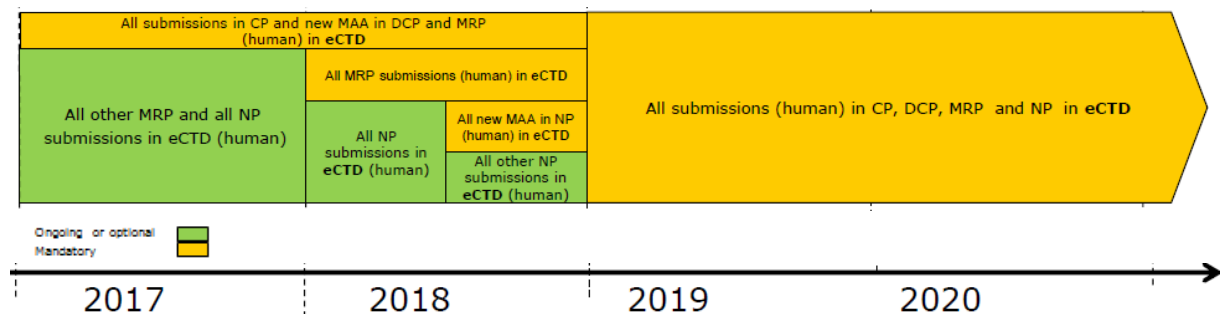


Q&A on how to handle ongoing procedures in relation to mandatory eCTD format



According to the [EU eSubmission Roadmap](#), eCTD format has been mandatory for all MRP submissions (human) since 1 January 2018 and will be mandatory for all submissions (human) in the National Procedures from 1 January 2019.¹

Questions

- Is the mandatory use of eCTD in MRP/DCP also applicable to submissions for ongoing regulatory activities that started up in NeeS or other non-eCTD formats (e.g. for the responses in ongoing procedures)?
- If so, is this applicable to all submission types, e.g. new MAAs, renewals and variations?
- Is the same handling applicable also for ongoing regulatory activities within National Procedures?

Answer

Yes, the mandatory use of eCTD in **MRP/DCP** is also applicable to **ongoing regulatory activities** even if the activity started in non-eCTD format. This applies to all submission types.

This means that submissions related to ongoing activities (e.g. responses or follow up submissions for variations, renewals or new MAAs) should be submitted in eCTD format, even if this means a format shift of the dossier at that time.²

On the contrary, for **National Procedures (NP)**, the applicant is recommended to continue to handle **ongoing regulatory activities** in non-eCTD format, even after the introduction of mandatory eCTD in NP by 1 January.

However, when a new regulatory activity is started within NP after 1 January 2019, it should be submitted in eCTD format and all following submissions for that product dossier should then always be submitted in eCTD format. This would also apply to subsequent submissions for any ongoing procedures concerning the same product dossier.

How to handle related sequences

Applicants are reminded to use the **<related-sequence> element** in the EU Envelope appropriately for the first and the following submissions for each regulatory activity as stated in the eCTD M1 specification.

¹ As for registrations according to article 14 or 16a of Directive 2001/83/EC (simplified registration procedure either for homeopathic medicinal products or traditional herbal medicinal products), the timelines of the eSubmission Roadmap are considered optional. Please refer to regional guidance of the member states.

² It is acknowledged that this is a contradiction of the recommendations set out in the Harmonised eCTD technical guidance, where it is stated that the change to eCTD format should preferably be done at the start of a regulatory activity.

However, if the change to eCTD format is done after a regulatory activity has already been started in another format, it would obviously not be possible to use the <related sequence> attribute correctly, since the start of the regulatory activity is not present as an eCTD sequence to refer to (i.e. there will be no 'initial' sequence in the lifecycle). In these cases, a technical validation would result in a P/F validation issue (criteria 14.7) and additional aspects need to be considered to avoid technical invalidation with rejection

14.7	Envelope Attributes	If the submission unit type is not equal to 'initial' or 'reformat' then the entry for related sequence must not be equal to the value for the current sequence.	P/F
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In these cases, the documents that started the activity and any updates to the activity that were earlier provided in other formats should be **resubmitted as an eCTD sequence** (normally 0000). If several submissions have been done over time (initial submission and subsequent responses to requests for information), the latest updated documents should be compiled and submitted in this sequence with clear reference to all earlier submissions in the cover letter. Then the response (or other follow up) documents for that same activity should be placed in a separate new sequence '0001' and be related to the starting sequence for that activity ('0000'). It should be clearly stated in the cover letter of the "resubmission sequence" for the ongoing regulatory activity that the content of the previously submitted documents has not been changed, only the format.

Example:

Sequence Number	Submission Description	Submission Type	Related Sequence	Submission Unit Type
0000*	e.g. Resubmission of Type II ASMF update variation *	'none'	0000	'reformat'
0001*	e.g. Response to Type II ASMF update variation	'var-type2'	0000	'response'

**) If the dossier is already switch to eCTD format, this should be the next available sequence number.*

In the case of ongoing procedures where significant documentation was provided, and/or the submission was made some time ago and assessment is ongoing, it might not be relevant to provide these documents in eCTD format by the time of a response. In these cases, it would be acceptable to clearly refer to earlier non-eCTD submissions in a cover letter provided as a separate starting sequence and then send the response as the following sequence, related to the cover letter sequence. The sequences should then be provided together in the same CESP delivery.

Applicants are also recommended, but not obliged, to move over to eCTD format by submission of a baseline sequence for the current approved dossier. If this is done, the above-mentioned scenario should also be followed for any ongoing regulatory activities in separate sequences.

Example:

Sequence Number	Submission Description	Submission Type	Related Sequence	Submission Unit Type
0000	e.g. Baseline module 3	none	0000	reformat
0001	e.g. Resubmission of Type II ASMF update variation	none	0001	reformat
0002	e.g. Response for Type II ASMF update variation	'var-type2'	0001	response

A baseline would also be accepted later in the lifecycle. For detailed guidance on that and on baselines in general, please refer to the [EU Harmonised Technical eCTD Guidance chapter 2.12.](#)