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SCOPE OF THE PROCEDURE

Question 1

*Which type of applications should be eligible for CMDh-referral?*

**Answer:** New applications including repeat use, extensions and renewals should go via CMDh. Also type II variations and, in case of a worksharing procedure, those variations (including grouping) according to Article 20(8) of the Commission Regulation 1234/2008 shall be within the scope of a CMDh-referral.

Question 2

*If the RMS in a DCP concluded that an application is not approvable, will the application be referred to CMDh if one or more CMSs are of the opinion that the application is approvable?*

**Answer:** No. Only a positive assessment by the RMS can be the reason for a CMS to raise a potential serious risk to public health concern. The DCP will end with a decision that the product is not approvable. All member states concerned need to take a final decision at national level rejecting the application, unless it is withdrawn by the applicant.

Question 2a

*If there is consensus among Member States concerned by the end of a CMDh referral procedure that the DCP application is not approvable, should the application be referred to CHMP?*

**Answer:** No, the application will not be referred to the CHMP since all Member States concerned reached consensus. The applicant can appeal the decision to refuse the application according to national legislation in each concerned Member State. If subsequently, an appeal is successful that leads to the grant of a marketing authorisation in an individual Member State, this marketing authorisation may then be the basis of the initiation of a mutual recognition procedure.

BEFORE START OF THE PROCEDURE

Question 3

*Should the RMS or the CMDh make validity test (e.g. compliance with the guideline on the definition of potential serious risks to public health) before initiation of the referral to CMDh?*

**Answer:** It is not up to the RMS to decide if the disagreeing CMS(s) has valid reasons for a referral or not as long as the reasons for disagreement are on grounds of potential serious risk to public health in relation to the submitted dossier and explained in detail by the disagreeing CMS(s). The discussion will take place in CMDh during the 60-days procedure.

Question 4

*Who are the members of CMDh?*

**Answer:** The names and background of the persons representing each Member State in CMDh are published on the CMDh website.

Question 5
The secretariat will put the referral on the agenda of the next CMDh meeting and propose a starting date for the 60-days procedure. Will a list of planned CMDh meetings be published on a yearly basis? Could a referral be delayed because of a ‘next CMDh meeting’ being fully booked?

**Answer:** The CMDh meetings are published on the CMDh web: [http://www.hma.eu/115.html](http://www.hma.eu/115.html)

A referral could not be delayed because of a ‘fully booked meeting’. In such a case CMDh will increase their normal meeting time.

**Question 6**

As the reason for referral must be based on potential serious risk to public health, will all decisions to start the referral procedure be initiated only after a very detailed explanation supported by scientific justification provided by the CMS not agreeing on the draft assessment report, draft SmPC, draft package leaflet and labelling?

**Answer:** Yes, and it is clearly stated that there could only be scientific reasons for a referral.

**Question 7**

Is it possible to begin the referral earlier than Day 90/210 in MRP/DCP?

**Answer:** In theory yes but in practice the Member States will try to reach agreement until day 90/210 of the procedure in order to avoid a referral.

**Question 8**

Could, in certain situations, the CMDh-referral be avoided and instead a CHMP arbitration procedure be started directly?

**Answer:** No, this is not possible. The directive set up an obligation for CMDh to process a 60-days procedure and this could not be disregarded. The EMA would not accept arbitration to CHMP unless CMDh discussed the health issues according to the relevant articles in the directive.

**INITIATING THE PROCEDURE**

**Question 9**

Is the applicant allowed to ask for a CMDh referral?

**Answer:** No.

**Question 10**

Who takes the decision about the referral: the chairperson and the RMS only, or is that done in collaboration with the applicant, or at least after a discussion with the applicant?

**Answer:** The decision to refer to CMDh is in a sense automatic because as soon as one Member State has potential serious risk to public health concerns the RMS must refer the issue to CMDh. The CMDh will discuss and have an opinion if the concern should be regarded as potential serious risk to public health.
TIMETABLE

Question 11

If the CMDh meetings take place every month, and the start date is set up at the 1st CMDh meeting after Day 90, with the recommendation to have Day 60 at least 5 days after a CMDh meeting, would the CMDh referral procedure be in length a total of 65 days (+ max 30 days before it start ?)

Answer: No, counting from the start date the procedure should end 5-10 days after the second CMDh meeting at Day 60. The start date is not the date for the first CMDh meeting but rather around 20 days before the first meeting.

Question 12

The secretariat will put the referral on the agenda of the next CMDh meeting. Is there intended to be a minimum time between Day 90/210 and Day 0 of the CMDh procedure/the initial discussion at CMDh?

Answer: No minimum time is foreseen. The timing of break-out sessions makes this scenario unlikely. There will always be sufficient time between end of MRP/DCP and the CMDh meeting 1 in line with the flow chart for the procedure.

Question 13

The CMDh procedure will start no later than 30 days after Day 90/210. Presumably this will be possible at all times of the year (e.g. August, Christmas holiday period), regardless of whether CMDh meetings are scheduled. Clarification on this would be appreciated.

Answer: In theory this is possible at any time of the year, although the Christmas holiday period should if possible be avoided.

Question 14

It is assumed that the second CMDh meeting will take place 30 days after the initial CMDh meeting. It would be helpful to specifically state this.

Answer: The CMDh meeting dates are already decided see http://www.hma.eu/115.html

LIST OF QUESTIONS

Question 15

On request by the CMS(s), other relevant information can be provided by the RMS. Clarification is requested on the kind of information that could be requested by the CMS(s) and provided by the RMS.

Answer: The intention of this wording is to make it possible for CMSs to ask for any information to help the understanding of the issue. No examples are given and it is difficult to foresee what kind of information could be needed in each situation.
Question 16

Could the applicant be informed on both the information requested by the CMS(s), and the information provided by the RMS in order that the applicant views are presented in best conditions?

Answer: No, this will be taken care of in the response document later in the procedure.

Question 17

For security reasons the use of Eudralink should be recommended for dispatch of Answers to Questions.

Answer: The applicant should check national recommendations for the sending of documents via Eudralink in ‘Requirements on electronic submissions (NeeS and eCTD) and paper documentation for New Applications within MRP, DCP or national procedures’, published on the CMDh website.

Question 18

Taking advice from one of the Committees will probably take too long. It has to be kept in mind that the CMDh procedure is a process where only Member States are involved. An involvement of the Committees is not foreseen in Art. 29 (1) - (3).

Answer: The possibility to use advice from Committees will be used only if time allows this.

Question 19

Applicants are allowed to provide comments to CMDh in writing only or have it presented orally at a CMDh meeting. Could the decision on an oral hearing be made after receiving the list of questions?

In case the applicant wants to present its points of view orally at a CMDh meeting, is it still needed to provide a written response to the list of questions?

Answer: Applicants should discuss with the RMS and will be asked by the EMA secretariat within two weeks of receipt of the list of questions about the wish to present its points of view orally at a CMDh meeting. The RMS informs the CMDh whether it will be an oral hearing or not. A written response to the list of questions is always needed, even if the applicant decides to have an oral hearing with the CMDh.

Question 20

What about new analyses in response to a question?

Answer: No new data are expected to be presented during the procedure. New data (e.g. results of studies never previously provided) should be distinguished from an elaboration, new presentation or clarification of data already presented. Submission of new supporting references, including published literature, will not in general be considered as new data as they provide a means of interpreting data already presented. Results of ongoing studies from which data were not available before are likely to be regarded as new data. The RMS view will be taken into account as to what additional supporting data may be accepted at this stage of the procedure.
Question 21

Are there recommendations on the format and submission of the response document?

Answer: Yes, recommendations are given in ‘Applicant’s Response Document in Mutual Recognition and Decentralised Procedures for Marketing Authorisation Applications’, published on the CMDh website.

Question 22

Pursuant to Art. 29 (3) of Directive 2001/83/EC, only the RMS and CMS shall reach an agreement on the action to be taken. They (RMS and CMS) shall allow the applicant the opportunity to make his point in writing. Does this not mean: those Member States that were not part of the initial MRP / DCP process are not involved in the procedure under Art. 29 (3) and (4). Therefore the applicant is not obliged to send the response document to the Member States not involved, and these Member States should not state their view on the response document. Consensus should only be reached between RMS and CMS and not with those Member States that were not part of the MRP / DCP.

Answer: As further explained below it is necessary for the "non-involved" Member States to be a part of the discussions. However they will not be involved in the formal agreement.

ISSUES FOR DISCUSSION

Question 23

Is it correct that the discussion shall only refer to the potential serious risk to public health as explained in detail by the disagreeing Concerned Member State(s) and no new items shall be brought up?

Answer: Yes.

Question 24

If an issue has already been discussed in CMDh, could the same question be raised once again?

Answer: The main idea with the referral procedure is to solve problems for the future and avoid repetition of discussions. Normally it would not be appropriate to reopen issues that have previously gone through the referral procedure. The legislation does not explicitly prohibit the issue to be brought up again so in exceptional circumstances this could occur. For example if development in a scientific area could have an impact on decisions or if only a small number of Member States had been involved in a previous referral procedure. See also Notice to Applicants, Chapter 1 and 3.

OUTCOME OF PROCEDURE

Question 25

Could CMDh confirm that Member States should reach consensus on the remaining issues, rather than taking a majority position as in the Centralised Procedure?

Answer: Consensus means that all involved Member States will be in agreement.

Question 26
Question 27

Will a referral to the CHMP be decided at day 60, or will that be decided one month later?

Answer: It will be decided at Day 60 and referred immediately to the EMA.

Question 28

This question was removed in February 2014.

Question 29

This question was removed in February 2014.

WITHDRAWALS

Question 30

It should be clarified that only withdrawals that are linked to serious public health concerns should be discussed by CMDh. Applications withdrawn for other reasons (e.g. marketing reasons) should not be.

Answer: It is already made sufficiently clear, that other reasons for withdrawal are out of the scope for a CMDh referral. However if a withdrawal has been made in a Concerned Member State after that Concerned Member State has raised potential serious risk to public health concerns a referral to CMDh is unavoidable. This applies regardless of the reason for withdrawal stated from the applicant.

Question 31

The CMDh is responsible for coordinating the discussion between the Member States where there is no agreement on the assessment report, the SmPC, labelling or PL. The outcome of the procedure is either approval or refusal of the application. Therefore, why would there be any need to continue the discussion of the disagreement if the applicant decides to withdraw the application in objecting Concerned Member States?

Answer: Withdrawals occurring after the MRP has started or after day 120 of the DCP in CMS having raised PSRPPh, will trigger a referral to CMDh since the intention of the legislation is to have a discussion on the scientific matters that is considered to be a potential serious risk to public health regardless if the applicant chooses to withdraw. This is clearly stated in the legislation and there is no room for interpretation to handle it differently.

Question 31a

Will the Concerned Member State(s) in which the application has been withdrawn by the applicant(s) be part of the decision by consensus at the end of the referral procedure at CMDh?

Answer: No. If the Member State(s) from which the application was withdrawn has raised a concern as a potential serious risk to public health and that Member State(s)
considers that the potential serious risk to public health is maintained following the CMDh referral, the RMS will refer the matter to CHMP.

IN INVOLVEMENT OF NON-CONCERNED MEMBER STATES

Question 32

All Concerned Member States that have raised risk to public health issues should be encouraged to participate. It is not clear why Concerned Member States should participate if they are not involved in the procedure and it is not necessary for them to have to be in agreement.

Answer: The reason for that is that the other Member States could have the same application filed in a repeat use procedure and normally the same issue cannot be brought up in CMDh more than once so this might be the only opportunity they have got to influence the discussion, see also Q number 22.

AFTER THE 60 DAYS PROCEDURE

Question 33

By when can a MS issue a marketing authorisation? Legally at day 1 of a recognition? Practically at the end of the referral to the CMDh?

Answer: In case of negative (non agreement) outcome in CMDh: A Member State that has approved the assessment report, SmPC, labelling and package leaflet may, on request from the applicant, authorise the product when the 60 days procedure is ended and not before.
In case of a positive outcome: All Member States should approve the product within the stipulated 30 days.

Question 34

When shall the national text for product information be submitted? Should it be during the 60-days procedure or after the finalisation of the procedure?

Answer: The national translations of the texts together with the request for MA should be submitted after finalisation of the 60-days procedure. Be aware that if the 60-days procedure results in changes to the SmPC, PL or labelling this shall not result in any variations submissions.

Question 35

Who should make the request for a MA, the applicant or a future MAH and to which MS should the request be directed, the RMS or CMS(s)

Answer: The request according to article 29 (6) must come from the applicant and the applicant may ask the competent authority in each MS for an approval. If the MAH should be different from the applicant the request normally should come from the applicant with consent from the future MAH but companies are advised to consult each competent authority because this might differ according to national law.

Question 36
Where a Member State agrees with the request from the Applicant to grant a marketing authorisation for a medicinal product according to Article 29(6), i.e. where the CMDh failed to reach an agreement within the 60-day period, what should the product information (SmPC, package leaflet and labelling) to be included in the marketing authorisation be?

**Answer:** For Member States which have approved the assessment report, draft SmPC, labelling and package leaflet, the product information submitted should be the proposed SmPC, package leaflet and labelling on Day 60 of the CMDh referral procedure. However, the authorisation granted shall be without prejudice to the outcome of the CHMP referral procedure, which will have to be implemented by all the Member States concerned in the procedure.