Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

MHRA baseline guidance

A baseline submission refers to submission of all current valid documents along with a statement that the content has not changed, only the format**.** For transparency reasons and ease of process it is recommended that baselines are applied when there are no pending regulatory activities for the product.

Baseline submissions are usually required when converting the format used for submission of procedures and/or correcting technical issues relating to previously supplied documents in the current submission format.

General guidance available from the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) is provided by the links below and the relevant text is italicised for easy reference.

Harmonised Technical Guidance for eCTD Submissions in the EU

Section 2.12 Technical Baseline Applications

A baseline submission is a compiled submission of the current status of the dossier, i.e. resubmission of currently valid documents that have already been provided to an agency but in another format. The sections provided to make up a baseline can be defined by the applicant, but any omissions should not render the submitted content misleading. A baseline would typically consist of the Module 3 documents that tend to change over time during the lifecycle of the product.

It is highly recommended but not mandatory to use a baseline as a start of an eCTD when changing from paper or NeeS and to provide as much content as possible in the eCTD. The baseline would preferably consist of high quality electronic source documents, but good quality scanned images would also be acceptable in these cases, preferably with Optical Character Recognition (OCR) to facilitate text searching.

It should be clearly stated in the cover letter of the "baseline eCTD sequence" that the content of the previously submitted dossier has not been changed, only the format. There is no need for the NCAs or EMA to assess baseline submissions and hyperlinks between documents are not needed. The submission type reformat should be used in the envelope for the baseline sequence.

When an up to date eCTD has already been used elsewhere in the procedure for other countries all previous sequences should be sent to the RMS and all CMSs

CMDH Best Practice Guide on the Use of the Electronic Common Technical Document (Ectd) in the Mutual Recognition and Decentralised Procedures

Section 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 elsewhere in the procedure for other countries, on agreement with the RMS, the lifecycle should continue and earlier sequences should be provided to the RMS and all CMSs.

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.

There may exist other scenarios where a baseline submission will be required by MHRA

Other Scenarios Requiring Baselines

You may be requested for a baseline following a submission in eCTD format where the MHRA does not have a current lifecycle established for this product. This may occur where the last submission in eCTD format was accepted using a tolerant validation to resolve issues of missing historical lifecycle e.g a missing baseline on conversion from NeeS to eCTD.

Reminders and Handy Tips

Baselines submitted through the portal should be submitted as Information updates

Once switched from NeeS to eCTD it is not possible to return to NeeS

Frequently asked Questions

1. *Are there any additional national requirements for national or EU approved products (other than the EU guidance)?*
    - Proof of payment where fees are applicable (implicit from the regulations) - in the eCTD
    - Consolidated Label & Leaflet - in the eCTD
    - SmPC fragments in the MHRA word template and included in the working documents folder – Outside of the sequence folder
    - Validated before submission - use a validation tool MHRA use EURS Validator
2. *What is the lifecycle management of national eCTD-submission in UK, internally at the MHRA?*
    - MHRA uses the Harmonised Guidance

http://esubmission.ema.europa.eu

- Currently we accept NeeS and eCTD
- For new MAA highly recommend starting in eCTD now
    - *Remember, eCTD mandatory for new MAA in DCP and MRP from Jan 2017*
- From Jan 2018 MHRA will only accept eCTD for all submissions
    - *In line with EU roadmap intentions*

3. *The guidance documents states it not a requirement to submit eCTD baseline whereas the MHRA have communicated that baseline are compulsory. Please can the MHRA validate the reason why it is a requirement or not.*
    - In the past we have accepted changes from older formats to eCTD without a baseline

- Creation of duplicate dossier streams are required to manage an eCTD without baseline
- With the increased use of eCTD we are now seeking to remove inconsistency from our approach
- However we will still be pragmatic in our approach, e.g. abbreviated baselines acceptable for very old products, best documentation possible..

4. *Could MHRA please advise on what is the best practice to follow for an eCTD baseline submission?*
    - (Re-)Submission of all current valid documents as a new sequence
    - Statement that the content has not changed, only the format
    - Applied when there are no pending regulatory activities for the product
5. *Why do some MS require only module 3 in e-CTD baseline, whereas the MHRA have stated they require module 1-5?*
    - All modules are clearly relevant and important to the lifecycle
    - MHRA recognise that for older dossiers some information may not be readily available or difficult to translate from previous formats into the appropriate modules
    - MHRA therefore recommend submission of the other modules at least at a higher level
    - Baseline should include everything available placed in the most appropriate placeholders within modules 1-5
6. *What are the requirements for submitting eCTD baselines for historical products that where approved before CTD format- how will the MAH compile the baseline of section/document that are not available?*
    - Choose the most appropriate placeholders
    - Within the declaration make their reasons clear why information is unavailable in a particular format and what has been presented
    - MHRA will take a pragmatic approach
    - Baselines are not assessed but will/may affect future applications if wrong
7. *In many large generic company portfolios, there are a lot of old licences (20 to 30 years old). If the entire dossier is not available for these kind of products, would it be acceptable to submit an abbreviated dossier with the key elements? This would be particularly useful for the Module 5 as the requirements have changed significantly over time.*
    - Yes
    - See responses 5 & 6
8. *What is the procedure for approving a baseline conversion? Would MHRA consider processing a bulk submission for UK National licences?*

- Yes
- If submitting an eCTD for a product line we would accept a baseline using a common document set for M2, M3-2-S, M4 & M5 – this is the same requirement we have for a new application submission as these documents are identical for different strengths/presentations. We would expect however to receive different M1 and M3-2-P sections within the same sequence which are product specific – again similar requirement to a new submission. However if justified we would accept differences to the above.

9. *Is eCTD format also requested for ASMFs?*

- Yes but MHRA still also accept NeeS submissions for ASMFs

CMDh QUESTIONS & ANSWERS ACTIVE SUBSTANCE MASTER FILE (ASMF)

The acceptable ASMF submission format(s) vary between Competent Authorities; please consult the CMDh and CMDv website for the submission requirements of each National Competent Authority or the Pre-submission guidance (human and veterinary) on EMA's website for the submission requirements in the centralised procedure.

For human medicinal products, submission in eCTD format is recommended.

- Also – see HMA Working Group on Active Substance Master File Procedures
    - ASMF work sharing will enable NCAs to identify when the same ASMF has been submitted in different European MAA and MAV procedures.
    - Share assessment outcomes of the same data supporting the quality of the active substance.
    - Version control is one of the key problem areas affecting assessors and eCTD and work sharing make a significant positive impact

10. *Concerning the 2018 deadline for the UK National licences and the very large portfolio of many generic companies will MHRA be flexible on the deadline implementation?*

- MHRA are anticipating that eCTD will be mandatory for all submissions after eCTD becomes mandatory for all procedures as outlined by the EU roadmap (Jan 2018)
- Not expecting conversion/baselines for existing licences on mass
- However, if no regulatory activity planned for these licences before 2018 MHRA would highly recommend a plan is introduced now.