Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary

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BEST PRACTICE GUIDE for Worksharing

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1. INTRODUCTION

1.1 This Best Practice Guide is the consequence of the implementation of *Commission Regulation (EC) No 1234/2008* of 24 November 2008 as amended by *Commission Regulation (EU) No 712/2012* of 3 August 2012.

1.2 Article 20 of the Regulation sets out the possibility for a Marketing Authorisation Holder (MAH) to submit the same type IB or type II variation, or the same group of variations affecting more than one marketing authorisations from the same holder in one application. In case a grouped application is applied within a worksharing application, this may also contain consequential IA changes.

1.3. A worksharing application cannot include extensions.

2. AIM AND SCOPE

2.1 This Best Practice Guide covers worksharing procedures for:

- a group of products from the same marketing authorisation holder[1] where none of the marketing authorisations is a centralised marketing authorisation. The worksharing application may include marketing authorisations granted via MRP/DCP as well as those authorisations issued on a purely-national basis.
- purely-national marketing authorisations held by the same MAH in more than one Member State (MS).

Where the worksharing procedure involves more than one Member State, the 'Reference Authority' shall be decided by CMDv after taking into consideration the applicants request. In cases where the worksharing procedure only contains products with the same RMS there is no need for the CMDv to choose the Reference Authority.

2.2 Some information on the submission of a worksharing procedure for a group of products from the same marketing authorisation holder where at least one of the products is centrally authorised is also provided. In these cases, the European Medicines Agency (EMA) shall be the Reference Authority.

2.3 This guidance does not cover the case of one or several changes to several different purely-national marketing authorisations which concern only one MS.

2.4 Harmonisation of the complete initial dossier or SPC and product literature is not a prerequisite for a worksharing procedure. The variation application form must reflect the same 'present' and 'proposed' situation applicable to all marketing authorisations included in the worksharing procedure.

[1] As per Commission Communication 98/C 229/03.

2.5 In order to benefit from a worksharing procedure, the application should include changes that are applicable to all the medicinal products concerned with either no or limited need for assessment of a potential product-specific impact. Therefore, applications that include changes to different marketing authorisations that require the submission of individual supportive data sets for each medicinal product concerned, which each require a separate product-specific assessment, should not be submitted as they will not benefit from worksharing and the Reference Authority may refuse to process the submission.

2.6 For the purpose of handling the worksharing procedure, the following definition of a marketing authorisation is used: all strengths and pharmaceutical forms of a certain product.

3. REFERENCES AND RELATED DOCUMENTS

3.1 Regulation 1234/2008 of 24 November 2008 as amended by Commission Regulation (EU) No 712/2012 of 3 August 2012 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products granted by a competent authority of a Member State.

3.2 NTA - Volume 6A - Chapter 5.

3.3 Commission guideline on the details of the various categories of variations.

3.4 CMDv BPG 006 Type II Variations
CMDv BPG 005 Type IB Variations
CMDv BPG 016 Grouped variations
CMDv GUI 003 Management of e-mail use during procedure and standardisation of subheadings
CMDv SOP 003 for the allocation of mutual recognition /decentralised procedure application numbers
CMDv SOP 001 Standard Operating Procedure for Disagreement in Procedures - Referral to CMDv .

4. PROCEDURE

4.1 Choice of Reference Authority

4.1.1 Where at least one of the marketing authorisations concerned has been authorised via the centralised procedure, the European Medicines Agency will be the Reference Authority. In all other cases, the applicant should propose a National Competent Authority (NCA) to act as the Reference Authority, except for Worksharing of products with the same RMS. However it should be noted that, after discussion of the proposed application, the CMDv may choose to appoint a different Reference

Authority if this is more appropriate to the marketing authorisations involved in the worksharing procedure.

4.2 Pre-submission notification (letter of intent)

4.2.1 MAHs should discuss an upcoming worksharing procedure with the proposed reference authority *before notifying* the CMDv *secretariat* by submitting a draft letter of intent, using the template published on the CMDv website (link). The letter of intent should contain the following information:

a. List of marketing authorisations concerned: name and respective MR/DC procedure numbers and/or MA number for purely-nationally authorised products.
b. Description of the change(s)* and proposed classification of those changes according to the European Commission variation classification guideline (2010/C 17/01).
c. Preferred Reference Authority.
d. Justification as to why the MAH believes that a worksharing procedure is suitable.
e. Planned submission date.
f. Explanation that all marketing authorisations concerned belong to the same MAH.
g. If applicable, details of submission/approval/rejection of the same variation(s) in any Member State(s).
h. If applicable, details of any marketing authorisations (MR/DC or purely-national) that have been excluded from the proposed worksharing procedure, with reasons.

* *If the proposed worksharing involves an update to the active substance master file, all individual changes should be specified because otherwise this can result in a delay whilst the CMDv asks for clarification from the applicant.*

4.2.2 Once the chosen national competent authority has agreed, in principle, to act as reference authority and has confirmed that the proposed variation classification(s) and any grouping(s) are acceptable, the final letter of intent should be submitted to the reference authority, copying the CMDv secretariat (CMDv@ema.europa.eu).

4.2.3 The CMDv secretariat will then include the details of the upcoming worksharing on the agenda of the next CMDv meeting. Letters of intent sent to the CMDv secretariat **15 days** in advance of the next CMDv meeting will be discussed at that meeting. A list of CMDv meetings is published on http://www.hma.eu/153.html. Letters of intent sent to the secretariat less than 15 days in advance of the CMDv meeting are unlikely to be discussed until the following month's meeting.

4.2.4 The reference authority will inform the MAH whether the worksharing application has been accepted by the CMDv within two weeks from the meeting taking place. The CMDv may – on its own initiative or if requested

by the MAH – give advice on the suitability and/or practicability of the proposed worksharing procedure.

4.3 Numbering

4.3.1 Each worksharing procedure will receive a new (non-product related) incremental variation procedure number, e. g. CC/V/xxxx/WS/vvv, to be requested from the Reference Authority.

Where:

CC	=	two letter Country Code of the Reference Authority
V	=	Veterinary domain
xxxx	=	placeholder : xxxx (is literally meant as 'xxxx')
WS	=	procedure qualifier for worksharing
vvv	=	sequential worksharing counter*.

*new counter starting from 1 for each Reference Authority

4.3.2 The MAH will insert the variation procedure number on the first page of the application form in the field 'Variation procedure number(s)' and in the cover letter.

4.3.3 A worksharing application needs to be visible in the lifecycle of individual products. It is required to identify each product included in the worksharing. This means that in addition to the variation procedure number an MRP variation number for each product has to be allocated. These MRP variation numbers should only be listed in the table 'Products concerned by this application' in the application form but not in the cover letter.

4.3.4 For purely-national marketing authorisations participating in a worksharing application no MRP variation number has to be allocated.

4.4 Application package and timelines

4.4.1 A variation or group of variations presented for worksharing should be submitted according to the normal rules applicable for variations, and should be provided as one integrated submission package covering all variations for all medicinal products. This will include a copy of the approval letter from CMDv, a common cover letter and application form together with separate supportive documentation and revised product information (if applicable) for each medicinal product concerned. This will allow the National Competent Authority to update the dossier of each marketing authorisation included in the worksharing procedure with the relevant amended/new information. The data should clearly indicate which of the variation(s) it is intended to support.

4.4.2 The Marketing Authorisation Holder shall submit the integrated submission package and any subsequent identical documentation for the worksharing procedure to all relevant authorities, i.e. the Reference Authority and all Member States where the products concerned are authorised.

4.4.3 Where the chosen Reference Authority is the Competent Authority of a Member State which has not granted a marketing authorisation for all the medicinal products affected by the application, the CMDv may on request of the Reference Authority ask another relevant authority to assist the Reference Authority in the evaluation of that application.

4.4.4 The Reference Authority will validate the application in line with the validation procedure followed for Type II variations.

4.4.5 In general, worksharing procedures will follow a 60-day evaluation timetable. However, this period may be reduced by the Reference Authority having regard to the urgency of the matter, particularly for safety issues, or may be extended by the Reference Authority to 90 days in case of complex groupings as well as for Type II variations if one of the variations is listed in Part 2 of Annex V of the *Commission Regulation EC No 1234/2008 of November 2008*[2], as amended.

4.4.6 The 30, 60 and 90 days procedures will follow the same timelines and principles as applicable for Type II variations; this includes the production of an assessment report. See *Best Practice Guide for Type II Variations* (CMDv/BPG/006). Please note this still applies even if the worksharing application only includes Type IB changes.

4.4.7 The Reference Authority can ask for advice from CMDv or any relevant Working Party during the procedure.

4.4.8 Worksharing procedures will be included in CTS for MRP/DCP products, to maintain the life-cycle management of each product.

4.4.9 The EMA will provide CMDv with a monthly overview of all on-going worksharing procedures at EMA level in which at least one of the marketing authorisations affected is not a centralised marketing authorisation. Member States provide their comments on these procedures through their respective CVMP members.

4.4.10 All communication relating to the worksharing procedure should be made via the Eudra-MRVE mailbox.

4.5 Discussion at CMDv meeting

[2] Variations relating to non-food target species, replacement or addition of serotypes, strains or antigens in vaccines against Avian Influenza, Foot and Mouth disease and Bluetongue, or replacement of strain for vaccines against equine influenza.

4.5.1 A systematic discussion of worksharing applications at CMDv meetings is not foreseen. The worksharing applications will be dealt with as normal variations; however, whenever the Reference Authority feels that discussion at CMDv could be useful the Reference Authority will propose its inclusion on the agenda.

4.6 Outcome of procedures

4.6.1 In order to avoid an unnecessary reassessment of already evaluated and agreed changes, an 'all or nothing' approach will not be adopted for worksharing procedures, i.e. a different outcome may be reached for different parts of the application; some changes may be accepted whilst other changes may be rejected. The outcome of a change will be applicable to all marketing authorisations concerned, i.e. a change will not be approved in relation to some marketing authorisations, but rejected for others.

4.6.2 The MAH may withdraw changes from a worksharing procedure when it becomes obvious that the change(s) is likely to be rejected.

4.6.3 At the end of the procedure the Reference Authority will inform the MAH and CMS of the outcome(s) of the application. In cases where some or all changes are rejected, the Reference Authority should provide a description of the reasoning for the outcome. The notification to the MAH and CMS should also include details of any changes that were withdrawn during the procedure.

4.6.4 The MAH and CMS are informed of the outcome by e-mail. The Reference Authority will also update the CTS record, which should state the reasons for rejection, if applicable.

4.6.5 For the purpose of CTS, it should be noted that a worksharing variation will be considered accepted if some or all changes are accepted; however, it will be considered rejected if all changes are rejected, or if some are rejected and some are withdrawn. If all changes are withdrawn, the application will be considered withdrawn.

4.6.6 The procedure for the submission of a revised SPC and product literature as well as national translations, in cases where these documents were affected by the variation(s), is the same as the one outlined in the *Best Practice Guides on Type II variations*.

4.6.7 Examples of suitable text for inclusion in the acceptance, acceptance/rejection or rejection notifications issued to the MAH on completion of the procedure are included in Annex 2.

4.6.8 In worksharing procedures in which the EMA acted as Reference Authority, the CMS shall approve the Final Opinion, inform the EMA and amend

accordingly the marketing authorisations concerned within 60 days, unless an Article 35 referral is initiated within 30 days following receipt of the opinion.

4.6.9 In worksharing procedures in which the Competent Authority of one of the Member States acted as Reference Authority, the CMS shall, without prejudice to article 13, approve the Final Opinion, inform the Reference Authority and amend accordingly the marketing authorisations concerned within 30 days.

4.6.10 For worksharing procedures involving authorisations approved on a national only basis; where the procedure leads to harmonisation of a section of the Summary of Product Characteristics then this must be maintained. It should not be possible for the authorisation holder to undermine this harmonisation at a later date by submitting variations to fewer Member States than included within the original worksharing procedure.

4.7 Referrals

4.7.1 If, in case of one or more variations, there is no agreement between the member states about whether they should be accepted or rejected, the procedure will, in cases of potential serious risk to human or animal health or to the environment, be referred to the CMDv. This still applies if the objection relates to a Type IB change.

4.7.2 The party in disagreement shall give a detailed statement of the reasons for its position to all member states concerned and to the MAH.

4.7.3 The Reference Authority collects the reasoning and notifies the matter to CMDv if the variation in question has not been withdrawn by the MAH before the finalisation of the worksharing procedure.

4.7.4 In situations where single changes in the worksharing are referred to the CMDv the whole procedure will not be closed until the referral is finalised. However, the CMDv discussion will only deal with the single change in question, not with the whole group.

4.7.5 Procedures may only be notified for referral to the CMDv by the Reference Authority and not by the MAH.

ANNEX 1

Template for letter of intent for the submission of a worksharing procedure to the CMDv : LINK

ANNEX 2

Sample text for inclusion in the acceptance, acceptance / rejection or rejection notifications issued to the MAH on completion of the procedure.

Example 1

ACCEPTANCE OF THE WORKSHARING APPLICATION

The Reference Authority accepts all the changes detailed in your application. The following changes have been notified:

<< enter changes applied for>>

The variations are considered acceptable on the basis that the application has been submitted simultaneously to all Concerned Member States and the relevant fees have been paid as required by national competent authorities. Failure to comply with this provision may subsequently deem the variations invalid.

[Please note the following changes were withdrawn from this application during the procedure]

Example 2

ACCEPTANCE / REJECTION OF THE WORKSHARING APPLICATION

The Reference Authority accepts some of the changes detailed in your application including the following:

<< enter changes applied for>>

The above variations are considered acceptable on the basis that the application has been submitted simultaneously to all Concerned Member States and the relevant fees have been paid as required by national competent authorities. Failure to comply with this provision may subsequently deem the variations invalid.

However, the Reference Authority rejects the following changes for the reasons given below:

[Please note the following changes were withdrawn from this application during the procedure]

Example 3

REJECTION OF THE WORKSHARING APPLICATION

The Reference Authority rejects all the changes detailed in your application for the following reasons:

<<enter reason for non-acceptance>>

[Please note the following changes were withdrawn from this application during the procedure]