

**CMDh BEST PRACTICE GUIDE
ON THE USE OF THE ELECTRONIC COMMON TECHNICAL
DOCUMENT (eCTD)
IN THE MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES**

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1. INTRODUCTION

Following experience gained both by industry and National Competent Authorities (NCAs), this best practice guidance has been developed in order to facilitate the use of the eCTD as a submission format in the Mutual Recognition Procedure (MRP) and Decentralised Procedure (DCP). The guidance shows the way for an applicant to meet their legal obligations within MRP and DCP in eCTD format. Some general principles apply to both procedures but there are some differences between the details for the MRP and DCP.

In order to greatly simplify this revised version of the guidance it has been agreed by CMDh and HMA to handle all national translations outside the eCTD. Hence this major change allows the new version of this guidance to focus almost exclusively on the mutual parts of the MRP and DCP and no longer also the national phase.

Although HMA announced in February 2005 that all NCAs should be ready for electronic-only submissions by the end of 2009, several NCAs will not be ready to accept fully paperless submissions by that date. Transparency on the situation for e-readiness is given by the HMA [<http://www.hma.eu>].

This guidance is only applicable to submissions in eCTD format and does not take into account specific issues that may arise if applicants need to provide documentation in eCTD, NeeS and paper formats for different Member States.

Applicants must therefore continue to comply with any national requirements to provide full or partial paper copies in addition to the eCTD as stated at the CMDh website [<http://www.hma.eu/277.html>] and to consider the provision of NeeS if needed by those NCAs, if any, that may not yet ready to receive eCTDs, particularly in support of the initiation of the MRP and Repeat Use Procedure. This might be achieved by use of an eCTD building tool with a function to print the current valid documents of an eCTD to paper or electronic media.

Where this guidance recommends submitting documents outside the eCTD, it is recommended that they are submitted according to the file naming principles of the eCTD standard.

2. GENERAL CONCEPTS

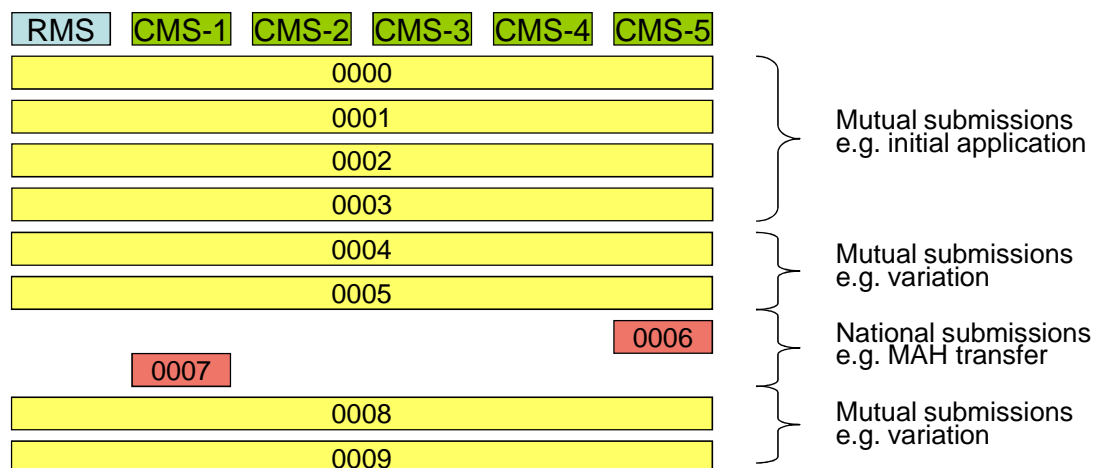
A key principle of this guidance is that the submissions made to the Reference Member State (RMS) and all Concerned Member States (CMSs) are managed as a single, comprehensive, eCTD. However at present, in the absence of a central repository for submission of MRP/DCP applications, it will be necessary to provide a copy of the eCTD to each NCA involved.

The content provided to each NCA will be identical for all the mutual stages of the procedures whereas activities such as transfers of ownership, applications for change in legal status and specific national requirements, if any, should normally be provided to the NCA concerned only. This means that it is allowable to submit submissions to NCAs in a non-sequential order e.g. CMS-1 may receive submission 0000, 0001 and 0002 while CMS-2 receives 0000 and 0002 but never 0001 if that sequence only concerned CMS-1. However, a sequence number should never be re-used except for resubmissions following a technical invalid submission, so the next submission (e.g. a variation) should utilise the next unused sequence number and so create a continuous numbering system.

The Applicant should maintain the full set of sequences as a comprehensive record.

Conceptually, this ‘comprehensive’ model is presented in Figure 1. More details of the model are presented in later sections of this best practice document.

Figure 1: The Comprehensive Model for the Use of the eCTD in MRP/DCP



There should always be a structured so called Tracking table included as an annex to the Cover Letter placed within the ‘common’ directory with the filename common-cover-tracking.pdf or common-cover-tracking.xml. The tracking table provides a history of the sequences that were provided to each NCA so that there can be confidence that sequences have not been omitted by oversight. The entries in the table should be consistent with the information in the envelope, namely that countries in the table should correspond to those included in the envelope and that the submission description used should be the same. This table should be updated with each sequence with the use of the operation attribute “new” and the ‘common’ country attribute. Examples of these tracking tables are provided later in this guidance.

It is strongly recommended that applicants should submit using this ‘comprehensive’ model since it ensures that the same sequence number is used for all mutual submissions and minimises and potential confusion between NCAs. However, in the short-term only, it remains acceptable but not recommended, to use the “parallel national model” i.e. to submit separate, national eCTDs to each NCA since it is recognised that at this time not all applicants can readily support the centralised submission management infrastructure that the use of the comprehensive model infers.

Conceptually, this ‘parallel national’ model is shown in Figure 2. No more detail regarding this model is provided in this guidance as its use should be regarded solely as an interim measure. Applicants should transition to the use of the ‘comprehensive’ model at the earliest opportunity. Appropriate times for migration from the national to the comprehensive model are at a Repeat Use Procedure or a change of RMS but it can also, after consultation with the RMS, occur at another time point in the procedure. Applicants should never migrate from the comprehensive to the national model.

Figure 2: The Parallel National Model for the use of eCTD in MRP/DCP

RMS	CMS-1	CMS-2	CMS-3	CMS-4	CMS-5
0000	0000	0000	0000	0000	0000
0001	0001	0001	0001	0001	0001
0002	0002	0002	0002	0002	0002
0003	0003	0003	0003	0003	0003
0004	0004	0004	0004	0004	0004
0005	0005	0005	0005	0005	0005
0006					0006
0007	0006	0006	0006	0006	0007
0008	0007	0007	0007	0007	0008

}

Mutual submissions
e.g. initial application

}

Mutual submissions
e.g. variation

}

National submissions
e.g. MAH transfer

}

Mutual submissions
e.g. variation

The Cover Letter should state which model is being used for the management of the eCTD and indicate when the model is changed from 'parallel national' to 'comprehensive'. Refer to the CMD(h) recommendations for the content of the cover letter for new applications and also a recommended template.

[\[http://www.hma.eu/91.html\]](http://www.hma.eu/91.html)

3. DECENTRALISED PROCEDURE (DCP)

3.1. Validation and Assessment

See Figures 3a, 3b and 3c, Tables 1a, 1b and 1c

The initial eCTD containing all common parts as well as any country-specific information should be submitted to the RMS and all CMSs. A separate Module 1 eCTD envelope should be used for each Member State included in the Procedure. Information for all countries will therefore be contained in this one submission. The organisation of the dossier and the use of the country attributes assigned to applicable documents will ensure that the CMSs will be easily able to find their country-specific information.

If there are updates to be made as a consequence of the regulatory validation process then it will depend upon the nature of the request as to whether the RMS and all CMSs or only a specific CMS receives an update.

During the validation period, the applicant can choose if any requested new or updated documents are sent as either new eCTD sequences or outside the eCTD.

If they are sent as eCTD sequences *during* the validation period it can be done in different ways.

- If there is a request for an update concerning Modules 2-5 or a common part of Module 1, the applicant should provide the updating sequence to the RMS and all CMSs. (Figure 3a, Table 1a)
- If the validation update concerns information regarding country-specific information (e.g. an application form) then this should be provided to the specific CMS only. (Figure 3b, Table 1b)
- If there are validation updates for both common and country-specific information then these can be combined in a single sequence and provided to the RMS and all CMSs.

If the validation has been handled outside the eCTD *during* the validation period, at the end of the validation period all submitted documents should be resubmitted to the RMS and all CMS with the relevant operation attribute in one eCTD sequence. It should be clearly stated in the cover letter that all documentation has been previously provided outside the eCTD during the validation period. (Figure 3a, Table 1a). However, if this validation sequence concerns country-specific information only then it need only be sent to those NCAs affected (Figure 3c, Table 1c).

If a submission is found to be *technically* invalid, a corrected sequence should always be submitted immediately, re-using the same sequence number.

During the Assessment Steps, any additional sequences, e.g. Responses to Questions, should also be submitted to the RMS and CMSs. If, due to the tight time limits, the responses are sent outside the eCTD, a new sequence should always follow with any new or updated documents placed in the dossier with the correct operation attribute. This also applies to the final agreed English product information (Summary of Product Characteristics, Package Leaflet and Labelling) that should also be submitted to the RMS and CMSs.

The common English product information texts communicated during the procedure should always be included in the eCTD as for all other relevant documents at the various key steps (e.g. in the initial application, responses to LoQ and final agreements). Word copies of the included PDFs, which are requested by some of the NCAs, should always be kept outside the eCTD as working documents.

Draft responses sent to the RMS during the ‘Clock-off Period’ should be handled outside the eCTD as they are not considered to be official submissions. Also procedural email correspondence should be exchanged outside the eCTD if not directly relating to the content of the dossier. Any other exemptions should be discussed with the RMS before submission.

Figure 3a: DCP: Assessment Phase – including a validation update for common information submitted either during the validation phase or at the end of the validation phase (See Table 1a)

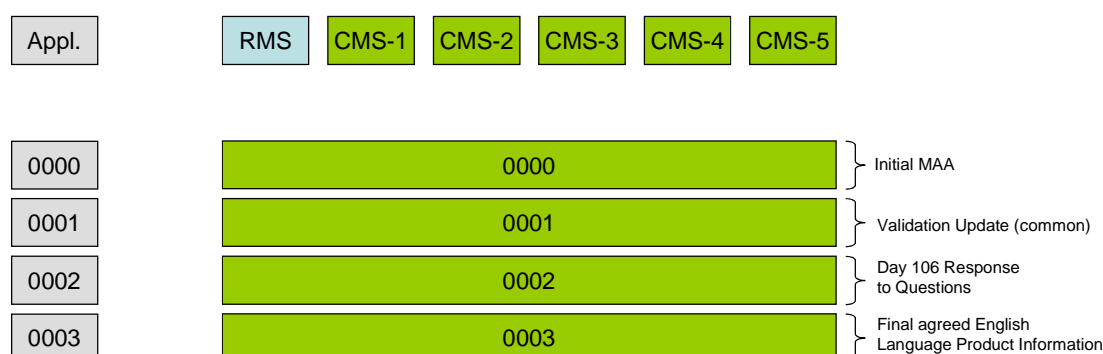


Figure 3b: DCP: Assessment Phase – including validation updates for country-specific information submitted during the validation phase (See Table 1b)

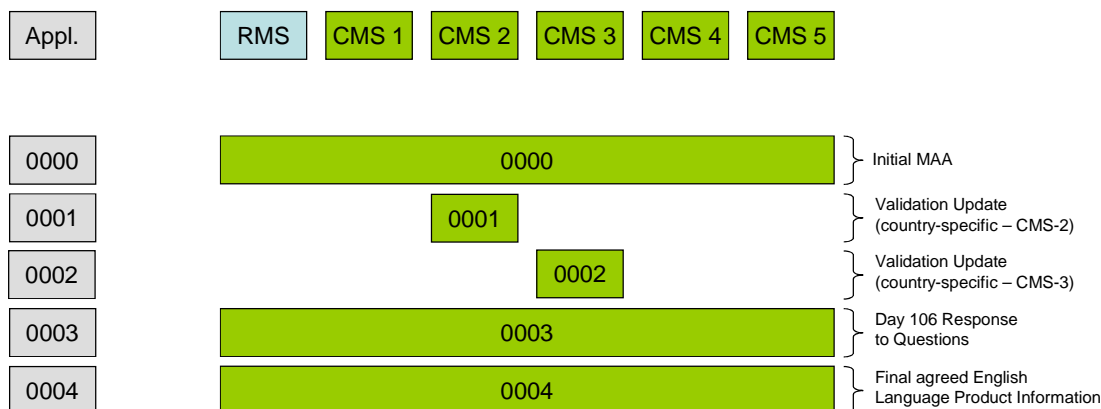
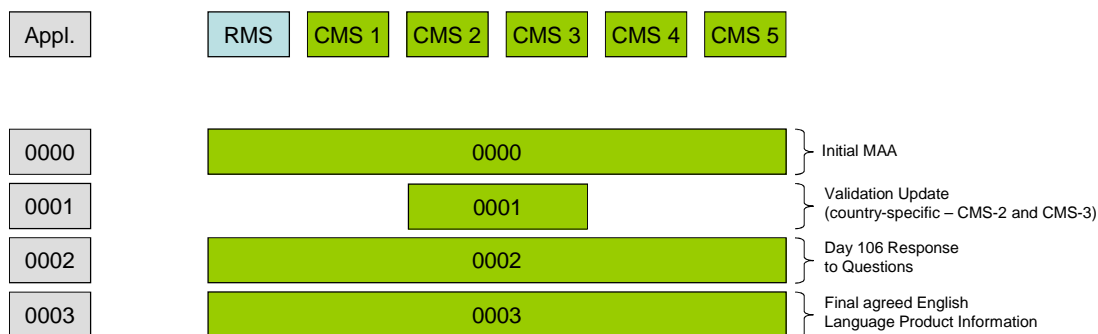


Figure 3c: DCP: Assessment Phase – including validation updates for country-specific information submitted after the end of the validation phase (See Table 1c)



3.2. Submission of National Translations of Product Information

The national translations should be handled outside the eCTD in MRP and DCP, since the national phases are a responsibility of each NCA and normally handled by local affiliates of the applicants.

3.3. Subsequent Lifecycle Submissions

Once initial authorisations are received the procedure is now that of an MRP. The envelope information for subsequent lifecycle submissions should have the <procedure_type> set to 'mutual-recognition'. The guidance in Section 4, Mutual Recognition Procedure should then be followed.

4. MUTUAL RECOGNITION PROCEDURE (MRP)

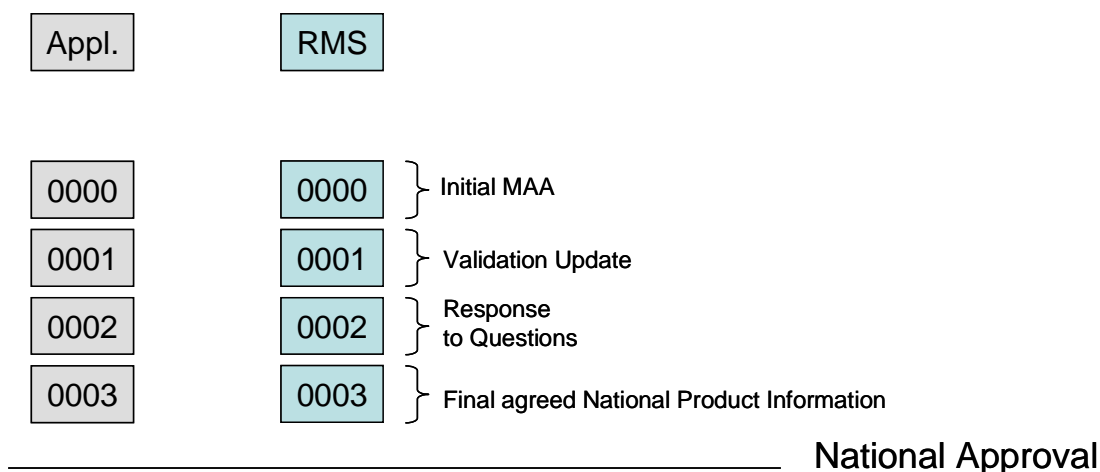
A number of differences exist between DCP and MRP and the best practices for the eCTD reflect these differences and are explained below.

4.1. National Phase

See Figure 4

An eCTD is submitted to the Member State that will become the Reference Member State (RMS). The envelope is specific to the RMS and the lifecycle is managed through from the initial submission to approval of the product nationally.

Figure 4: MRP: National Approval with RMS



4.2. Start of MRP

See Figures 5a, 5b, Tables 2a, 2b

A key principle of this best practice is that for a submission managed as an eCTD it is not necessary to produce an updated dossier for provision to the Concerned Member States (CMSs). For a process that utilises paper an updated dossier would be provided to any CMSs but within the eCTD review tools, the ‘current view’ of the set of sequences provided to the RMS as the initial filing and any further submissions will provide the equivalent of the updated dossier. It is noted that the ‘current view’ created from the RMS eCTD sequences and submitted to the CMSs will include the RMS specific documents submitted during the National Phase. However, the CMSs can easily identify these documents using the available metadata and disregard content not applicable to them.

When the application is submitted as an MRP, the submission type should be set to “initial maa” in the MRP initiation sequence (i.e. sequence 0004 in Figures 5a and 5b).

There are two basic options for the applicant to use to initiate the MRP and it is at their discretion which to utilise.

Option A: Managing a combined sequence for all NCAs (preferred from an authority perspective)

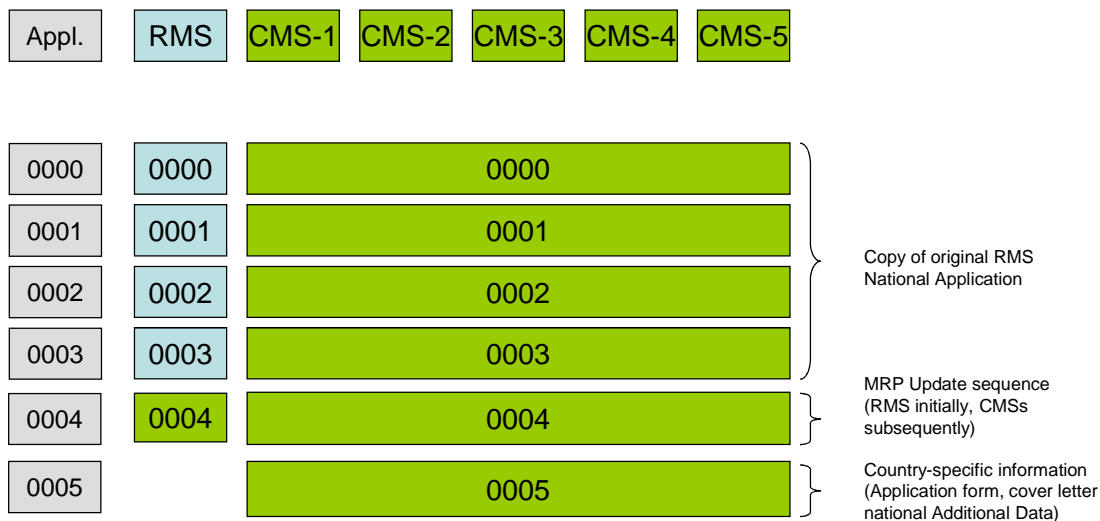
Option B: Managing individual sequences for each NCA

Description of Option A:

The RMS continues with their national submission which evolves into the MRP submission. This allows the RMS to maintain their records and links to other systems. In advance of the initiation of the MRP, the RMS is provided with an updating sequence (sequence 0004 in the figure below) and

when the RMS is satisfied then the MRP can be initiated with provision of the initial RMS sequences (0000 – 0003), the update sequence (0004) and the country specific information e.g. cover letter, application forms and additional nationally required documents included in a single sequence covering all CMSs (0005). The organisation of the dossier and the use of the country attributes assigned to documents will ensure that the CMSs will be easily able to find their specific information. The RMS does not need to receive the country specific information as there is nothing contained within that is of relevance to them.

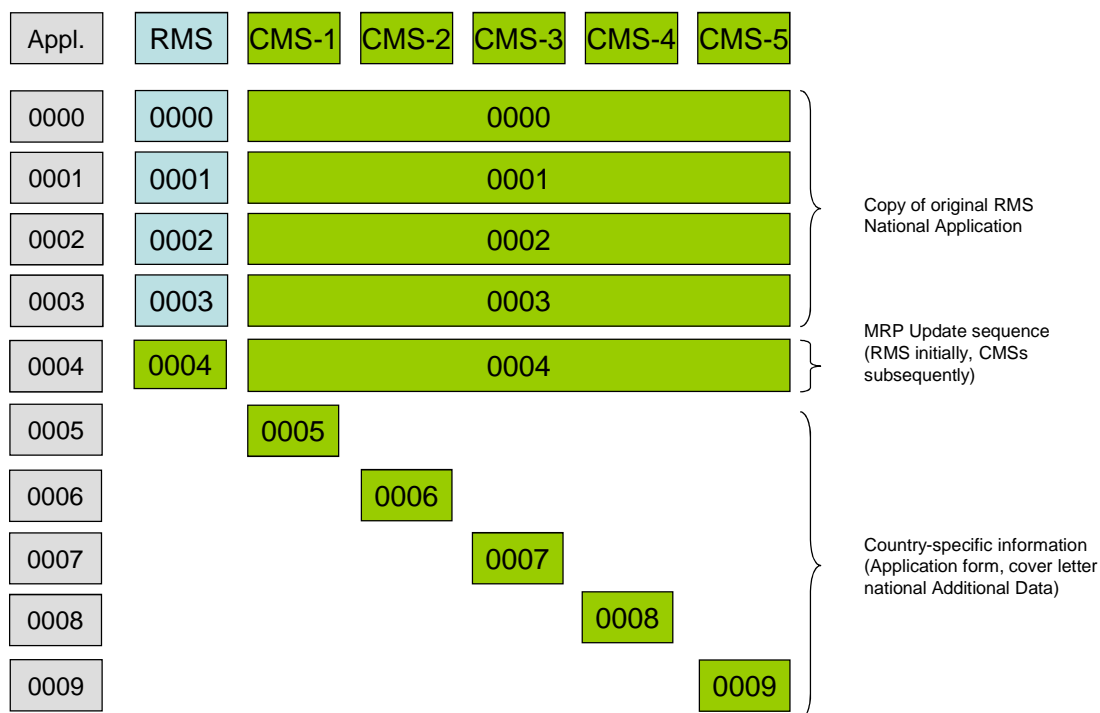
Figure 5a: MRP: Initial filing (Option A – combined submission) (See Table 2a)



Description of Option B:

The RMS continues with their national submission which evolves into the MRP submission. This allows the RMS to maintain their records and links to other systems. In advance of the initiation of the MRP, the RMS is provided with an updating sequence (sequence 0004 in the figure below) and when the RMS is satisfied then the MRP can be initiated with provision of the initial RMS sequences (0000 – 0003), the update sequence (0004) and a separate sequence for each CMS with their country specific information e.g. cover letter, application forms and additional nationally required documents (0005 through 0009). The RMS does not need to receive any of these country specific sequences as there is nothing contained within that is of relevance to them.

Figure 5b: MRP: Initial filing (Option B – individual submissions) (See Table 2b)



4.3. Validation and assessment (for both option A or B)

See Figures 6a, 6b, 6c & 7, Tables 3a, 3b, 3c & 4

During the validation period, the applicant can choose if any requested new or updated documents are sent as either new eCTD sequences or outside the eCTD.

If they are sent as eCTD sequences *during* the validation period it can be done in different ways.

- If there is a request for an update concerning Modules 2-5 or a common part of Module 1, the applicant should provide the updating sequence to the RMS and all CMSs. (Figure 6a, Table 3a)
- If the validation update concerns information regarding country-specific information (e.g. an application form) then this should be provided to the specific CMS only. (Figure 6b, Table 3b).
- If there are validation updates for both common and country-specific information then these can be combined in a single sequence and provided to the RMS and all CMSs.

If the validation has been handled outside the eCTD *during* the validation period, all submitted documents should be resubmitted to the RMS and all CMS with the relevant operation attribute in one eCTD sequence at the end of the validation period. It should be clearly stated in the cover letter that all documentation has been previously provided outside the eCTD during the validation period (Figure 6a, Table 3a). However, if this validation sequence concerns country-specific information only then it need only be sent to those NCAs affected. (Figure 6c, Table 3c)

If a submission is found to be *technically* invalid, a corrected sequence should always be submitted immediately, re-using the same sequence number.

It should be noted that sequences submitted earlier within the national procedure (the current dossier) before the start of the MRP will need to be part of the technical validation to ensure no new validation issues have been introduced during the processes of copying and submitting the sequences to the CMSs. However, when these sequences were validated originally by the RMS, and earlier set of validation criteria may have been used and/or Category B and C failures may have been addressed in subsequent corrective submissions. Therefore, the results from the validation by the CMSs should be considered carefully and pragmatically. Only errors introduced because of poor copying should need to be addressed. There should be no requests to update sequences that would involve the provision of revisions to the RMS.

During the Assessment Steps, any additional sequences, e.g. Responses to Questions, should be submitted to the RMS and CMSs. If, due to the tight time limits, the responses are sent outside the eCTD, a new sequence should always follow with any new or updated documents placed in the dossier with the correct operation attribute. Final agreed English language product information should always be submitted to the RMS and CMSs. (Figure 7, Table 4).

The common English product information texts communicated *during* the procedure should always be included in the eCTD as all other relevant documents at the different key steps (e.g. in the initial application, responses to LoQ and final agreements). Word copies of the included PDFs, which are requested by some of the NCAs, should always be kept outside the eCTD as working documents.

Draft responses sent to the RMS should be handled outside the eCTD as they are not considered to be official submissions.

Figure 6a: MRP: Validation update for common information submitted either during the validation phase or at the end of the validation phase

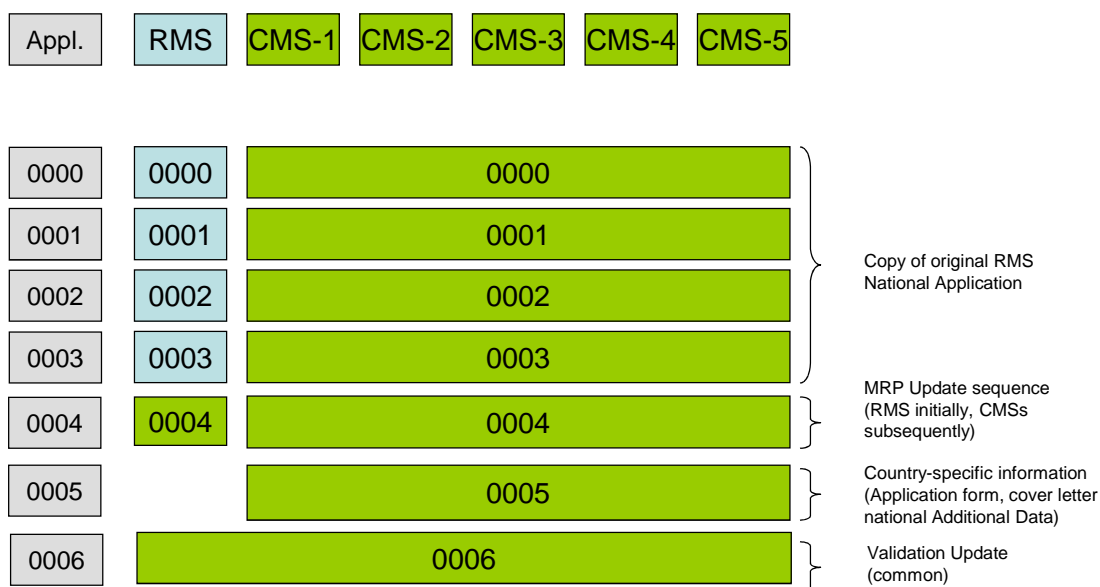


Figure 6b: MRP: Validation updates for country-specific information submitted during the validation phase

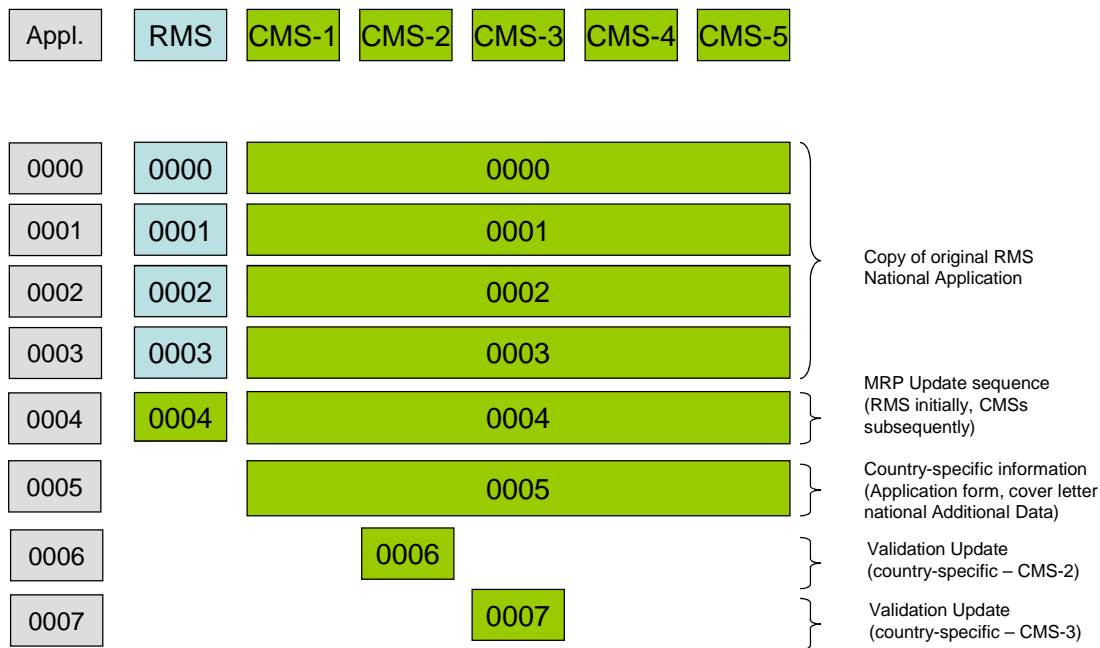


Figure 6c: MRP: Validation updates for country-specific information submitted after the end of the validation phase

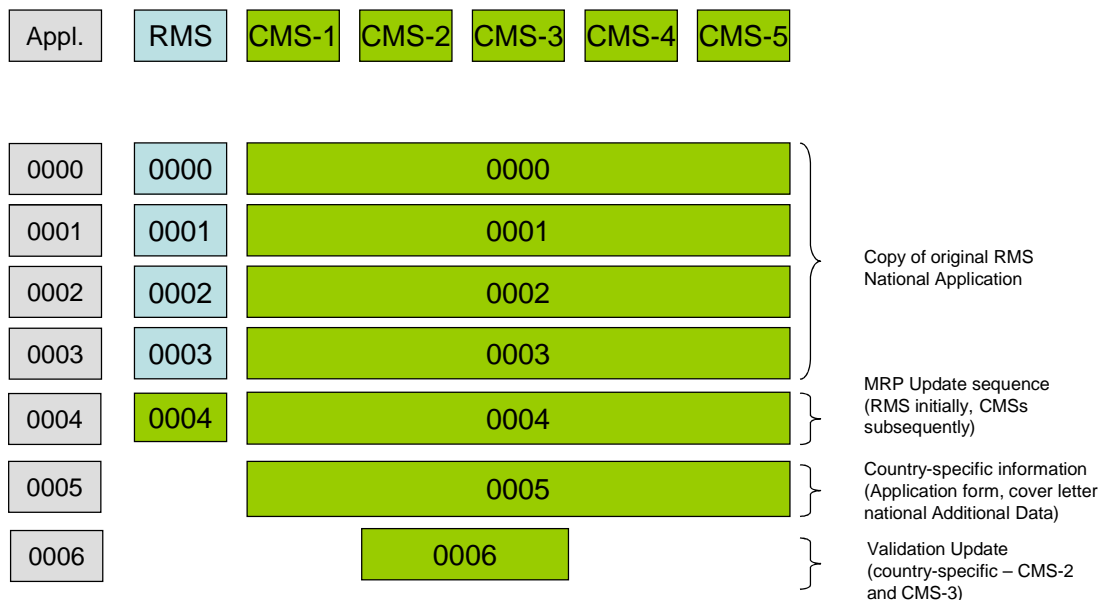
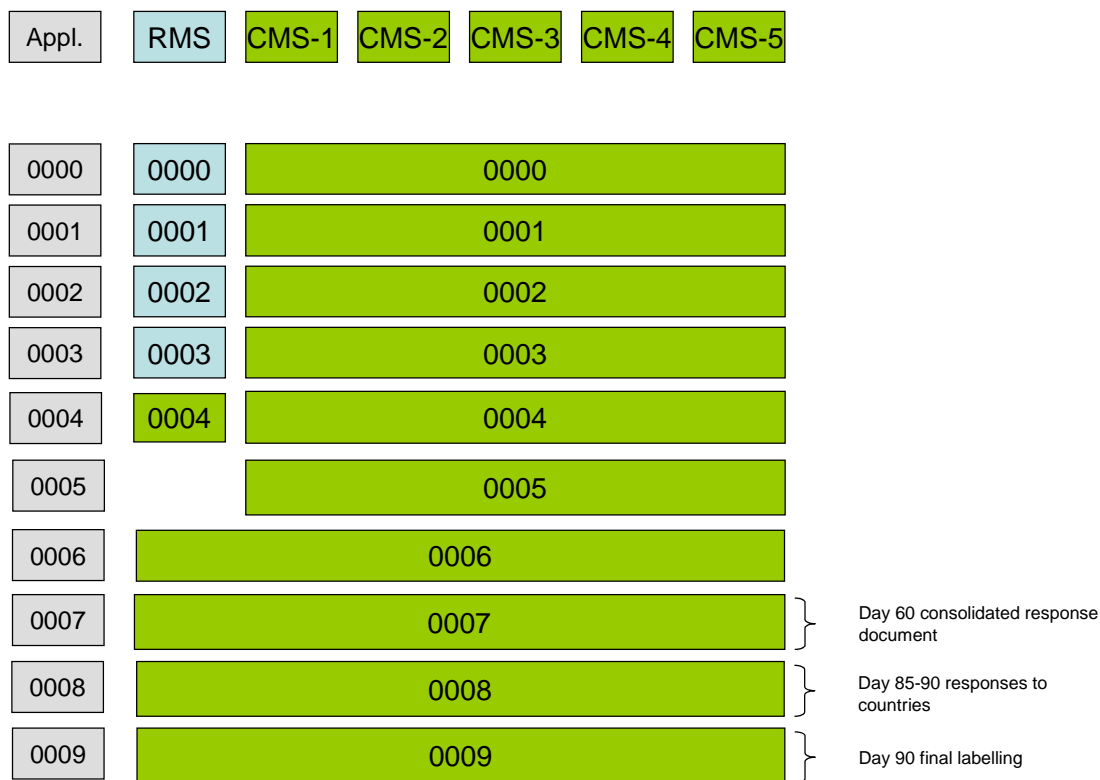


Figure 7: MRP: Review following provision of a single common validation sequence (i.e. based on Figure 6a) (See Table 4)



4.4. Submission of National Translations of Product Information

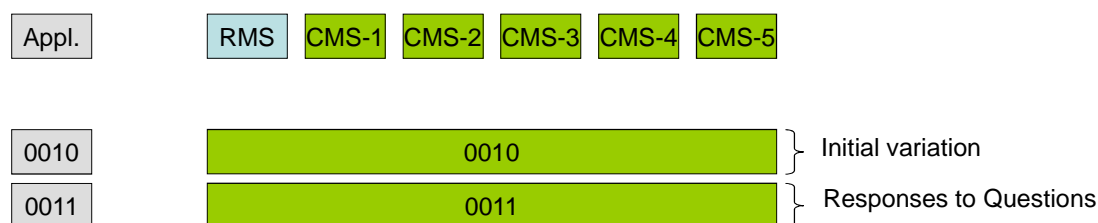
The national translations should be handled outside the eCTD in MRP and DCP, since the national phases are a responsibility of each NCA and normally handled by local affiliates of the applicants.

4.5. Variations and Other Procedures that Affect the RMS and all CMSs (Generally-Applicable Lifecycle Submissions)

See Figure 8, Table 5

Subsequent lifecycle submissions such as variations should be submitted to the RMS and all CMSs as a single sequence containing all documentation for all NCAs and any subsequent responses to questions should also be provided to the RMS and all CMSs. Again, for simplicity, only the sequence scheme based upon Option A for the MRP is presented. When translations of the product information are required at the time of submission of a variation, these should be provided outside the eCTD but on the same CD/DVD in (a) separate folder(s) including country codes in the folder name.

Figure 8: MRP: Generally-applicable lifecycle submissions (See Table 5)



In the case where a variation is rejected, or partially rejected by member states it is important that the authority maintains the rejected application within the eCTD to refer to. However, the continued inclusion of rejected information can cause confusion regarding what is ‘current’. Applicants should refer to the “eCTD Variations Q&A document” at the EMA eSubmission website regarding the provision of a consolidation sequence.

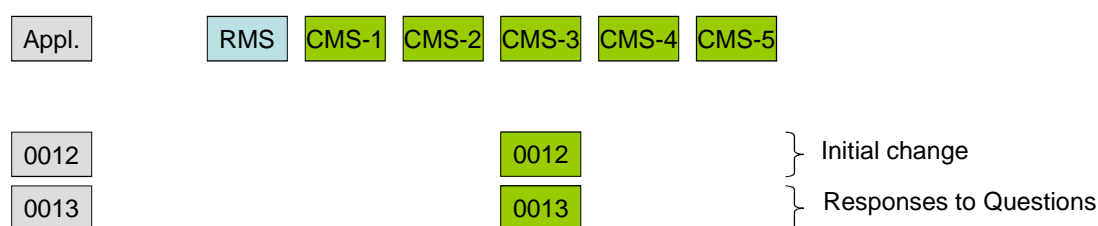
[\[http://esubmission.ema.europa.eu/doc/QA%20eCTD%20variations%20vers%205%20\(Jan%2010\)%20-%20clean%20version.doc\]](http://esubmission.ema.europa.eu/doc/QA%20eCTD%20variations%20vers%205%20(Jan%2010)%20-%20clean%20version.doc)

4.6 Procedures that Affect Only a Single CMS (Country-Specific Lifecycle Submissions)

See Figure 9, Table 6

An MAH transfer or an application for change in legal status would be relevant to one CMS only and therefore the sequence should be provided to that CMS only and not to the RMS or any other CMSs. Subsequent submissions, e.g. Responses to Questions, associated with this activity should also only be submitted to that specific CMS. Again, for simplicity, only the sequence scheme based upon Option A above is presented.

Figure 9: MRP: Country-specific lifecycle submissions (See Table 6)



4.7 Repeat Use Procedures

See Figure 10, Table 7

As with the MRP, a key principle of this best practice is that for a submission managed as an eCTD it is not necessary to produce an updated dossier for provision to the Concerned Member States (CMSs). For a process that utilises paper an updated dossier would be provided to any CMSs but within the eCTD review tools, the ‘current view’ of the set of sequences provided to the RMS as the initial filing and any further submission will provide the equivalent of the updated dossier.

When the application is submitted as an RUP application, the submission type should be set to “initial-maa” in that RUP initiation sequence (i.e. sequence 0014 in Figure 10)

As for the initial MRP there are two options available to the applicant and it is at their discretion which to use but they should be consistent in the approach within the eCTD overall.

Option A: Managing a combined sequence for all NCAs (preferred from an authority perspective)

Option B: Managing individual sequences for each NCA

For simplicity, only the sequence scheme based upon Options A is presented.

Description of Option A:

The RMS and existing CMSs continue with their eCTD submission as this allows them to maintain their records and links to other systems. In advance of the initiation of the RUP, the RMS is provided with an initiating sequence (sequence 0014 in the figure below) and when the RMS is satisfied then the RUP can be initiated with the new CMSs through provision of the relevant (generally-applicable) sequences from the MRP, the initiating sequence (0014) and a combined sequence for all new CMS with their country specific information e.g. cover letter, application forms and additional nationally required specific documents if any (0015). The RMS does not need to receive the country specific information and the existing CMSs should receive neither the initiating sequence (0014) nor the country specific information (0015) since there is nothing contained within these sequences which is of relevance to them.

During the validation period, the applicant can choose if any requested new or updated documents are sent as new sequences or are sent outside the eCTD. If they are sent as eCTD sequences *during* the validation period it could be done in different ways.

- If there is a request for an update concerning a common part of Module 1, the applicant should provide the updating sequence to the RMS and all CMSs.
- If the validation update concerns information regarding country-specific information (e.g. an application form) then this should be provided to the specific CMS only.
- If there are validation updates for both common and country-specific information then these can be combined in a single sequence and provided to the RMS and all CMSs.

If the validation has been handled outside the eCTD *during* the validation period, all submitted documents should be resubmitted to the RMS and all CMS involved in this RUP with the relevant operation attribute in one eCTD sequence when the validation period ends, clearly stating in the cover letter that all documentation has been previously provided outside the eCTD during the validation period. However, if this validation sequence concerns country-specific information only then it need only be sent to those NCAs affected.

If the RUP specific sequence is found *technically* invalid, a corrected sequence has to be submitted immediately re-using the same sequence number.

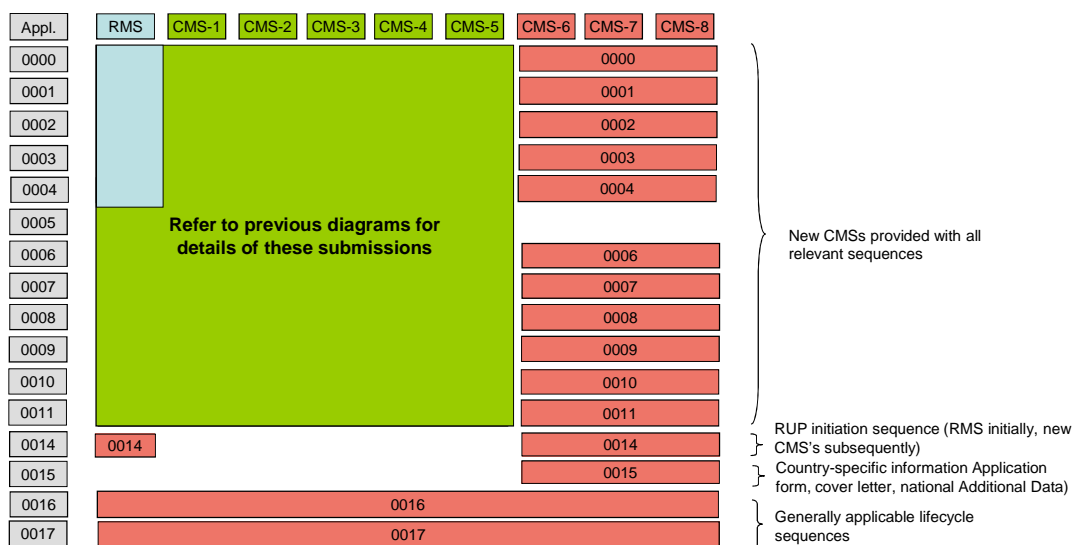
It should be noted that sequences submitted earlier within the DCP/MRP procedure (the current dossier) before the start of the Repeat use will need to be part of the technical validation to ensure no new validation issues have been introduced during the processes of copying and submitting the sequences to the new CMSs. However, when these sequences were validated originally by the RMS and/or existing CMSs, and earlier set of validation criteria may have been used and/or Category B and C failures may have been addressed in subsequent corrective submissions. Therefore, the results from the validation by the new CMSs should be considered carefully and pragmatically. Only errors

introduced because of poor copying should need to be addressed. There should be no requests to update sequences that would involve the provision of revisions to the RMS and existing CMSs.

After finalisation of the RUP, the RMS, existing CMSs and new CMSs should all receive generally-applicable lifecycle sequences (0016 & 0017) for example if a variation is needed as a consequence of questions during the RUP.

Subsequent RUPs should be managed in the same way as described for this first RUP.

Figure 10: MRP: Repeat Use Procedure followed by generally-applicable lifecycle submission (See Table 7)



4.8 Change of RMS

According to the CMD(h) procedural advice on changing the RMS, the MAH must notify the change of RMS to all CMS(s) before the change of the RMS takes effect.

The notification of the RMS transfer can take place in different ways (e-mail, telephone or letter). With regards to eCTD, the notification of RMS transfer is considered to be part of communication which is not relevant for the eCTD Life Cycle Management of the product. The RMS transfer notification is therefore regarded to be out of scope of the eCTD.

This means that it is not required to submit a new eCTD sequence to the involved Member States (RMS and CMS) for the notification of the RMS transfer.

For the submission of the next sequence in eCTD format (i.e. variation, renewal, etc), the applicant will change the procedure number in the envelope information and ensure that the RMS is changed from this point onwards in the Tracking table. Note: The current DTD for the tracking table in XML-format is not able to be utilised when there is a change of RMS.

In cases that the Marketing Authorisation (MA) of the country that previous acted as RMS is withdrawn, the withdrawal of the MA should be covered by submission of a sequence in eCTD format. The cover letter for the withdrawal of the MA should be submitted as an eCTD sequence. In this eCTD sequence, the procedure-MR-number from the new RMS will be displayed.

4.9 Switch from paper or NeeS to eCTD

When an applicant wants to switch from paper or NeeS to eCTD in a specific CMS and has already an up to date eCTD used in the procedure, earlier sequences should normally be provided as requested by the CMS. However, the “old” sequences should in these cases not be technically validated by this CMS, but accepted as they are. However, if there are problems with loading or reading the submitted files the applicant should be assisting in solving the problems.

4.10 Use of the eCTD format for “Mixed Format Applications”

All applications have to be in CTD format in accordance with the directive 83/2001 as amended. If an already existing paper dossier is only in the old NtA Part format, the structure has to be updated before going into an MRP or a RUP initial application as stated in the Notice to Applicant, CTD Q&A (Q4b). [http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-2/b/ctd-qa-updatev3_2008-02.pdf]. There it is stated that it is *acceptable* to have a mixed dossier with Module 1-3 in CTD format and Module 4-5 (Part III and IV) in the old NtA format.

In principle this would also be acceptable if the dossier is to be submitted in an electronic format. However, if submitted in eCTD format it is recommended to re-format the whole dossier into the eCTD format. Much of the documentation in Parts 1 and 2 would need to be re-worked into Modules 1-3 but most of the documents in Parts III and IV could be scanned and be put at the correct location in the eCTD structure.

If the applicant does not find it possible to place the document into the eCTD structure, the old Part documentation (IC, III and IV as relevant) should be handled outside the eCTD, either as paper (if preferred by the applicant and accepted by the RMS/CMS) or in a separate NtA Part folder structure for these documents submitted on the same CD/DVD. Relevant filenames should be used following the NtA Part structure and PDF TOCs with functional links should be included. The old Expert Reports should in that case also be handled outside the eCTD but a statement should be included in the eCTD Module 2 referring to these Reports (see NtA Q&A 4b).

5. SUMMARY

The approach outlined allows the applicant to maintain a single eCTD that covers all NCAs involved in the MRP/DCP throughout the life of the product. It also ensures that the RMS and each CMS has the set of sequences that are relevant to the mutual assessment phases and their country-specific information. The RMS and CMSs will not have to needlessly load each and every sequence, some of which may not be relevant to them but they will be able to identify efficiently which has been submitted in their country and which has not.

The principle of the updated dossier at the beginning of the MRP and Repeat Use Procedure is achieved by provision of a set of sequences of the generally-applicable information combined with the ability of the review tools to view the ‘current’ submission.

However, during the period through to end-2009 not all NCAs may be in a position to accept eCTD-only submissions. Although HMA announced in February 2005 that all NCAs should be ready for eCTD-only submissions by the end of 2009, several NCAs will not be ready to accept fully paperless

submissions by that date. Transparency on the situation is given by the HMA [<http://www.hma.eu/>]. Applicants must therefore continue to comply with any national requirements to provide full or partial paper copies in addition to the eCTD [<http://www.hma.eu/277.html>] and to consider the provision of NeeS if needed by those NCAs, if any, that may not yet be ready to receive eCTDs, particularly in support of the initiation of the MRP and Repeat Use Procedure. This might be achieved by use of an eCTD building tool with a function to print the current valid documents of an eCTD to paper or electronic media.

Review tools should provide the functionality to filter country-specific information from within multiple country information through use of the country attributes applied to specific Module 1 documents (i.e. Cover Letters, Forms, Product Information, Responses and Additional Data). It should be noted however that not all review tools provide this ability currently.

TABLES

Examples of the Sequence Tracking Table that should be included as an attachment to the Cover Letter for each sequence

Principles of Layout for the Tracking Table

- i) The Member State acting as the RMS should be identified and be the first Member States listed
- ii) The 'first wave' CMSs should be listed alphabetically and grouped under a heading 'CMSs - First Wave'
- iii) Subsequent waves should be grouped under a similar heading e.g. 'CMSs - Second Wave', 'CMSs - Second Wave' etc. and listed alphabetically
- iv) The RMS and CMSs should be identified by the two character country code
- v) The date presented should be month and year. This is defined by the applicant and should equate to the intended date of submission

Note : The inclusion of the identifier CMS-1, CMS-2 etc in the following tables is purely to allow cross-reference from the figures to the tables. The entries in the table should be consistent with the information in the envelope, namely that countries in the table should correspond to those included in the envelope and that the submission description used should be the same.

Table 1a: DCP Assessment Phase – including a validation update for common information (See Figure 3a)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0003	Final agreed En product information	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10
0002	Day 106 Responses to questions	May 10	May 10	May 10	May 10	May 10	May 10
0001	Validation update	Dec 09	Dec 09	Dec 09	Dec 09	Dec 09	Dec 09
0000	Initial MAA	Dec 09	Dec 09	Dec 09	Dec 09	Dec 09	Dec 09

Table 1b: DCP Assessment Phase – including a validation update for country-specific information (See Figure 3b)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0004	Final agreed En product information	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10
0003	Day 106 Responses to questions	May 10	May 10	May 10	May 10	May 10	May 10
0002	Validation update (FR)				Dec 09		
0001	Validation update (ES)			Dec 09			
0000	Initial MAA	Dec 09	Dec 09	Dec 09	Dec 09	Dec 09	Dec 09

Table 1c: DCP Assessment Phase – including a validation update for country-specific information submitted at the end of the validation phase (See Figure 3c)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0003	Final agreed En product information	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10
0002	Day 106 Responses to questions	May 10	May 10	May 10	May 10	May 10	May 10
0001	Validation update (ES & FR)			Jan 10	Jan 10		
0000	Initial MAA	Dec 09	Dec 09	Dec 09	Dec 09	Dec 09	Dec 09

Table 2a: MRP: Initial filing : Option A (Combined submission : Single sequences for all CMSs) (See Figure 5a)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0005	Country specific information (All)		Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09

Table 2b: MRP: Initial filing : Option B (Individual submissions - Separate sequences for each CMS) (See Figure 5b)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0009	Country specific information (SK)						Feb 09
0008	Country specific information (SE)					Feb 09	
0007	Country specific information (FR)				Feb 09		
0006	Country specific information (ES)			Feb 09			
0005	Country specific information (AT)		Feb 09				
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09

Table 3a: MRP: Validation update for common information submitted either during the validation phase or at the end of the validation phase (See Figure 6a)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0006	Validation update	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09
0005	Country specific information (All)		Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09

Table 3b: MRP: Validation updates for country-specific information submitted during the validation phase (See Figure 6b)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0007	Validation update (FR)				Mar 09		
0006	Validation update (ES)			Mar 09			
0005	Country specific information (All)		Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09

Table 3c: MRP: Validation updates for country-specific information submitted after the end of the validation phase (See Figure 6c)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0006	Validation update (ES & FR)			Mar 09	Mar 09		
0005	Country specific information (All)		Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09

Table 4: MRP : Review (See Figure 7)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0009	Day 90 – Final En product information	Nov 09	Nov 09	Nov 09	Nov 09	Nov 09	Nov 09
0008	Day 85-90 Responses	Oct 09	Oct 09	Oct 09	Oct 09	Oct 09	Oct 09
0007	Day 60 Consolidated Response Document	Sep 09	Sep 09	Sep 09	Sep 09	Sep 09	Sep 09
0006	Validation update	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09
0005	Country specific information (All)		Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09

Table 5: MRP : Generally applicable lifecycle submissions (See Figure 8)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0011	Responses to Questions	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10
0010	Manufacturing change variation	Mar 10	Mar 10	Mar 10	Mar 10	Mar 10	Mar 10
0009	Day 90 – Final En product information	Nov 09	Nov 09	Nov 09	Nov 09	Nov 09	Nov 09
0008	Day 85-90 Responses	Oct 09	Oct 09	Oct 09	Oct 09	Oct 09	Oct 09
0007	Day 60 Consolidated Response Document	Sep 09	Sep 09	Sep 09	Sep 09	Sep 09	Sep 09
0006	Validation update	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09
0005	Country specific information (All)		Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09

Table 6: MRP : Country-specific lifecycle submissions (See Figure 9)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0013	Responses to Questions – change in legal status (FR)					Aug 10	
0012	Change in legal status (FR)					Jul 10	
0011	Responses to Questions	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10
0010	Manufacturing change variation	Mar 10	Mar 10	Mar 10	Mar 10	Mar 10	Mar 10
0009	Day 90 – Final En product information	Nov 09	Nov 09	Nov 09	Nov 09	Nov 09	Nov 09
0008	Day 85-90 Responses	Oct 09	Oct 09	Oct 09	Oct 09	Oct 09	Oct 09
0007	Day 60 Consolidated Response Document	Sep 09	Sep 09	Sep 09	Sep 09	Sep 09	Sep 09
0006	Validation update	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09
0005	Country specific information (All)		Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09

Table 7: MRP : Repeat Use Procedure followed by generally-applicable lifecycle submission (See Figure 10)

Sequence	Submission description	RMS	CMSs – First Wave					CMSs – Second Wave		
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)	FI (CMS-6)	LV (CMS-7)	NL (CMS-8)
0017	Responses to Questions	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11
0016	Manufacturing change variation	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11	Apr 11
0015	Country specific information							Jan 11	Jan 11	Jan 11
0014	RUP initiation sequence	Dec 10						Jan 11	Jan 11	Jan 11
0013	Responses to Questions – change in legal status (FR)				Aug 10					
0012	Change in legal status (FR)				Jul 10					
0011	Responses to Questions	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10	Jun 10	Jan 11	Jan 11	Jan 11
0010	Manufacturing change variation	Mar 10	Mar 10	Mar 10	Mar 10	Mar 10	Mar 10	Jan 11	Jan 11	Jan 11
0009	Day 90 – Final En product information	Nov 09	Nov 09	Nov 09	Nov 09	Nov 09	Nov 09	Jan 11	Jan 11	Jan 11
0008	Day 85-90 Responses	Oct 09	Oct 09	Oct 09	Oct 09	Oct 09	Oct 09	Jan 11	Jan 11	Jan 11
0007	Day 60 Consolidated Response Document	Sep 09	Sep 09	Sep 09	Sep 09	Sep 09	Sep 09	Jan 11	Jan 11	Jan 11
0006	Validation update	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Jan 11	Jan 11	Jan 11
0005	Country specific information (All)		Feb 09	Feb 09	Feb 09	Feb 09	Feb 09	Jan 11	Jan 11	Jan 11
0004	MRP update sequence	Jan 09	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09	Jan 11	Jan 11	Jan 11
0003	Final agreed National product information	Dec 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09	Jan 11	Jan 11	Jan 11
0002	Responses to questions	Sep 08	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09	Jan 11	Jan 11	Jan 11
0001	Validation update	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09	Jan 11	Jan 11	Jan 11
0000	Initial MAA	Dec 07	Feb 09	Feb 09	Feb 09	Feb 09	Feb 09	Jan 11	Jan 11	Jan 11