



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

April 2008

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1. INTRODUCTION

Following experience gained both by industry and national Competent Authorities (NCAs), 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. It is expected that as more experience is gained these best practices will be updated as needed.

The guidance is applicable to applications in eCTD format only and at this stage is not applicable to non-eCTD electronic submissions (NeeS). Also, the guidance is not applicable to paper-based submissions. Thus there may be restrictions of applicability if an applicant is attempting to manage a procedure in eCTD, NeeS and paper formats. During the period through to end-2009 not all NCAs may be in a position to accept eCTD-only submissions. Applicant must continue to comply with any national requirements to provide full or partial paper copies in addition to the eCTD (see http://www.hma.eu/uploads/media/eSubmissions_requirements_new_applications.pdf) and to consider the provision of NeeS to those NCAs 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.

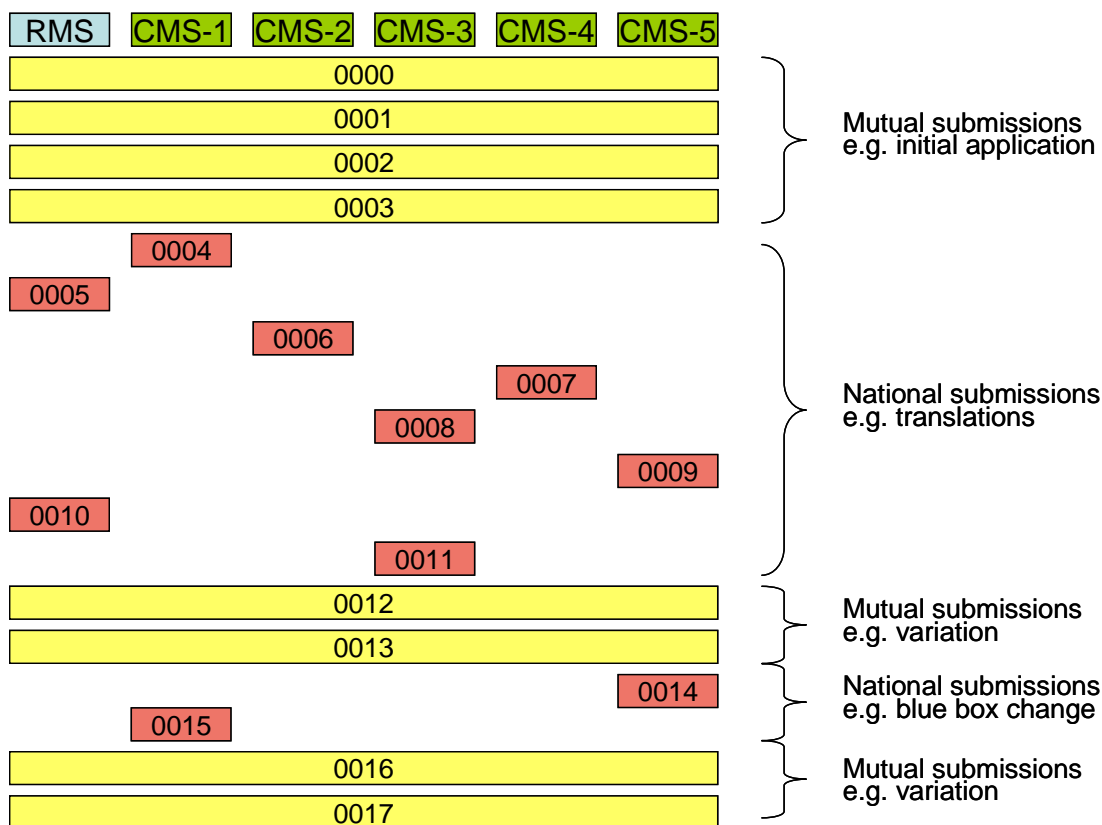
2. GENERAL CONCEPTS

A key principle 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 translations, transfers of ownership and changes to 'blue box' text will normally be provided to only the NCA concerned. 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. All eCTD building and viewing tools must therefore be able to support these omissions. 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



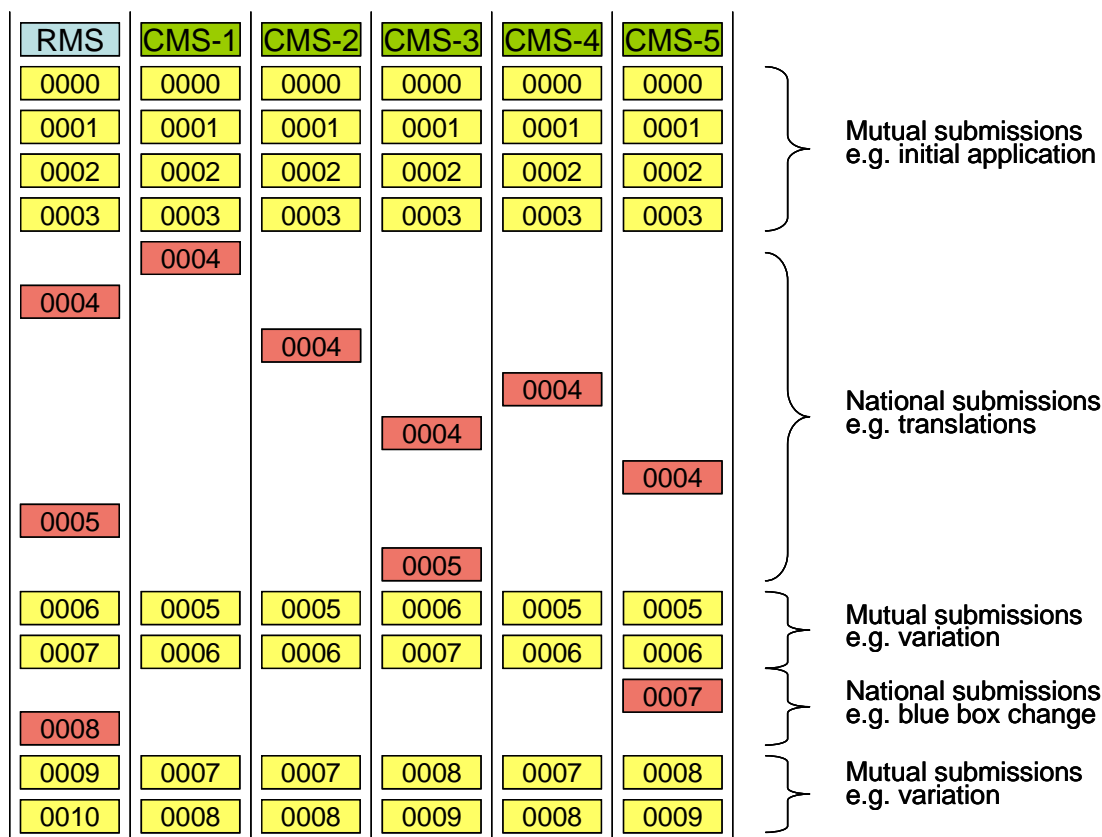
There should always be a structured table included as an annex to the Cover Letter that provides a history of the sequences that were provided to each NCA so that there can be confidence that sequences have not been omitted by oversight. This table should be updated with each sequence with the use of the ‘replace’ operation attribute and the ‘common’ country attribute. Examples of these tracking tables are provided later in this guidance.

Applicants should aim to 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 is acceptable but not recommended, to submit separate, national eCTDs to each NCA since it is recognised that 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.

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 (http://www.hma.eu/uploads/media/Recommendations_Cover_letter_NA_MRP-DCP_Rev2.pdf) or use the CMD(h) template for cover letter (<http://www.hma.eu/219.html>).

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



The guidance provided in this best practice describes the use of the recommended, ‘comprehensive’ model for the use of the eCTD in DCP and MRP.

3. DECENTRALISED PROCEDURE (DCP)

3.1 Assessment Phase

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

The initial eCTD containing all common parts as well as any country-specific information (e.g. as per Chapter 7 of the NTA) 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. For example, 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 1b**, 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.

During the Assessment Steps, any additional sequences, e.g. Responses to Questions, should also be submitted to the RMS and CMSs. Final agreed pivot language product information (Summary of Product Characteristics, Package Leaflet and Labelling) should also be submitted to the RMS and CMSs.

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. It is recommended that all documents should be handled at least according to Nees standard.

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

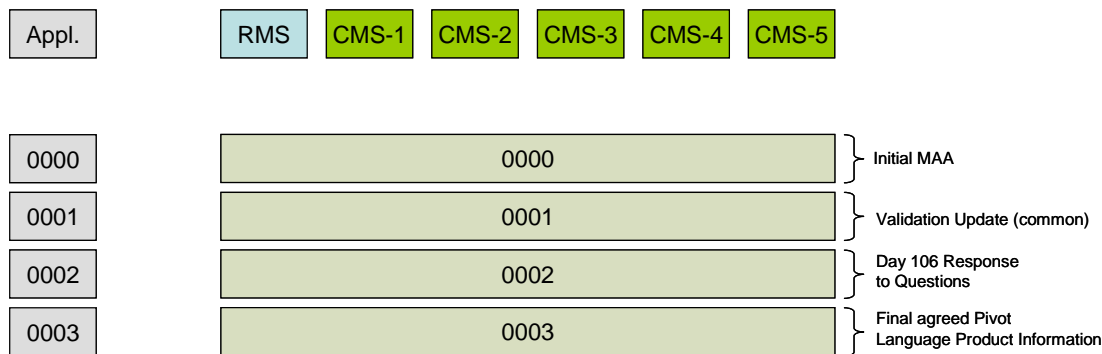
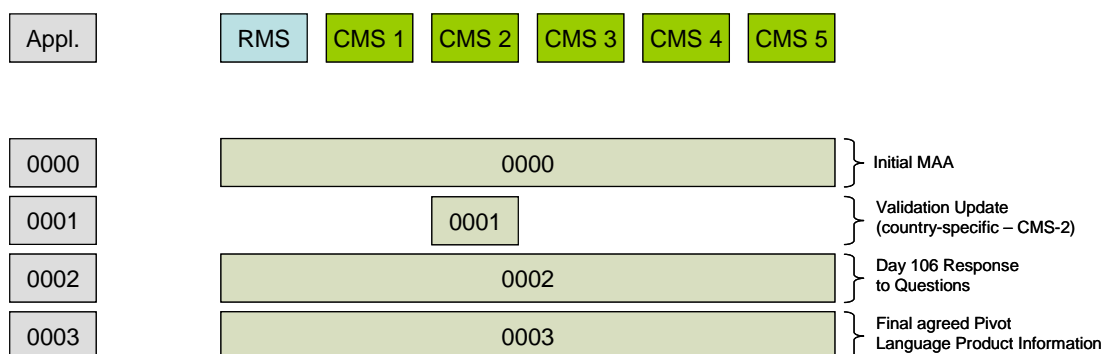


Figure 3b: DCP: Assessment Phase – including a validation update for country-specific information (See Table 1b)



3.2 Submission of National Translations of Product Information

See **Figures 4a, 4b & 4c**, Tables 2a, 2b & 2c

There are three basic options for the applicant and it is at their discretion which to utilise.

The decision which to use will be a balance between the number of sequences being produced versus the speed at which national review and approval can occur. Since the review of the national product information is part of the national phase of the DCP they can and do run at different speeds.

Option A: Managing individual sequences for each NCA. (**Figure 4a**, Table 2a).

Option B: Manage a combined sequence for all NCAs (**Figure 4b**, Table 2b).

Option C: Manage grouped NCAs (**Figure 4c**, Table 2c).

There may be some intermediate position where the submissions of the translations are grouped eg.

- as they become available for submission - a sequence containing all those ready early followed by another sequence for those available a bit later
- to NCAs where there is a shared language – Germany/Austria

The key principle is that an NCA should never be sent a sequence which does not contain any information that is relevant for their review and this is particularly relevant to resubmission of amended product information so, for example, if Germany and Austria receive a grouped sequence for the initial translation but Austria requests a change (but Germany does not) then a country-specific sequence should be provided to Austria containing the change but should not be provided to Germany. (**Figure 4c**, Table 2c)

Figure 4a: DCP: National Phase – Submission of Translations (Option A – individual submission) (See Table 2a)

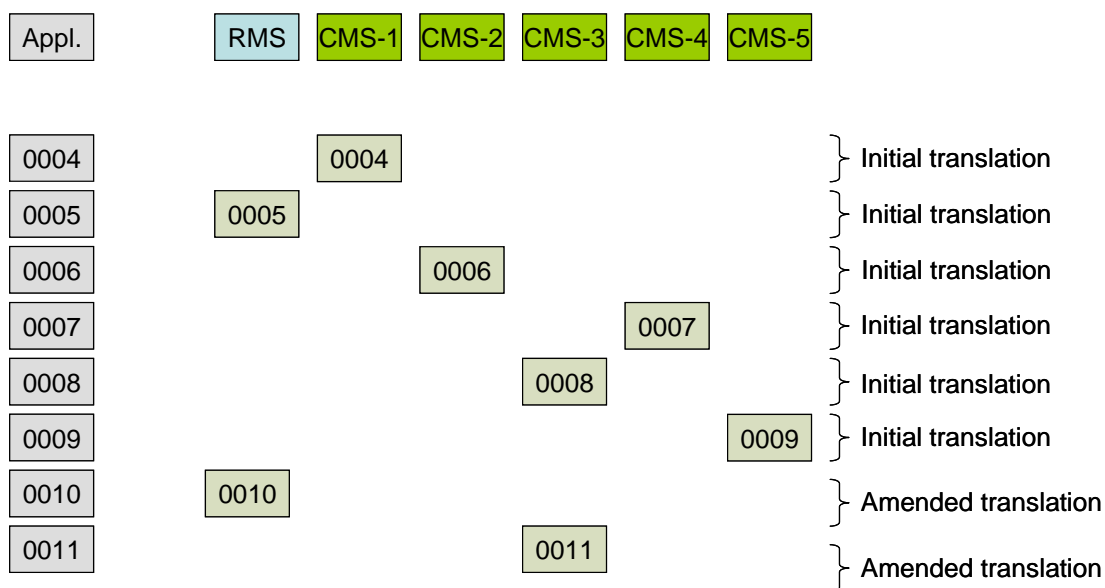


Figure 4b: DCP: National Phase – Submission of Translations (Option B – combined submission) (See Table 2b)

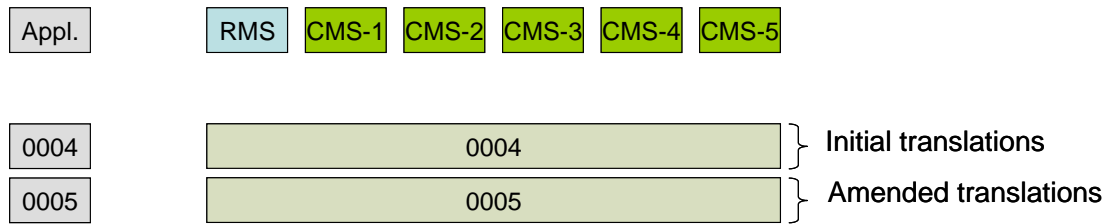
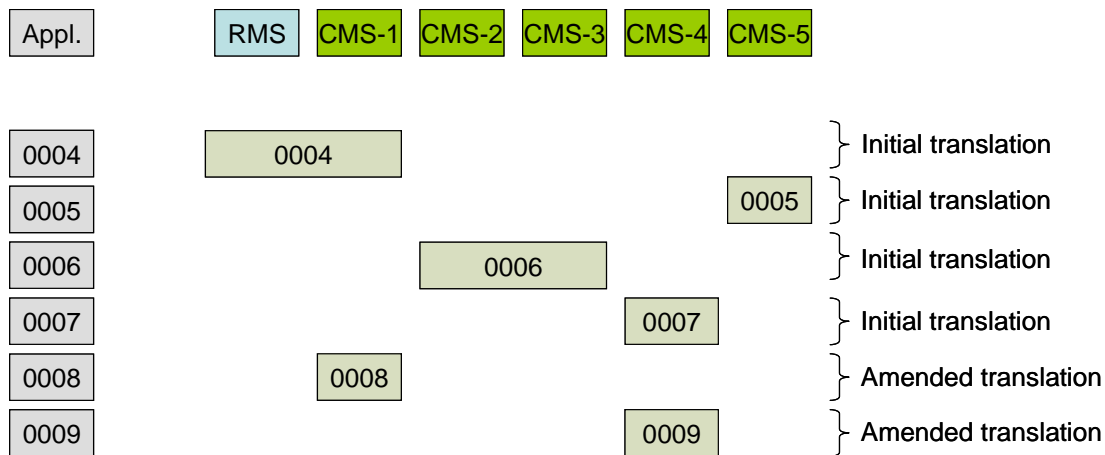


Figure 4c: DCP: National Phase – Submission of Translations (Option C – grouped submission) (See Table 2c)



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)

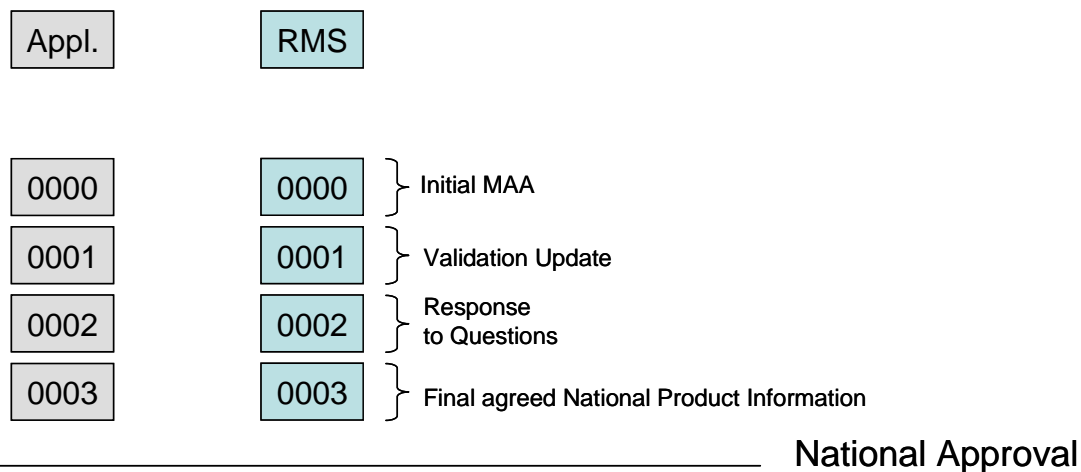
A number of differences exist between DCP and MRP and the best practices for the eCTD reflect these differences and are explained below.

4.1 National Phase

See **Figure 5**

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 5: MRP: National Approval with RMS



4.2 MRP

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

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.

In agreement with the RMS, any RMS’s country-specific documents should preferably not be submitted to the CMSs if this can be handled easily by taking out such sequences.

Similar to the submission of translations which were described for the DCP (**Figures 4a, 4b and 4c**) 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 individual sequences for each NCA

Option B: Managing a combined sequence for all NCAs

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 a separate sequence for each CMS with their country specific information e.g. cover letter, application forms and additional documents as per Chapter 7 of the NTA (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.

If there are any validation issues raised that necessitate the addition to or replacement of any country-specific documents these should be provided only to the specific CMS that raised the issue (0010). (**Figure 6a**, Table 3a).

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 the country specific information e.g. cover letter, application forms and additional documents as per Chapter 7 of the NTA 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.

If there are any validation issues raised that necessitate the addition or replacement of any country-specific documents these should be provided only to the specific CMS that raised the issue (0006). (**Figure 6b**, Table 3b).

Extension of Options A & B (Figure 7, Table 4):

During the Assessment Steps, any additional sequences, e.g. Responses to Questions, should also be submitted to the RMS and CMSs. Final agreed pivot language product information should also be submitted to the RMS and CMSs. For simplicity only the extension of Option A (sequences 00011 – 0013) is shown in as a Figure (**Figure 7**) but the applicant can, of course, use this principle for extension also for Option B.

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

Figure 6a: MRP: Initial filing and validation (Option A – individual submissions)
(See Table 3a)

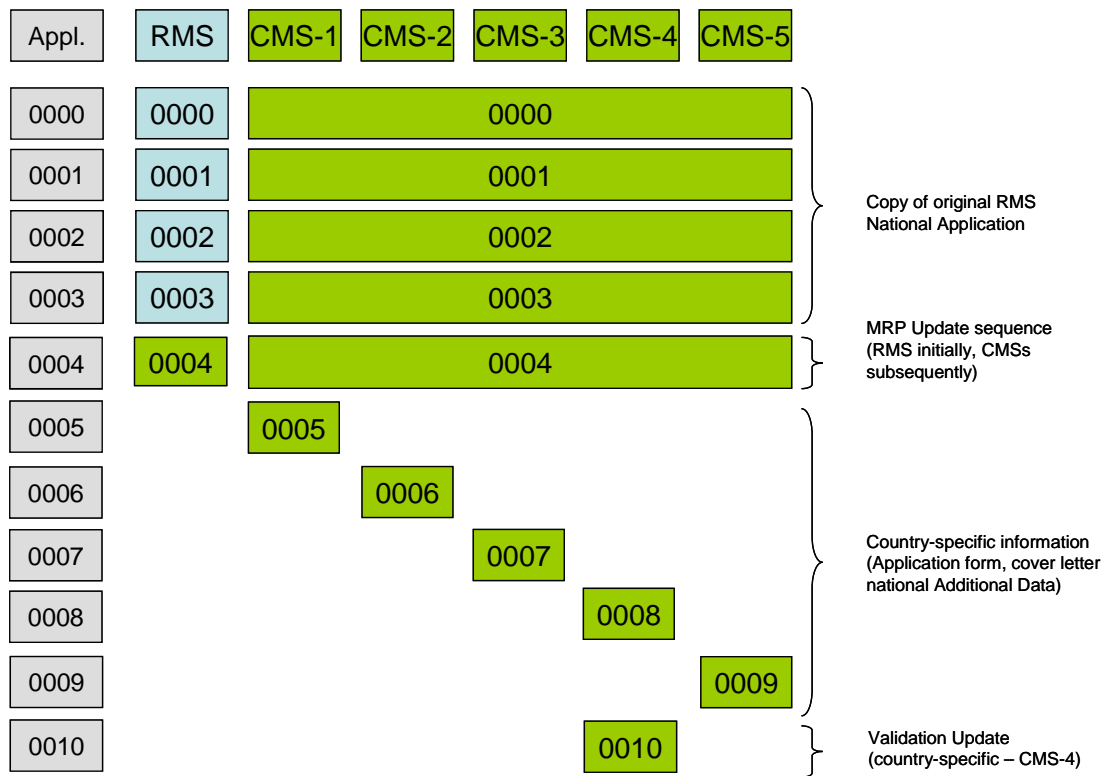


Figure 6b: MRP: Initial filing and validation (Option B – combined submission)
(See Table 3b)

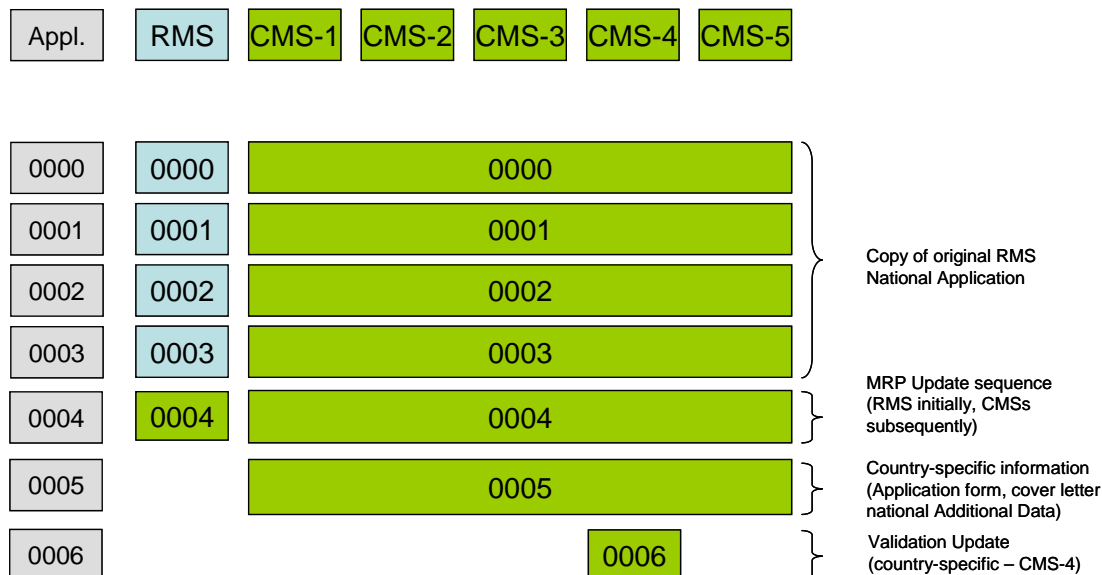
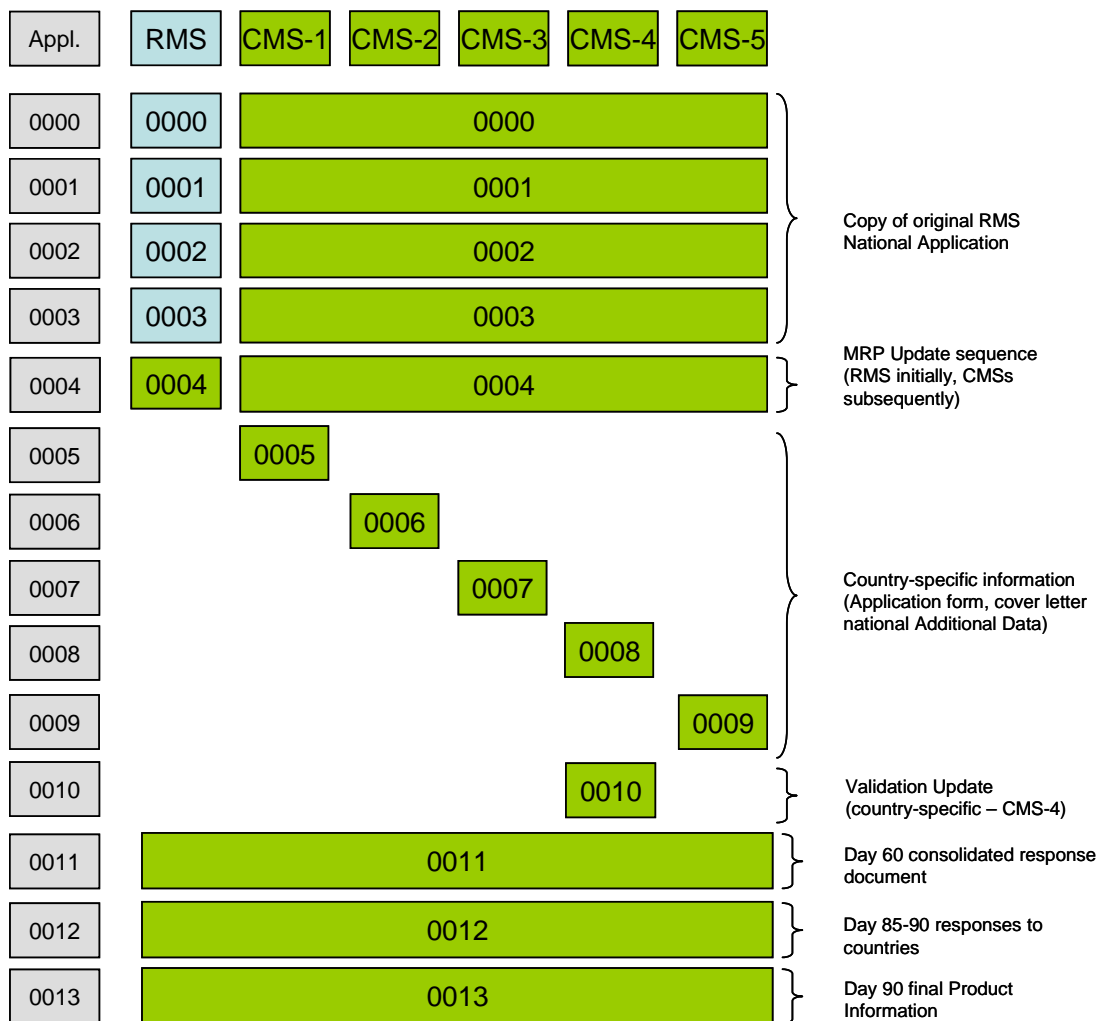


Figure 7: MRP: Review (See Table 4)



4.3 Submission of National Translations of Product Information

See **Figures 8a, 8b & 8c**, Tables 5a, 5b & 5c

The same options as for DCP are open to applicants for the submission of national product information in the national phase following MRP. For completeness and clarity the figures and tables are re-presented with representative sequence numbers continuing from the previous MRP steps. For simplicity, only the sequence scheme based upon Option A described for the MRP above is presented.

Figure 8a: MRP: National Phase – Submission of Translations (Option A – individual submission) (See Table 5a)

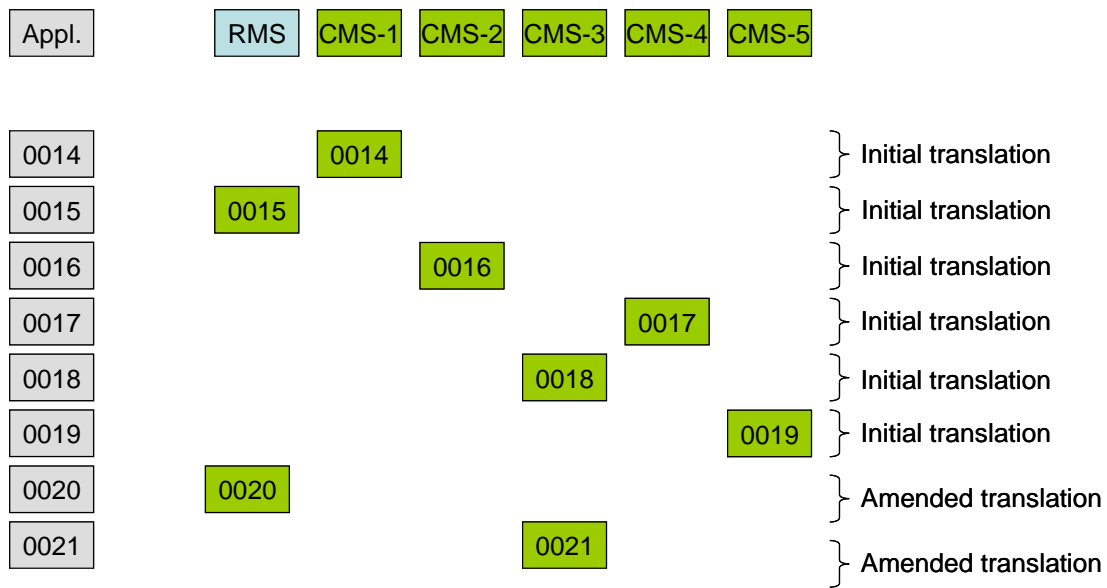


Figure 8b: MRP: National Phase – Submission of Translations (Option B – combined submission) (See Table 5b)

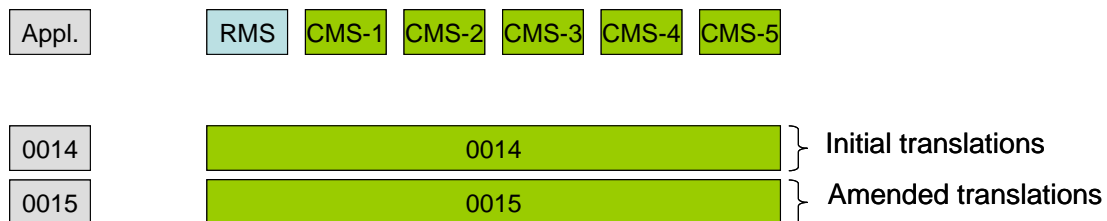
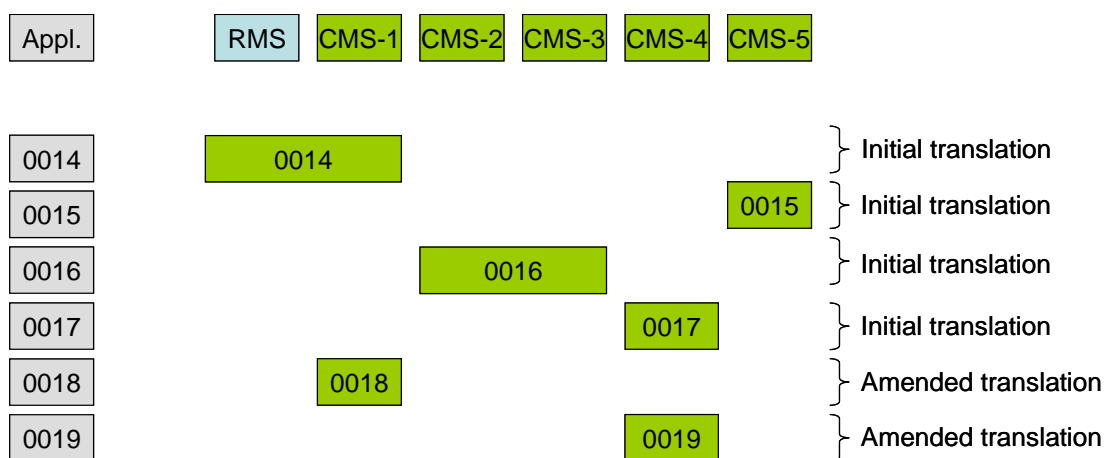


Figure 8c: MRP: National Phase – Submission of Translations (Option C – grouped submission) (See Table 5c)

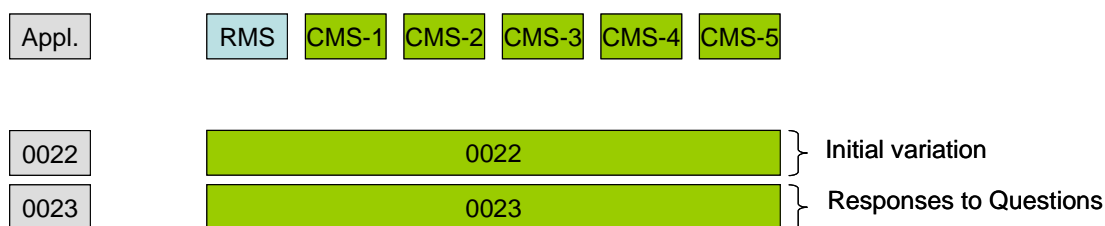


4.4 Variations and Other Procedures that Affect the RMS and all CMSs (Generally-Applicable Lifecycle Submissions)

See **Figure 9**, Table 6

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 and for the Submission of Translations above is presented.

Figure 9: MRP: Generally-applicable lifecycle submissions (See Table 6)

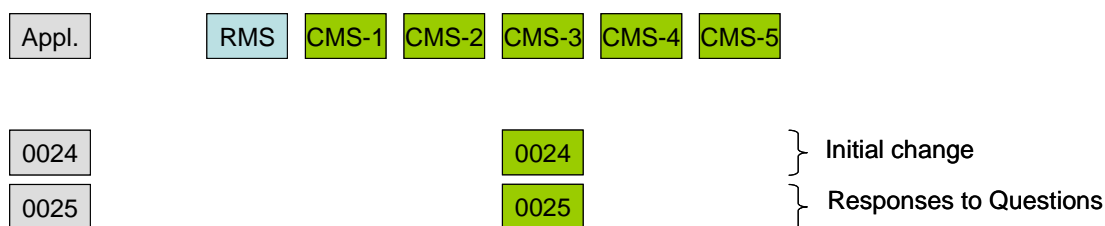


4.5 Procedures that Affect Only a Single CMS (Country-Specific Lifecycle Submissions)

See **Figure 10**, Table 7

A change of blue box information on the patient leaflet or a change of MAH is relevant to one CMS only and so the sequence should be provided to that CMS and not to the RMS or any other CMSs. Subsequent submissions, e.g. Responses to Questions, associated with this activity should only be submitted to the specific CMS. Again, for simplicity, only the sequence scheme based upon Option A above is presented.

Figure 10: MRP: Country-specific lifecycle submissions (See Table 7)



4.6 Repeat Use Procedures

See **Figure 11**, Table 8

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.

In agreement with the RMS, any RMS's country-specific documents should preferably not be submitted to the CMSs if this can be handled easily by taking out such sequences.

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 individual sequences for each NCA

Option B: Managing a combined sequence for all NCAs

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

Description of Option A

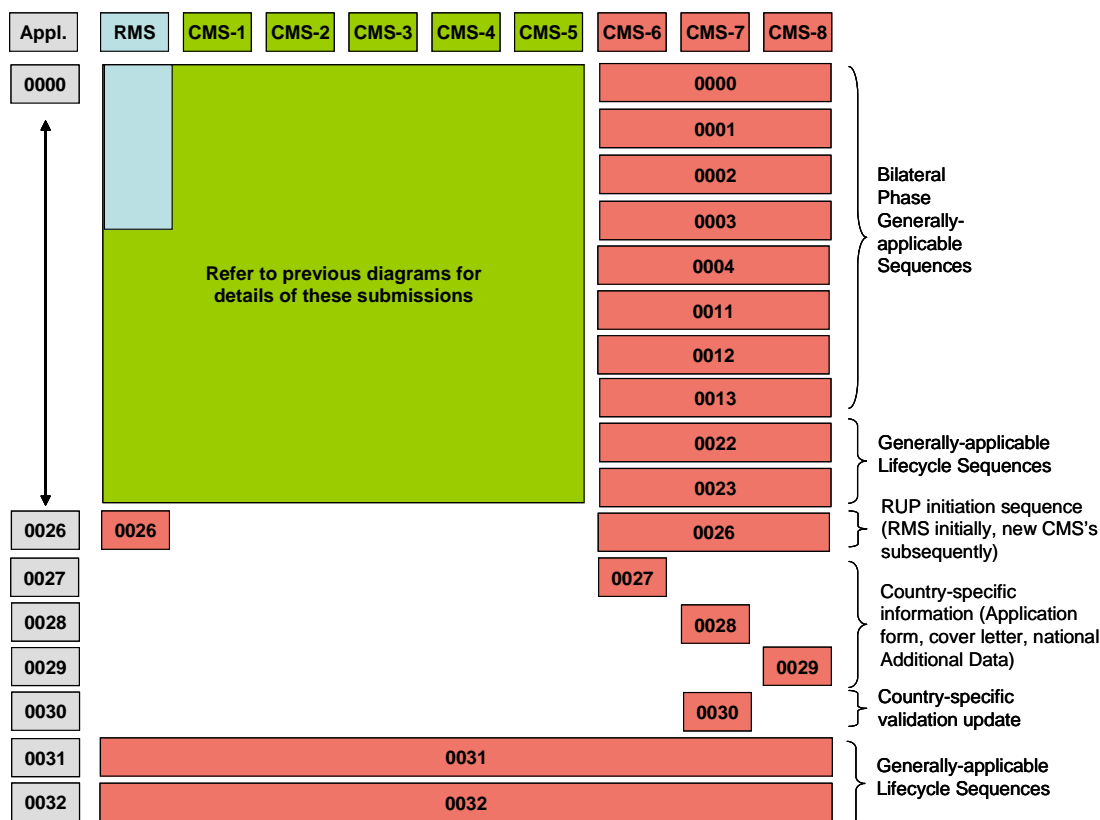
The RMS and existing CMSs continue with their eCTD submission as this allows them to maintain their records and links to other systems. In advance of the initiation of the RUP, the RMS is provided with an initiating sequence (sequence 0026 in the figure below) and when the RMS is satisfied then the RUP can be initiated with the new CMSs through provision of the relevant (generally-applicable) sequences from the MRP, the initiating sequence (0026) and a separate sequence for each new CMS with their country specific information e.g. cover letter, application forms and additional documents as per Chapter 7 of the NTA (0027, 0028 & 0029). The RMS does not need to receive the country specific information and the existing CMSs do not need to receive either the initiating sequence (0026) or the country specific information (0027, 0028 & 0029) since there is nothing contained within these which is of relevance to them.

If there are any validation issues raised that necessitate the addition or replacement of any country-specific documents these should be provided only to the specific CMS that raised the issue (0030).

As the RUP progresses the RMS, existing CMSs and new CMSs should all receive generally-applicable lifecycle sequences (0031 & 0032).

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

Figure 11: MRP: Repeat Use Procedure (See Table 8)



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. Applicant must continue to comply with any national requirements to provide full or partial paper copies in addition to the eCTD and to consider the provision of NeeS to those NCAs not yet ready to receive eCTDs, particularly in support of the initiation of the MRP and Repeat Use Procedure.

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

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 08	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08
0002	Day 106 Responses to questions	May 08	May 08	May 08	May 08	May 08	May 08
0001	Validation update	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07
0000	Initial MAA	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07

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)
0003	Final agreed En product information	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08
0002	Day 106 Responses to questions	May 08	May 08	May 08	May 08	May 08	May 08
0001	Validation update (ES)			Dec 07			
0000	Initial MAA	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07

Table 2a: DCP National Phase – Submission of Translations (Option A – individual submission) (See Figure 4a)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0011	Amended product information (FR)				Aug 08		
0010	Amended product information (DE)	Jul 08					
0009	Translations of agreed En product information (SK)						Jul 08
0008	Translations of agreed En product information (FR)				Jul 08		
0007	Translations of agreed En product information (SE)					Jul 08	
0006	Translations of agreed En product information (ES)			Jul 08			
0005	Translations of agreed En product information (DE)	Jun 08					
0004	Translations of agreed En product information (AT)		Jun 08				
0003	Final agreed En product information	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08
0002	Responses to questions	May 08	May 08	May 08	May 08	May 08	May 08
0001	Validation update	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07
0000	Initial MAA	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07

Table 2b: DCP National Phase – Submission of Translations (Option B – combined submission) (See Figure 4b)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0005	Amended product information	Aug 08	Aug 08	Aug 08	Aug 08	Aug 08	Aug 08
0004	Translations of agreed En product information	Jul 08	Jul 08	Jul 08	Jul 08	Jul 08	Jul 08
0003	Final agreed En product information	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08
0002	Day 106 Responses to questions	May 08	May 08	May 08	May 08	May 08	May 08
0001	Validation update	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07
0000	Initial MAA	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07

Table 2c: DCP National Phase – Submission of Translations (Option C – grouped submission) (See Figure 4c)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0009	Amended product information (SE)					Aug 08	
0008	Amended product information (AT)		Jul 08				
0007	Translations of agreed En product information (SE)					Jul 08	
0006	Translations of agreed En product information (ES & FR)			Jul 08	Jul 08		
0005	Translations of agreed En product information (SK)						Jul 08
0004	Translations of agreed En product information (DE & AT)	Jun 08	Jun 08				
0003	Final agreed En product information	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08	Jun 08
0002	Responses to questions	May 08	May 08	May 08	May 08	May 08	May 08
0001	Validation update	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07
0000	Initial MAA	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07	Dec 07

Table 3a: MRP: Initial filing and validation Option A (Individual submissions - separate sequences for each CMS) (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)
0010	Validation update (SE)					Mar 08	
0009	Country specific information (SK)						Feb 08
0008	Country specific information (SE)					Feb 08	
0007	Country specific information (FR)				Feb 08		
0006	Country specific information (ES)			Feb 08			
0005	Country specific information (AT)		Feb 08				
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08

Table 3b: MRP: Initial filing and validation Option B (Combined submission : Single sequences for all CMSs) (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)
0006	Validation update (SE)					Mar 08	
0005	Country specific information (All)		Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08

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)
0013	Day 90 – Final En product information	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08
0012	Day 85-90 Responses	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08
0011	Day 60 Consolidated Response Document	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08
0010	Validation update (SE)					Mar 08	
0009	Country specific information (SK)						Feb 08
0008	Country specific information (SE)					Feb 08	
0007	Country specific information (FR)				Feb 08		
0006	Country specific information (ES)			Feb 08			
0005	Country specific information (AT)		Feb 08				
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08

Table 5a: MRP: National Phase – Submission of Translations (Option A – individual submission) (See Figure 8a)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0021	Amended Product information (FR)				Jan 09		
0020	Amended Product information (DE)	Nov 08					
0019	Translations of agreed En product information (SK)						Nov 08
0018	Translations of agreed En product information (SE)				Nov 08		
0017	Translations of agreed En product information (FR)					Nov 08	
0016	Translations of agreed En product information (ES)			Nov 08			
0015	Translations of agreed En product information (DE)	Nov 08					
0014	Translations of agreed En product information (AT)		Nov 08				
0013	Day 90 – Final En product information	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08
0012	Day 85-90 Responses	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08
0011	Day 60 Consolidated Response Document	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08
0010	Validation update (SE)					Mar 08	
0009	Country specific information (SK)						Feb 08
0008	Country specific information (SE)					Feb 08	
0007	Country specific information (FR)				Feb 08		
0006	Country specific information (ES)			Feb 08			
0005	Country specific information (AT)		Feb 08				
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08

Table 5b: MRP: National Phase – Submission of Translations (Option B – combined submission) (See Figure 8b)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0015	Amended product information	Jan 09	Jan 09	Jan 09	Jan 09	Jan 09	Jan 09
0014	Translations of agreed En product information	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08
0013	Day 90 – Final En product information	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08
0012	Day 85-90 Responses	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08
0011	Day 60 Consolidated Response Document	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08
0010	Validation update (SE)					Mar 08	
0009	Country specific information (SK)						Feb 08
0008	Country specific information (SE)					Feb 08	
0007	Country specific information (FR)				Feb 08		
0006	Country specific information (ES)			Feb 08			
0005	Country specific information (AT)		Feb 08				
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08

Table 5c: MRP: National Phase – Submission of Translations (Option C – grouped submission) (See Figure 8c)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0019	Amended Product information (SE)					Jan 09	
0018	Amended Product information (AT)		Nov 08				
0017	Translations of agreed En product information (SE)					Nov 08	
0016	Translations of agreed En product information (ES & FR)			Nov 08	Nov 08		
0015	Translations of agreed En product information (SK)						Nov 08
0014	Translations of agreed En product information (DE & AT)	Nov 08	Nov 08				
0013	Day 90 – Final En product information	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08
0012	Day 85-90 Responses	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08
0011	Day 60 Consolidated Response Document	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08
0010	Validation update (SE)					Mar 08	
0009	Country specific information (SK)						Feb 08
0008	Country specific information (SE)					Feb 08	
0007	Country specific information (FR)				Feb 08		
0006	Country specific information (ES)			Feb 08			
0005	Country specific information (AT)		Feb 08				
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08

Table 6: MRP: Generally applicable 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)
0023	Responses to Questions	Jun 09	Jun 09	Jun 09	Jun 09	Jun 09	Jun 09
0022	Manufacturing change variation	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09
0021	Amended Product information (FR)				Jan 09		
0020	Amended Product information (DE)	Nov 08					
0019	Translations of agreed En product information (SK)						Nov 08
0018	Translations of agreed En product information (SE)				Nov 08		
0017	Translations of agreed En product information (FR)					Nov 08	
0016	Translations of agreed En product information (ES)			Nov 08			
0015	Translations of agreed En product information (DE)	Nov 08					
0014	Translations of agreed En product information (AT)		Nov 08				
0013	Day 90 – Final En product information	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08
0012	Day 85-90 Responses	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08
0011	Day 60 Consolidated Response Document	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08
0010	Validation update (SE)					Mar 08	
0009	Country specific information (SK)						Feb 08
0008	Country specific information (SE)					Feb 08	
0007	Country specific information (FR)				Feb 08		
0006	Country specific information (ES)			Feb 08			
0005	Country specific information (AT)		Feb 08				
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08

Table 7: MRP: Country-specific lifecycle submissions (See Figure 10)

Sequence	Submission description	RMS	CMSs – First Wave				
		DE	AT (CMS-1)	ES (CMS-2)	FR (CMS-3)	SE (CMS-4)	SK (CMS-5)
0025	Responses to Questions – address change (FR)				Aug 09		
0024	Variation – address change (FR)				Jul 09		
0023	Responses to Questions	Jun 09	Jun 09	Jun 09	Jun 09	Jun 09	Jun 09
0022	Manufacturing change variation	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09
0021	Amended Product information (FR)				Jan 09		
0020	Amended Product information (DE)	Nov 08					
0019	Translations of agreed En product information (SK)						Nov 08
0018	Translations of agreed En product information (SE)				Nov 08		
0017	Translations of agreed En product information (FR)					Nov 08	
0016	Translations of agreed En product information (ES)			Nov 08			
0015	Translations of agreed En product information (DE)	Nov 08					
0014	Translations of agreed En product information (AT)		Nov 08				
0013	Day 90 – Final En product information	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08
0012	Day 85-90 Responses	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08
0011	Day 60 Consolidated Response Document	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08
0010	Validation update (SE)					Mar 08	
0009	Country specific information (SK)						Feb 08
0008	Country specific information (SE)					Feb 08	
0007	Country specific information (FR)				Feb 08		
0006	Country specific information (ES)			Feb 08			
0005	Country specific information (AT)		Feb 08				
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08

Table 8: MRP: Repeat Use Procedure - including country-specific validation update (See Figure 11)

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)
0032	Responses to Questions	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10
0031	Manufacturing change variation	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10	Apr 10
0030	Validation update (LV)								Feb 10	
0029	Country specific information (NL)									Jan 10
0028	Country specific information (LV)								Jan 10	
0027	Country specific information (FI)							Jan 10		
0026	RUP initiation sequence	Dec 09						Jan 10	Jan 10	Jan 10
0025	Responses to Questions – address change (FR)				Aug 09					
0024	Variation – address change (FR)				Jul 09					
0023	Responses to Questions	Jun 09	Jun 09	Jun 09	Jun 09	Jun 09	Jun 09	Jan 10	Jan 10	Jan 10
0022	Manufacturing change variation	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Mar 09	Jan 10	Jan 10	Jan 10
0021	Amended Product information (FR)				Jan 09					
0020	Amended Product information (DE)	Nov 08								
0019	Translations of agreed En product information (SK)						Nov 08			
0018	Translations of agreed En product information (SE)				Nov 08					
0017	Translations of agreed En product information (FR)					Nov 08				
0016	Translations of agreed En product information (ES)			Nov 08						
0015	Translations of agreed En product information (DE)	Nov 08								
0014	Translations of agreed En product information (AT)		Nov 08							
0013	Day 90 – Final En product information	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Nov 08	Jan 10	Jan 10	Jan 10
0012	Day 85-90 Responses	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08	Oct 08	Jan 10	Jan 10	Jan 10
0011	Day 60 Consolidated Response Document	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08	Sep 08	Jan 10	Jan 10	Jan 10
0010	Validation update (SE)					Mar 08				
0009	Country specific information (SK)						Feb 08			
0008	Country specific information (SE)					Feb 08				
0007	Country specific information (FR)				Feb 08					
0006	Country specific information (ES)			Feb 08						
0005	Country specific information (AT)		Feb 08							
0004	MRP update sequence	Jan 08	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08	Jan 10	Jan 10	Jan 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)
0003	Final agreed National product information	Dec 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08	Jan 10	Jan 10	Jan 10
0002	Responses to questions	Sep 07	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08	Jan 10	Jan 10	Jan 10
0001	Validation update	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08	Jan 10	Jan 10	Jan 10
0000	Initial MAA	Dec 06	Feb 08	Feb 08	Feb 08	Feb 08	Feb 08	Jan 10	Jan 10	Jan 10