS immediately forwards this to CMS
Day 70	RMS circulates assessment of response to LOQ to applicant and CMS
Day 77/78	CMD(v) meeting RMS informs applicant of outcome of discussions immediately after the meeting
Day 82	Applicant sends new drafts of SPC, PL and labelling to RMS. Translations may be included. RMS immediately forwards this to CMS
Day 85	If necessary, final drafts of SPC, PL and labelling
Day 88	CMS send final comment to RMS
Day 89	RMS circulates final AR, SPC PL and labelling to CMS and applicant
Day 90	If consensus reached, the RMS will close the procedure If consensus not reached, referral to CMD(v).
National step	
Day 95	Applicant sends high quality translations to all member states concerned
Day 120	Granting of national marketing authorisation in RMS and CMSs if no referral to the Co-ordination group. (National Agencies will adopt the decision and will issue the marketing authorisation subject to submission of acceptable translations/mock-ups).
Day 180	Granting of national marketing authorisation in RMS and CMSs if positive conclusion by the Co-ordination group and no referral to the CHMP/CVMP. (National Agencies will adopt the decision and will issue the marketing authorisation subject to submission of acceptable translations/mock-ups).

Annex II:

FLOW CHART for the DECENTRALISED PROCEDURE	
At least 3 months before the DCP	Applicant discusses the application with RMS
- 3 Months	RMS will • Allocate procedure number • Create procedure in CTS • Inform CMS of proposed start date
-14 Days	Submission of the dossier to the RMS and CMS Validation of the application (may be extended to 30 days for generics when the reference product is not authorised in the RMS)
Assessment step I	
Day 0	RMS starts the procedure
Day 70	RMS circulates drafts of LOQ, SPC, Pl and labelling & preliminary AR to CMS
Day 100	CMS send comments to RMS
Day 105	RMS forwards LOQ to the applicant and CMS
Clock-off period	Applicant has 3 (6) months to submit response
Day 106	Valid submission of response. RMS re-starts the clock
Assessment step II	
Day 120 (0)	RMS forwards to applicant and CMS Draft AR, and drafts of SPC, PL and labelling Start of Assessment step II If consensus reached, the RMS can close the procedure
Day 145 (25)	CMS send comments to RMS and applicant (via RMS)
Day 150 (30)	RMS circulates LOQ to applicant and CMS If consensus reached, the RMS can close the procedure
Day 170 (50)	Applicant sends response to LOQ to RMS RMS immediately forwards this to CMS
Day 190 (70)	RMS circulates assessment of response to LOQ to applicant and CMS
Day 197/198 (77/78)	CMD(v) meeting RMS informs applicant of outcome of discussions immediately after the meeting
Day 202 (82)	Applicant sends new drafts of SPC, PL and labelling to RMS. Translations may be included. RMS immediately forwards this to CMS
Day 205 (85)	If necessary, final drafts of SPC, PL and labelling
Day 208 (88)	CMS send final comment to RMS
Day 209 (89)	RMS circulates final AR, SPC PL and labelling to CMS and applicant
Day 210 (90)	If consensus reached, the RMS will close the procedure If consensus not reached, referral to CMD(v)

National step	
Day 125/155/215/275	Applicant sends high quality translations to all member states concerned
Day 150/180/240	Granting of national marketing authorisation in RMS and CMSs if no referral to the Co-ordination group. (National Agencies will adopt the decision and will issue the marketing authorisation subject to submission of acceptable translations/mock-ups).
Day 300	Granting of national marketing authorisation in RMS and CMSs if positive conclusion by the Co-ordination group and no referral to the CHMP/CVMP. (National Agencies will adopt the decision and will issue the marketing authorisation subject to submission of acceptable translations/mock-ups).