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CHAPTER 3

Community Referral Procedures

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CHAPTER 3 Community Referral Procedures

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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 29 of Directive 2001/83/EC ("Mutual Recognition and Decentralised referral")

2. Article 30 of Directive 2001/83/EC ("Divergent decision referral")

3. Article 31 of Directive 2001/83/EC ("Community interest referral")

4. Articles 35[1] and 36 of Directive 2001/83/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 Human Use (CHMP) of the European Medicines Agency's (EMEA/Agency) or, in specific cases, by the Committee for Herbal Medicinal Products (HMPC). 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).

Part A of this chapter sets out the details for the above procedures.

Community pharmaceutical legislation has also created a mechanism by which Member States may refer certain matters to the Committee for Herbal Medicinal Products (HMPC) of the EMEA, but which does not lead to a binding Community procedure. These situations are foreseen in:

1. Article 16c(1)(c) of Directive 2001/83/EC ("Adequacy of evidence of the long standing use referral")

2. Article 16c(4) of Directive 2001/83/EC ("Traditional use less than 15 years referral")

These referrals to the HMPC lead to an opinion and also in some cases the Article 16c(4) referrals may lead to a monograph which Member States shall take into account.

Part B of 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.

PART A : REFERRALS UNDER ARTICLES 29, 30, 31, 35 AND 36 OF DIRECTIVE 2001/83/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 public health is necessary) Member States may take unilateral action whilst waiting for the outcome of a Community referral. These cases are illustrated in section 6.

The procedural elements of the referral procedure to the CHMP are laid down in Articles 32, 33 and 34 of Directive 2001/83/EC. These procedural elements are the same for all types of referrals to the CHMP and are described in section 7.

Please note that for traditional herbal medicinal products, as defined in Article 1(29) of Directive 2001/83/EC, the referrals of this Part A of this Chapter are also applicable and, in this case, the HMPC is the competent Committee, assuming the tasks which are normally carried out by the CHMP (Article 16h(1)(c) of Directive 2001/83/EC).

2. Article 29(4) of Directive 2001/83/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 29(1) to (3) of Directive 2001/83/EC, a referral according to Article 29(4) shall be triggered[2].

The referral shall be triggered by the reference Member State, on the grounds of potential serious risk to public health, 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 public health, the Commission has adopted a guideline, available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm.

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 public health are answered, and that all 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 public health has been raised in accordance with Article 29(1) by a concerned Member State, a withdrawal of the application in some of the Member States

[2] Homeopathic medicinal products subject to the special simplified registration procedure foreseen in Article 14 of Directive 2001/83/EC may not be referred to the CHMP. If agreement within the coordination group procedure is not reached, national authorities are competent to decide on the registration.

will not stop the matter from being discussed within the Coordination Group (CMD(h)) and, eventually, from a referral procedure being triggered.

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

2.3 Procedural steps leading to an Article 29 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 32, 33 and 34 of Directive 2001/83/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 public health grounds and should be precise. A notification form for a referral to the CHMP/EMEA 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 8, 10, 10a, 10b or 10c and 11 of Directive 2001/83/EC.

2.4 Scope of the referral

The CHMP 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 medicinal product concerned might present a “potential serious risk to public health”.

The term 'risk' related to the use of medicinal products is defined in Directive 2001/83/EC, Article 1(28, first indent), as 'any risk relating to the quality, safety or efficacy of the medicinal product as regards to patients' health or public health'. In addition, on the basis of Article 29(2) of Directive 2001/83/EC, the Commission has adopted a guideline to define a potential serious risk to public health, available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm.

If the CHMP is asked about "potential serious risk to public health" 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 CHMP and to the decision of the Commission as provided in Articles 32, 33 and 34 of Directive 2001/83/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 CHMP opinion.

In cases where the assessment of the CHMP 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 CHMP 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 29(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 medicinal product without waiting for the outcome of the procedure laid down in Article 32. 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 30 of Directive 2001/83/EC ("Divergent decision referral")

3.1 Basic principles

Any Member State, the Commission or the applicant/marketing authorisation holder of a particular medicinal product may trigger a referral if divergent decisions on the authorisation, suspension or revocation of a particular 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 30(1) of Directive 2001/83/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 30(1) may be invoked, for instance, in the following cases:

- Where a particular medicinal product has been nationally authorised in two or more Member States and the authorisations diverge;

- Where a particular 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 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.

According to Article 30(2) of Directive 2001/83/EC, "in order to promote harmonisation of authorisations for medicinal products authorised in the Community, Member States shall, each year, forward to the coordination group a list of medicinal products for which a harmonised summary of product characteristics should be drawn up. The coordination group shall lay down a list taking into account the proposals from all Member States and forward this list to the Commission. The Commission or a Member State, in agreement with the Agency and taking into account the views of interested parties, may refer these products to the Committee in accordance with paragraph 1".

Thus, the "divergent decision referral" may be used as a tool for the harmonisation of summary of product characteristics referred to in the second paragraph of Article 30.

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 30 referral

The referrer (Member State, applicant/marketing authorisation holder or the Commission) sends the question to the CHMP for consideration, together with a detailed explanation of the issue(s) raised. A notification form for a referral to the CHMP/EMEA 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 30(1), he is recommended to have a pre-referral meeting with the EMEA. 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 CHMP 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 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 31 of Directive 2001/83/EC ("Community interest referral")

4.1 Basic principles

Article 31 states that Member States, the Commission or the applicant(s)/marketing authorisation holder(s) of the concerned 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 public health related to medicinal products on the market in the Community in the light of quality, safety and efficacy data and to the free movement of products within the Community.

Whenever a Member State or the Commission or applicant(s)/marketing authorisation holder(s) invokes Article 31, it should duly identify the relevant interests of the Community and set out how they are involved.

An Article 31 referral may concern only one medicinal product or a range or class of medicinal products (an active substance, which is present in several different medicinal products with different invented names and different marketing authorisation holders, or different active substances and medicinal products belonging to the same therapeutic class) - so-called 'class referral'.

When the referral concerns a range of medicinal products or a therapeutic class the specific provisions of Article 31(2) will apply. In this case, the legislation expressly states that the Agency/CHMP 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 31 referral

The referrer (Member State(s), applicant(s)/marketing authorisation holder(s) or the Commission) clearly identifies the question which is referred to the CHMP 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 CHMP/EMEA 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 EMEA. Pre-referral meetings between the applicant/marketing authorisation holder and the EMEA 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 medicinal product(s).

4.4 Scope of the referral

4.4.1 Referral relating to a specific medicinal product

The CHMP is called upon to issue an opinion on a matter involving Community interests, on the basis of a question referred to it. However, the CHMP may consider aspects other than those explicitly mentioned in the referral which are necessary to evaluate quality, safety and efficacy of the 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 status.

4.4.2 Class referral

Where the referral to the Committee concerns a range of 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 35 referral may only apply to those medicinal products if they were covered by the authorisation procedures referred to in Chapter 4 of Directive 2001/83/EC (i.e. mutual recognition and decentralised procedures) or when, having been granted purely national marketing authorisations, they have been subject to a referral[3]. Where a Community interest referral procedure related to so-called “purely national” marketing authorisations has been limited to specific parts of the authorisations, Member States may continue to vary them using national procedures.

Centrally authorised medicinal products belonging to a class subject to an Article 31 referral may not be part of the referral procedure itself but may be handled where necessary via a parallel procedure according to Article 20 of Regulation (EC) No 726/2004 triggered by the Commission.

3 With the exception of a partial harmonisation within the meaning of paragraps 48 and 49 of the judgement of the European Court of Justice in case C-39/03 P "Artegodan" (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).

5. Articles 35 and 36 of Directive 2001/83/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 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 35 of Directive 2001/83/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 35 of Directive 2001/83/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 public health, by reference to Article 36 of Directive 2001/83/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 35 of Directive 2001/83/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 35 of Directive 2001/83/EC and 6(13) of Regulation (EC) No 1084/2003.

Article 37 of Directive 2001/83/EC extends the scope of Articles 35 and 36 referrals to human medicinal products authorised by Member States following an opinion of the CPMP given in accordance with Article 4 of Directive 87/22/EEC before 1 January 1995 (ex-concertation 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 35 and 36 referrals

For Article 35 and Article 36 referrals the procedural steps of Article 29 and Article 31 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 35(2) of Directive 2001/83/EC (i.e. the procedure for referral to CHMP) shall apply where it has not been possible to achieve agreement under the mutual recognition procedure for a variation.

Article 36 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 2001/83/EC (mutual recognition or decentralised procedures) or its suspension or withdrawal is necessary for protection of public health.

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

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

6. Unilateral Action by Member States in urgent cases

When concerns about a 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 public health and until a definitive action is adopted. In accordance with Article 36 (2) of Directive 2001/83/EC, in these specific cases, the Member States may temporarily adopt national measures suspending the marketing and use of a 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 107 of Directive 2001/83/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 any variation or the suspension or revocation, in accordance with the guidelines referred to in Article 106(1) of the same Directive, of a marketing authorisation for any medicinal product – even purely nationally authorised products – resulting from the evaluation of pharmacovigilance data.

Article 107(2) of Directive 2001/83/EC also allows Member States, “where urgent action to protect public health is necessary”, to suspend the marketing authorisation of a specific 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 107, that a Member State is considering suspension or revocation of a marketing authorisation, or that urgent action was undertaken by a Member State, by suspending a marketing authorisation, the CHMP 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 121(3).

When the Agency is informed, on the basis of Article 107, that a Member State is considering a variation of a marketing authorisation, the CHMP may, at request of a Member State, prepare an opinion to address the issue.

7. Procedural elements

Notwithstanding the legal provisions described below (Articles 32, 33 and 34 of Directive 2001/83/EC as amended), it is suggested to carry out some 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 CHMP, indicating the medicinal product concerned, pharmaceutical forms and/or strengths, route of administration, 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 CHMP, each Member State is asked to make available to the Agency before the end of the first CHMP meeting following the referral a list of the names of the 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) and route(s) of administration.

In the case of Article 29 referrals triggered in the frame of a repeat use mutual recognition procedure, the list of the names of the medicinal product affected by the referral shall also include those authorised by the previous mutual recognition procedure(s).

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

For Article 30(1) and Article 31 referrals initiated by the applicant(s)/marketing authorisation holder(s), the Agency will inform the applicant(s)/marketing authorisation holder(s) of the appropriate fee to be paid.

7.1 Organisation of work within the CHMP/EMEA

The CHMP 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 CHMP on a case-by-case basis.

In cases of a 'class referral', according to Article 31(2), it is not necessary to appoint a (co-) rapporteur for each 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 CHMP 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 CHMP meeting following the initiation of the referral, the CHMP 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 fist CHMP meeting following the initiation of the referral, the CHMP starts its assessment of the issues referred. A list of questions may be adopted at day 30 of the procedure.

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

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

7.2 Hearing of the applicant/marketing authorisation holder

Before issuing its opinion, the CHMP 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 CHMP considers the matter and issues a reasoned opinion within 60 days of the date of the referral.

For Article 30 and Article 31 referrals, the CHMP 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 CHMP 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 CHMP takes to assess the data provided. The CHMP will not exceed the overall timeframe provided in the legislation.

The CHMP 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 CHMP 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 CHMP/EMEA Secretariat
Day 1	First meeting of the CHMP following notification of referral. The CHMP discusses the question(s) referred during the plenary meeting. Rapporteur/(Co)-Rapporteur appointed/confirmed, as applicable
	Adoption of CHMP List of questions to be addressed by the MAHs/ applicant(s) and timetable
Clock stop	For the MAHs/applicant(s) to answer CHMP 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 CHMP 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 CHMP members on the (Co-)Rapporteur(s) assessment report(s) and draft SPC/Labelling/PL (if applicable)
Day 30	Discussion at the CHMP:
	Adoption of the CHMP Opinion, or
	Adoption of CHMP 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 CHMP opinion (with annexes as provided in Article 32 of Directive 2001/83/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 CHMP/EMEA Secretariat
Day 1	CHMP 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 CHMP discusses the question(s) referred during the plenary meeting. Rapporteur/(Co)-Rapporteur appointed/confirmed. Adoption of the CHMP 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 CHMP members on the (Co-)Rapporteur(s) assessment reports and draft SPC/Labelling/PL (if applicable)
Day 30	Discussion at the CHMP: Adoption of the CHMP Opinion, or Adoption of CHMP 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 CHMP opinion (with annexes as provided in Article 32 of Directive 2001/83/EC)

7.4 CHMP opinion and re-examination mechanism

The opinion of the CHMP may have implications for the applicant(s)/marketing authorisation holder(s), i.e., where the CHMP 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 11 of Directive 2001/83/EC should be amended, or
- The authorisation should be granted subject to conditions, considered essential for the safe and effective use of the medicinal product including pharmacovigilance, or
- The marketing authorisation should be suspended, varied or revoked.

Once the opinion of the CHMP 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 CHMP 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 CHMP, 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 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 medicinal product concerned, in accordance with Article 32(5) of Directive 2001/83/EC, the following documents are annexed to the opinion:

i. List of the 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 medicinal product including pharmacovigilance, if applicable;

iv. Details of any recommended conditions or restrictions with regard to the safe and effective use of the medicinal product, if applicable;

v. The proposed text of the labelling and package leaflet;

vi. Scientific conclusions justifying the outcome of the referral.

Applicants are recommended to take into account the need for appropriate design and layout of the information to be included within the package leaflet and any associated consultation with target patient groups (“user testing”) to ensure that it is legible, clear and easy to use.

In the cases of an Article 29 or Article 31(2) referral where only parts of the summary of products characterictics 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 in that sense.

In the event of an opinion recommending the suspension or revocation of the marketing authorisation(s) for the 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 medicinal product addressed to the applicant/marketing authorisation holder according to Article 32(4)(c) and (5)(b) and (c) of Directive 2001/83/EC

In the cases foreseen in Article 32(4)(c) and (5)(b) and (c) of Directive 2001/83/EC the authorisation should be granted subject to certain conditions, in view of conditions considered essential for the safe and effective use of the medicinal product including pharmacovigilance or other recommended conditions or restrictions with regard to the safe and effective use of the medicinal product.

The opinion/assessment report of the CHMP 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 (risk management plan) 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 CHMP.

8. Decision making procedure at Community level

After the reception of the final opinion of the CHMP, 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 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 medicinal product including pharmacovigilance, and any conditions or restrictions with regard to the safe and effective use of the 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 CHMP

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 proving 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 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 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 medicinal product has been subject to multiple applications for marketing authorisation.

In the case of a subsequent application for the same 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 public health or issues which have not been previously considered. Any Member State or the Commission would as appropriate refer the new scientific issue to the CHMP in order to start a new referral procedure.

The same applies in case where a marketing authorisation is pending for the 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 medicinal products with the same active substance(s) can be submitted. For

instance, if an Article 30 referral concerns the "originator" medicinal product, applications for "generic" medicinal products of this "originator" 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 31 "class" referrals, if applications for marketing authorisations of 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 medicinal product is involved in a referral. However, when a referral procedure based on Article 29 is ongoing it is recommended that no new variation procedure is started for the medicinal product concerned, unless it relates to public health matters.

9.3 Subsequent applications occurring after finalisation of the referral

Subsequent applications for a specific medicinal product which has been the subject of a referral must use the harmonisation achieved following the referral. After Articles 29, 30 and 31 referrals subsequent applications for the same 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 public health. In accordance with Articles 8(3)(l) and 18 of Directive 2001/83/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 30(1) and Article 31 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 31(2) referral, there may be a large number of products. In this case, different Reference Member States can be chosen for different medicinal products but the harmonisation should be maintained.

In the case of Article 30 or Article 31 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.

PART B : REFERRALS UNDER ARTICLE 16C OF DIRECTIVE 2001/83/EC

1. Introduction

Part B of Chapter 3 deals with the situations where a referral is made to the Committee for Herbal Medicinal Products (HMPC) under Article 16c of Directive 2001/83/EC and intends to provide practical guidance on the referral procedure.

Please note that for traditional herbal medicinal products, as defined in Article 1(29) of Directive 2001/83/EC, the referrals of Part A of this Chapter are also applicable and, in this case, the HMPC is the competent Committee, assuming the tasks which are normally carried out by the CHMP (Article 16h(1)(c) of Directive 2001/83/EC).

For all other herbal medicinal products the CHMP remains the competent Committee for referrals. However, the HMPC is called to give its opinion on the herbal substance contained in the herbal medicinal product concerned, where appropriate (Article 16h(1)(d) of Directive 2001/83/EC).

2. Article 16c(1)(c) of Directive 2001/83/EC (“adequacy of evidence of the long standing use referral”)

This referral may be started at the request of a Member State where an application for traditional use registration for a traditional herbal medicinal product has been submitted.

The HMPC is asked to draw up an opinion on the adequacy of the evidence of the long-standing use of the product, or of the corresponding product, where it has been in medicinal use throughout a period of at least 30 years preceding the date of the application, including at least 15 years in the Community. Namely, it shall assess whether the data on long standing use and experience of the traditional herbal medicinal product are sufficient to demonstrate plausible efficacy and pharmacological effects. A notification form for a referral to the HMPC/EMEA is added in the annex.

Although the legislation does not provide for a specific timeframe, the HMPC has agreed to endeavour to issue a reasoned opinion within 60 days of the date of referral. This time frame is indicative and may be subject to prolongation, namely when the applicant(s) is provided with an opportunity to present written or oral explanations.

It should be noted, nevertheless, that the limit of 210 days foreseen in Article 17(1) of Directive 2001/83/EC for the finalisation of the procedure for granting a marketing authorisation has to be respected.

3. Article 16c(4) of Directive 2001/83/EC ("Traditional use < 15 years referral")

This referral shall be started at the request of a Member State where an application for traditional use registration for a traditional herbal medicinal product has been submitted, in the specific case where the medicinal product has been used in the Community for less than 15 years, but is otherwise eligible for the simplified registration as determined by the referring Member State.

According to Article 16c(4) of Directive 2001/83/EC as amended, the Member States shall refer the matter to the HMPC for an opinion before taking a decision on an application for a traditional use registration.

The HMPC is called upon to issue an opinion on whether the medicinal product is eligible for simplified registration, although it has been used in the Community for less than 15 years. A notification form for a referral to the HMPC/EMEA is added in the annex.

Although the legislation does not provide for a specific timeframe, the HMPC has agreed to endeavour to issue a reasoned opinion within 60 days of the date of referral. This time frame is indicative and may be subject to prolongation, namely when the applicant(s) is provided with an opportunity to present written or oral explanations.

It should be noted, nevertheless, that the limit of 210 days foreseen in Article 17(1) of Directive 2001/83/EC for the finalisation of the procedure for granting a marketing authorisation has to be respected.

In addition to issuing this opinion, the HMPC shall evaluate the possibility of establishing a Community herbal monograph for that medicinal product. When the monograph is established it shall be taken into account by the Member State when taking its final decision to register the product.

4. Organisation of work within the HMPC

In order to consider the matter, the HMPC 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 HMPC on a case-by-case basis. Once the appointment of the (co-) rapporteur(s) has been made, the EMEA informs the applicant(s) and all Member States.

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

At the first HMPC meeting following the submission of the referral, the HMPC adopts the question(s) to be addressed to the applicant(s) if any and discusses, on the basis of the proposal from the Member State making the referral, the scope of the documentation actually requested or needed. The HMPC may also take into account any other information at its disposal which concerns the quality, safety and the plausibility of the pharmacological effects or efficacy of the medicinal product and which may help in arriving at its opinion.

ANNEX: Notification forms

NOTIFICATION TO THE CHMP*/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 29(4) OF DIRECTIVE 2001/83/EC FAX NUMBER –44 20 75237051

This notification is an official referral for arbitration to the CHMP made by the Reference Member State following the procedure in the Coordination Group (CMDh)

Reference Member State (RMS):----------

Concerned Member States (CMS):----------

Member State(s) who raised the potential serious risk to public health:----------

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

Product Name <in the RMS>, if appropriate, Strength and Pharmaceutical Form**	
Active substance	
Applicant/Marketing Authorisation Holder(s)	
Mutual Recognition Procedure number	

< Member State(s) who raised the potential serious risk to public health> CONSIDER(S) THAT THE AUTHORISATION OF THIS MEDICINAL PRODUCT MAY PRESENT A POTENTIAL SERIOUS RISK TO PUBLIC HEALTH ON THE FOLLOWING GROUNDS

(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):

Signed

Date

* In case of herbal medicinal products as referred to in Article 16a, which are refered to the Agency under Chapter 4 of Title III, this form should be used by replacing CHMP by HMPC.
** In case of herbal medicinal products as referred to in Article 16a, which are refered to the Agency under Chapter 4 of Title III, this form should be used by including under "Product Name , if appropriate, Strength and Pharmaceutical Form" the following: <Herbal substance(s), preparation(s) or combination(s) thereof>

<Qualitative/Quantitative composition>

NOTIFICATION TO THE CHMP/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 30 OF DIRECTIVE 2001/83/EC
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 30 of Directive 2001/83/EC to the CHMP 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 CHMP MEMBERS

Name(s) of particular 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>	
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 medicinal product} (and associated names):
Rationale for the notification of the Article 30 referral

The above-mentioned 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 30 of Directive 2001/83/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, rutes of administration and presentations of the medicinal product in all EU Member States (Iceland and Norway, if appropriate) should be mentioned

NOTIFICATION TO THE CHMP/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 30 OF DIRECTIVE 2001/83/EC AS AMENDED
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 30 of Directive 2001/83/EC as amended to the CHMP made by the European Commission.

THIS NOTIFICATION IS COPIED TO APPLICANT/ MARKETING AUTHORISATION HOLDER AND ALL CHMP MEMBERS

Name(s) of particular medicinal product	
Active substance(s)	
Pharmaceutical form(s)	
Strength(s)	
Route of administration(s)	
Presentations	
Marketing Authorisation Holder(s)	

Harmonisation of Summary of Product Characteristics (SPC) for {name of medicinal product}(and associated names):
Rationale for the notification of the Article 30 referral

{name of medicinal product}was included in the list of products for SPC harmonisation, drawn up by the CMD(h), in accordance with Article 30(2) of Directive 2001/83/EC, as amended.

Having analysed the medicinal products included in such list, and after obtaining the Agency's agreement, the European Commission has decided to trigger a referral on the basis of Article 30(2) of Directive 2001/83/EC, to promote harmonisation of the authorisations granted for this medicinal product.

The CMD(h) carried out the task of identifying the divergences between the available SPCs for this product and has came to the conclusion that the above-mentioned medicinal product {name of medicinal product}(and associated names) does not have the same SPC across all EU Member States, Iceland and Norway with respect to <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 products, the European Commission notifies the EMEA of an official referral under Article 30 of Directive 2001/83/EC, as amended, in order to resolve divergences amongst the nationally authorised SPCs for the above-mentioned products and thus to harmonise its divergent SPCs across the EU.

Signed
Date

NOTIFICATION TO THE CHMP/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 31 of Directive 2001/83/EC to the CHMP made by the <following
Member State>, <Applicant(s)>, <Marketing Authorisation Holder(s), <European Commission>:

<Product Name(s), if appropriate, Strength(s) and Pharmaceutical Form(s)> <Active Substance(s)/Therapeutic class>	

<Applicant(s)/Marketing Authorisation Holder(s)> <In the referring Member State>

The <above mentioned Member State>, <above mentioned applicant(s)>, < above mentioned Marketing Authorisation Holder(s)>, <European Commission> consider(s) that it is in the interest of the Community to refer the above mentioned <medicinal product(s)><range of medicinal product(s)> <therapeutic class> to the CHMP/EMEA Secretariat.

(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):

Signed

Date

NOTIFICATION TO THE CHMP*/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 5(11) OF COMMISSION REGULATION (EC) No 1084/2003
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 5(11) of Commission Regulation (EC) No 1084/2003 to the CHMP 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 CHMP MEMBERS

Product Name<in the RMS>, if appropriate, Strength and Pharmaceutical Form**	
Marketing Authorisation Holder(s)	
Mutual Recognition variation procedure No.	

(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):

Signed

Date

* In case of herbal medicinal products as referred to in Article 16a, which are referred to the Agency under Chapter 4 of Title III, this form should be used by replacing CHMP by HMPC.
** In case of herbal medicinal products as referred to in Article 16a, which are referred to the Agency under Chapter 4 of Title III, this form should be used by including under “Product Name , if appropriate, Strength and Pharmaceutical Form” the following: <Herbal substance(s), preparation(s) or combination(s) thereof> <Qualitative/Quantitative composition>

NOTIFICATION TO THE CHMP*/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 6(12) OF COMMISSION REGULATION (EC) No 1084/2003
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 6(12) of Commission Regulation (EC) No 1084/2003 to the CHMP 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 CHMP MEMBERS

Product Name<in the RMS>, if appropriate, Strength and Pharmaceutical Form**	
Marketing Authorisation Holder(s)	
Mutual Recognition variation procedure No.	

(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):

Signed

Date

* In case of herbal medicinal products as referred to in Article 16a, which are referred to the Agency under Chapter 4 of Title III, this form should be used by replacing CHMP by HMPC.
** In case of herbal medicinal products as referred to in Article 16a, which are referred to the Agency under Chapter 4 of Title III, this form should be used by including under "Product Name , if appropriate, Strength and Pharmaceutical Form" the following: <Herbal substance(s), preparation(s) or combination(s) thereof> <Qualitative/Quantitative composition>

NOTIFICATION TO THE CHMP*/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 6(13) OF COMMISSION REGULATION (EC) No 1084/2003
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 6(13) of Commission Regulation (EC) No 1084/2003 to the CHMP 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 CHMP MEMBERS

Product Name<in the RMS>, if appropriate, Strength and Pharmaceutical Form**	
Marketing Authorisation Holder(s)	
Mutual Recognition variation procedure No.	

(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):

Signed

Date

* In case of herbal medicinal products as referred to in Article 16a, which are referred to the Agency under Chapter 4 of Title III, this form should be used by replacing CHMP by HMPC.
** In case of herbal medicinal products as referred to in Article 16a, which are referred to the Agency under Chapter 4 of Title III, this form should be used by including under "Product Name , if appropriate, Strength and Pharmaceutical Form" the following: <Herbal substance(s), preparation(s) or combination(s) thereof> <Qualitative/Quantitative composition>

NOTIFICATION TO THE CHMP*/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 36 OF DIRECTIVE 2001/83/EC
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 36 of Directive 2001/83/EC to the CHMP 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 and Pharmaceutical Form>** <Active Substance(s)>	
Mutual recognition Procedure No, when applicable	
Marketing Authorisation Holder(s)	

The above mentioned Member State, considers that it is necessary for the protection of public health to refer the above-mentioned <medicinal product(s)> <active substance(s)> to the CHMP/EMEA Secretariat.

(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):

Signed

Date

* In case of herbal medicinal products as referred to in Article 16a, which are referred to the Agency under Chapter 4 of Title III, this form should be used by replacing CHMP by HMPC.
** In case of herbal medicinal products as referred to in Article 16a, which are referred to the Agency under Chapter 4 of Title III, this form should be used by including under "Product Name , if appropriate, Strength and Pharmaceutical Form" the following: <Herbal substance(s), preparation(s) or combination(s) thereof> <Qualitative/Quantitative composition> and by deleting <Active Substance(s)>

NOTIFICATION TO THE HMPC/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 16c(1)c OF DIRECTIVE 2001/83/EC

FAX NUMBER +44 20 75237051

This notification is an official referral under Article 16c(1)c to the HMPC made by the following Member State: ----------

THIS NOTIFICATION IS COPIED TO APPLICANT AND ALL MEMBER STATES

Product Name, if appropriate, Strength(s) and Pharmaceutical Form(s)	
< Herbal substance(s), preparation(s) or combination(s) thereof> <Qualitative/Quantitative composition>	
Applicant	

Grounds for and scope of referral

THE ABOVE-MENTIONED MEMBER STATE HEREBY REFERS THIS TRADITIONAL HERBAL MEDICINAL PRODUCT, WHICH CLAIMS TO HAVE BEEN IN MEDICINAL USE THROUGHOUT A PERIOD OF AT LEAST 30 YEARS PRECEDING THE DATE OF THE APPLICATION, INCLUDING AT LEAST 15 YEARS IN THE COMMUNITY.

(please provide a summary of background information and clearly precise the question(s) that triggers the referral)
(if this space is not sufficient, please summarise and add annex):

Signed
Date

NOTIFICATION TO THE HMPC/EMEA SECRETARIAT OF A REFERRAL UNDER ARTICLE 16c(4) OF DIRECTIVE 2001/83/EC

FAX NUMBER +44 20 75237051

This notification is an official referral under Article 16c(4) to the HMPC made by the following Member State: ----------

THIS NOTIFICATION IS COPIED TO APPLICANT AND ALL MEMBER STATES

Product Name, if appropriate, Strength(s) and Pharmaceutical Form(s)	
< Herbal substance(s), preparation(s) or combination(s) thereof> <Qualitative/Quantitative composition>	
Applicant	

Grounds for and scope of referral

THE ABOVE-MENTIONED MEMBER STATE REFERS THIS TRADITIONAL HERBAL MEDICINAL PRODUCT, WHICH CLAIMS TO HAVE BEEN IN MEDICINAL USE THROUGHOUT A PERIOD OF AT LEAST 30 YEARS PRECEDING THE DATE OF THE APPLICATION BUT LESS THAN 15 YEARS IN THE COMMUNITY, AND IS OTHERWISE ELIGIBLE FOR SIMPLIFIED REGISTRATION.

(please provide a summary of background information and clearly precise the question(s) that triggers the referral)
(if this space is not sufficient, please summarise and add annex):

Signed
Date