How can baseline dossiers support global eSubmissions?

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What is a baseline submission?

- Single eCTD submission capturing all the appropriate information that
  - reflects what has been submitted
    - –All module
    - –Module 3 only (32S, 32P, 32A and/or 32R)
  - Corresponds to approved marketing license of a drug
  - Merges per eCTDs per strength to single eCTD lifecycle

Content of a baseline

- Module 1
  - Cover letter (state content has not changed, only its format)
- Module 2
  - Integrated overviews and summaries for Quality, Nonclinical and Clinical or a clear combination of those
  - Cumulative list of all clinical trials
  - Individual study synopses
- Module 4+5
  - All study reports as is

Content of a baseline

- Module 3
  - No chronological cumulative presentation, but a "current view"
  - Hyperlinks not necessary
  - Do not
    - Exclude any information form original dossier (unless updated by a regulatory process)
    - Include any information not submitted before in the original dossier
  - Document granularity that fits best with the lifecycle of documents

Document granularity Module 3

- Coursest and finest granularity defined by ICH M4 on organisation of Module 3
- Determine granularity based on likelihood of:
  - Future changes
  - Reusability across products
  - Reusability across regions
- Apply meaningful names for now, here and the future

Subsequent sequences should match granularity of the previous sequences

Granularity and future?

- Only replace or delete whole documents, not sections or pages in eCTD
  - –e.g. single 32P33 vs. Formulation, filling, packaging and labelling
- Mention information only once and in a single document
  - –e.g. Batch numbering in 32P33 only and not repeated in 32P54
- Do not mention the reason for submitting a document
  - –e.g. Do not mention “to support the change of.....”

Granularity and regional difference

- Additional specifications beyond the Ph.Eur. in a subset of countries
  - –S41 Specifications Ph.Eur. Vs. S41 Specifications polymorphism
- Different level of detail in a limited number of documents
  - –e.g. Details around control of critical steps, whereas the remainder is identical

Granularity and reuse across products

- Separate content from context
  - –Drug substance documentation not refering to the context of use
  - –Analytical procedures across substances and products
  - –P1 Description and composition vs. Container description
  - –P4 Compendial combined vs. Compendial individual
  - –P7 Container material information, rather usage

How to define the granularity?

- By use of an ToC outline capturing granularity and naming

Analytical procedure "Test C by Method D" is not product specific and can be reused across products

Module	Section	Shared/Dup	eDMS N	CTD Title	Output File Name
3.2.P.5 Control of Drug Product					
3.2.	P.5.1		P.5.1 Qdrug	Qdrug	specifications-qdrug
3.2.	P.5.2		P.5.2 Test A by Method B Qdrug	Test A by Method B Qdrug	analytical-procedure-testamethodbqdrug
3.2.	P.5.2	cross-product	P.5.2 Test C by Method D	Test C by Method D	analytical-procedure-testcmethodd
3.2.	P.5.3		P.5.3 Test A by Method B Qdrug	Test A by Method B Qdrug	validation-analytical-procedure-testamethodbqdrug
3.2.	P.5.3	cross-product	P.5.3 Test C by Method D	Test C by Method D	validation-analytical-procedure-testcmethodd

When to be created and submitted?

- At start of an eCTD lifecycle for an existing dossier
  - –0000=Baseline
  - –0001=Major variation or renewal

- During the eCTD lifecycle

Submission type: reformat

Pros of baseline submissions 1

- Ability to remove repeating and therefore redundant information, such as
  - –Scale at other sections than S22 and P33
  - –Manufacturer names at other sections than S21, P31 and A1
  - –Buildings at other sections than A1
- Ability to create content in context in appropriate sections
  - –Manufacturing process development and Pharmaceutical development
- Ability to apply specific information at relevant sections only
  - –In text and in header and footer

Pros of baseline submissions 2

- Ability to start a clear lifecycle and audit trail
- Ability to create documents for reuse across products, e.g.
  - Filling, packaging and labelling processes
  - Selection and justifications for excipients
  - Suitability of container
  - Excipients
  - Analytical procedures (and Quality by design)
  - Container closure systems
  - Facilities and equipment
- Ability to create documents for reuse across countries

Pros of baseline submissions 3

- Greatly improves the review process
  - Within the company
  - For agencies
- Improves transparency
  - What document has been submitted where?
  - What products are supported by a document?
- EU agencies encourage/recommend baseline submissions; US accepts these

Cons of baseline submissions

- Time consuming (up to 15 days)
  - Requires limited content knowledge and advanced Word knowledge
- Insufficiencies and incompliance becomes apparent; e.g.
  - Lack of validation because it got approved before it was required
  - Lack of stability data because it was OK at time of registration
- Inability to
  - Add more recent though never submitted information
  - Correct erroneous information
  - Remove out-dated though never replaced information

To be corrected with variations

How can baseline dossiers support global eSubmissions?

- Preparation of a baseline
  - Cleaning the Module 3 documents
  - Allow for reuse of documents across products
  - Allow for reuse of documents across countries
  - Audit trail of what has been submitted where as captured within an eDMS
- Submission of a baseline
  - Starting a clean and clear lifecycle to ease future audit trail within a dossier
- No need to prepare a baseline for Modules 1, 2, 4 and 5
- No need to submit a baseline to benefit internally

Thank you

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