Switching from Paper/NeeS to eCTD: The importance of baseline eCTDs

userBridge 2010

21.09.2010 - 23.09.2010, Frankfurt

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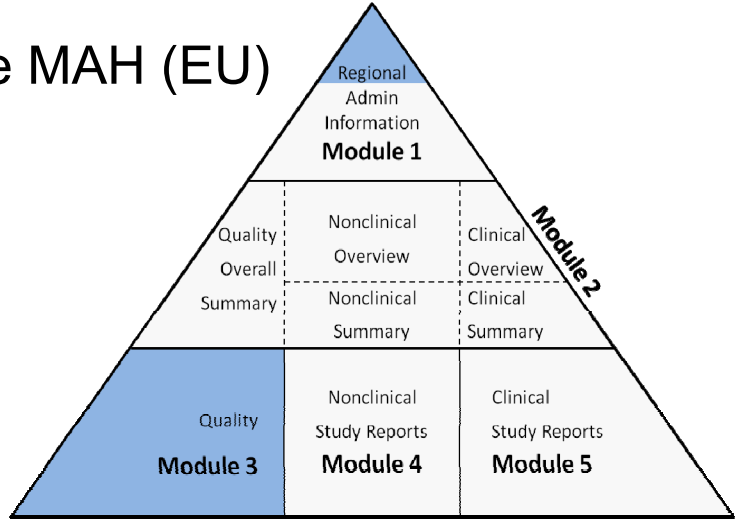
What is an eCTD baseline?

- Formal eCTD life cycle initiation step for existing drug dossiers:
  - Post-approval phase
  - Type “reformat”, no new contents, no hyperlinks
  - No assessment, only upload into agencies review system
  - Ideally in timely context of a new regulatory activity
- Can occur multiple times during eCTD life cycle

eCTD baseline Content

- Should include:
  - Complete and approved Quality information in Module 3
  - Cover letter + signed declaration from the MAH (EU) additional M1 requirements in CH
  - “Common” approved Product Information
- Additional content optional
- Supplements during later eCTD life cycle possible



eCTD baseline Requirements

- The eCTD baseline is an European concept
  - Not yet mentioned in guidelines from US, CA and other regions
  - On EU level “encouraged” (EMA) or “highly encouraged” (TIGes)
  - On NCA level “preferred” or “strongly recommended”
  - In CH highly recommended
  - **But not mandatory (yet)!**

eCTD baseline
Feedback from clients

- Although it`s purpose and benefits seem to be obvious the reaction from new clients is often:
  - *„Do I really need to do a baseline first?“*
  - *„We don´t have the ressources right now, we just want to start with the eCTD“*
  - *„What´s the benefit of redoing all that documentation ?“*
  - *„Base... Sorry?“*

eCTD baseline
Strategic challenges

- Business focus on new / initial drug applications (“fancy” projects)
  - Management support for switching to eCTD limited
  - Resources limited
- Sometimes less experienced staff responsible
  - Awareness of eCTD requirements limited
  - Additional software licenses required

eCTD baseline
Practical challenges

- Reworking of documentation required:
  - “Historic” documentation, not available in CTD format
  - Granularity
  - “Section overview” docs, explanatory docs, TOCs, placeholders, etc..
  - Paper and scanned PDFs
- Switch in business practice: from parallel “old paper world” to sequential “new eCTD world”

eCTD baseline
Consequences

- An eCTD baseline costs time + money!

- ”...Default industry position to not require the supply of a baseline for existing applications and that the decision is owned and managed by the applicant...”

  Efpia Presentation Nov 2009 at HMA meeting

Real-life example
Without eCTD baseline

- National licensed product (Spain), post-approval phase
  - Single, simple dossier containing 1 x 3.2.S and 1 x 3.2.P
  - To be switched from paper to eCTD
    without prior submission of a baseline eCTD

"The switch from paper to electronic-only can be made at the start of any phase in the life cycle of a medicinal product, initial application or a later variation… ***Historical data does not need to be re-submitted electronically****... "* [AEMPS website, 2009]

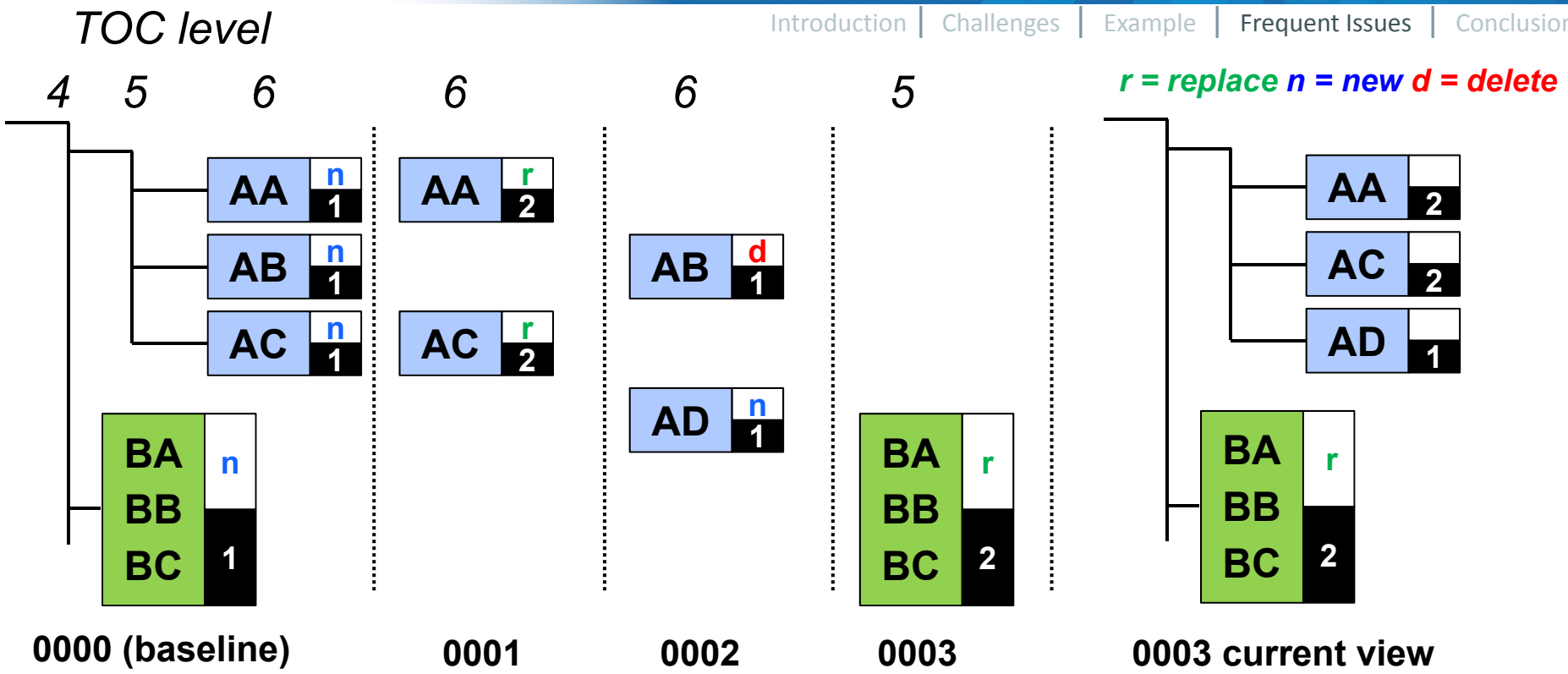
Real-life example
Starting point (2009)

- No baseline submission due to time and resource constraints
- Trigger: subsequent renewal procedure
- eCTD life cycle to start with a type II variation,
  further sequences filed in “close timely context”
- M3 documents to be reformatted in CTD format from NtA at the time of filing *only as required per life cycle sequence concerned*

Real-life example
Problems experienced

- Typical practical challenges as with eCTD baseline!
- Referencing to background information was not possible
- No “complete picture” of the registration dossier; paper and electronic archive in parallel
- Updated content (compared to “paper baseline”) submitted as “new” instead of “replace”
- **Difficulties in establishing optimal level of granularity**
- **Problems assigning correct life cycle “operation” attributes**

“Fixed” granularity with baseline – dos



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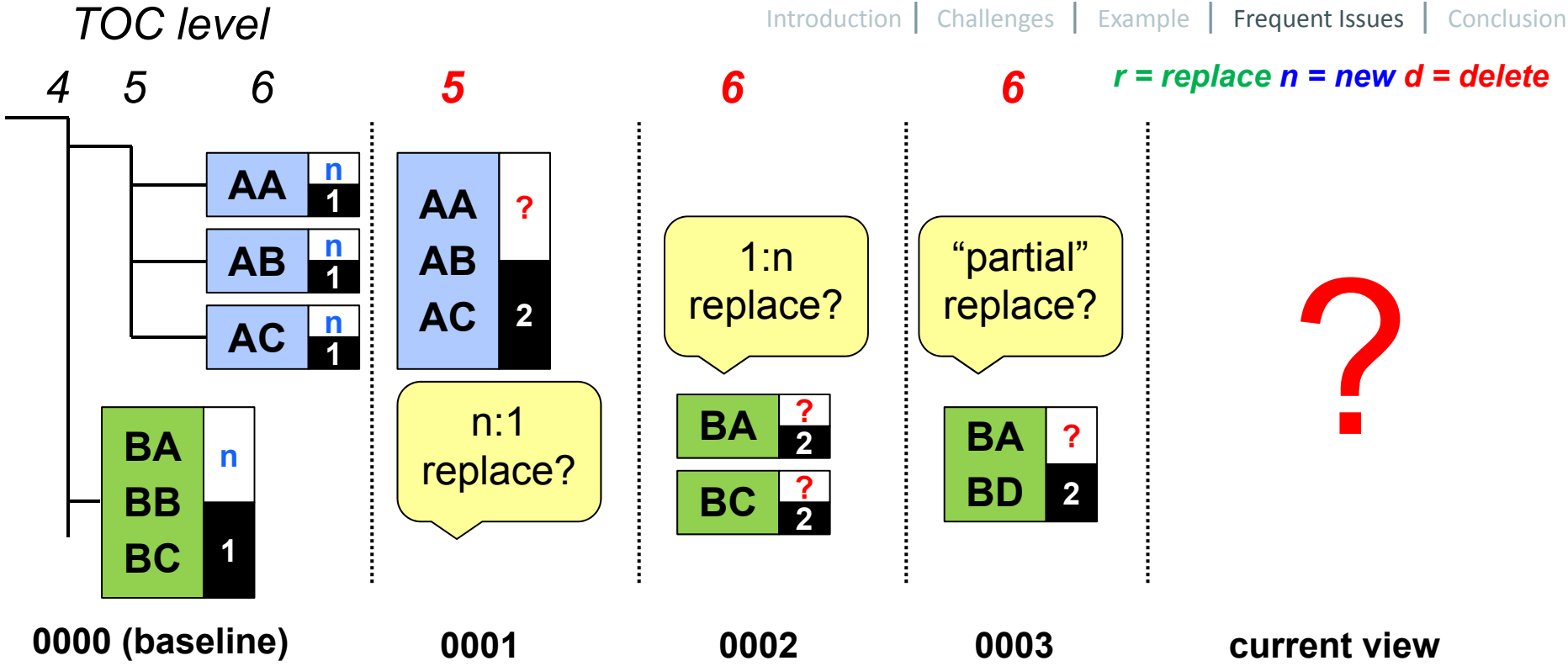
“Fixed” granularity with baseline – don’ts



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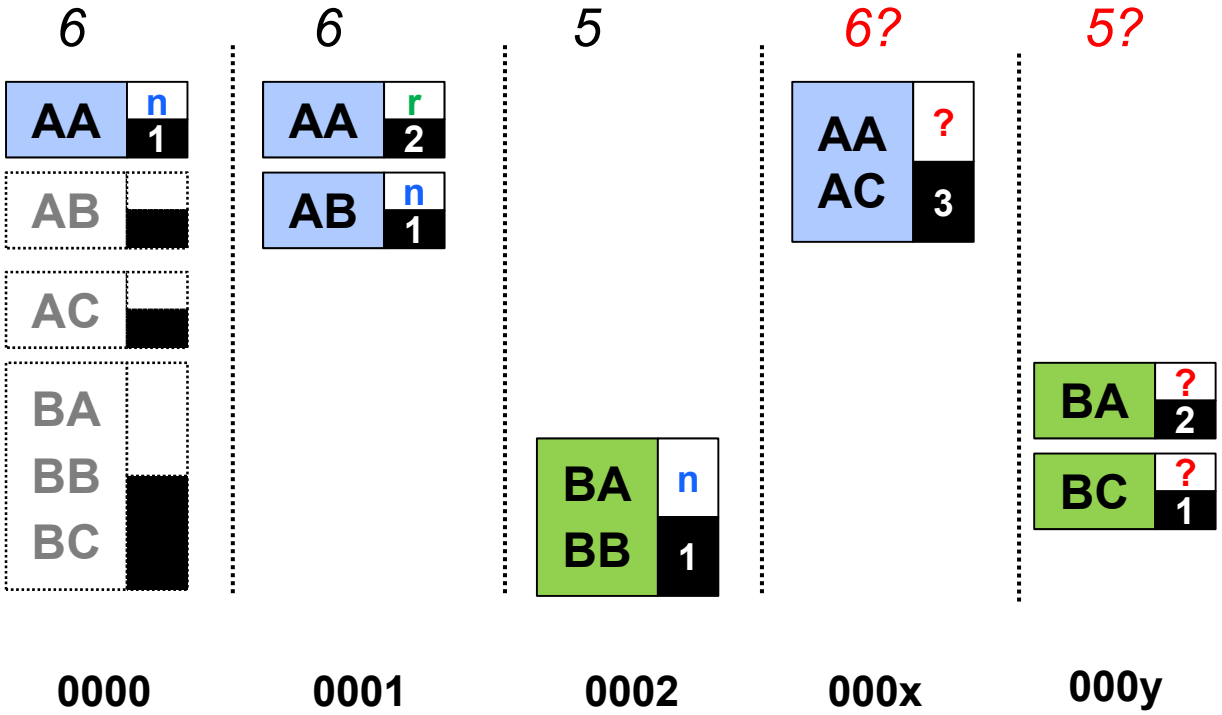
And now... without baseline

TOC level



r = replace n = new d = delete

What if.... several months are between 0002, 000x, 000y?

What if.... the responsible person has changed?

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Granularity issues without baseline

0000

3.2.S.2.3 **Doc 1**
1) Control A (1)
2) Control B (1)

3.2.S.2.3 **Doc 2**
3) Control C (1)
4) Control D (1)

5) Control E
6) Control F
not submitted

000n

3.2.S.2.3 **Doc 3**
1) Control A (2)
5) Control E (1)

New ?

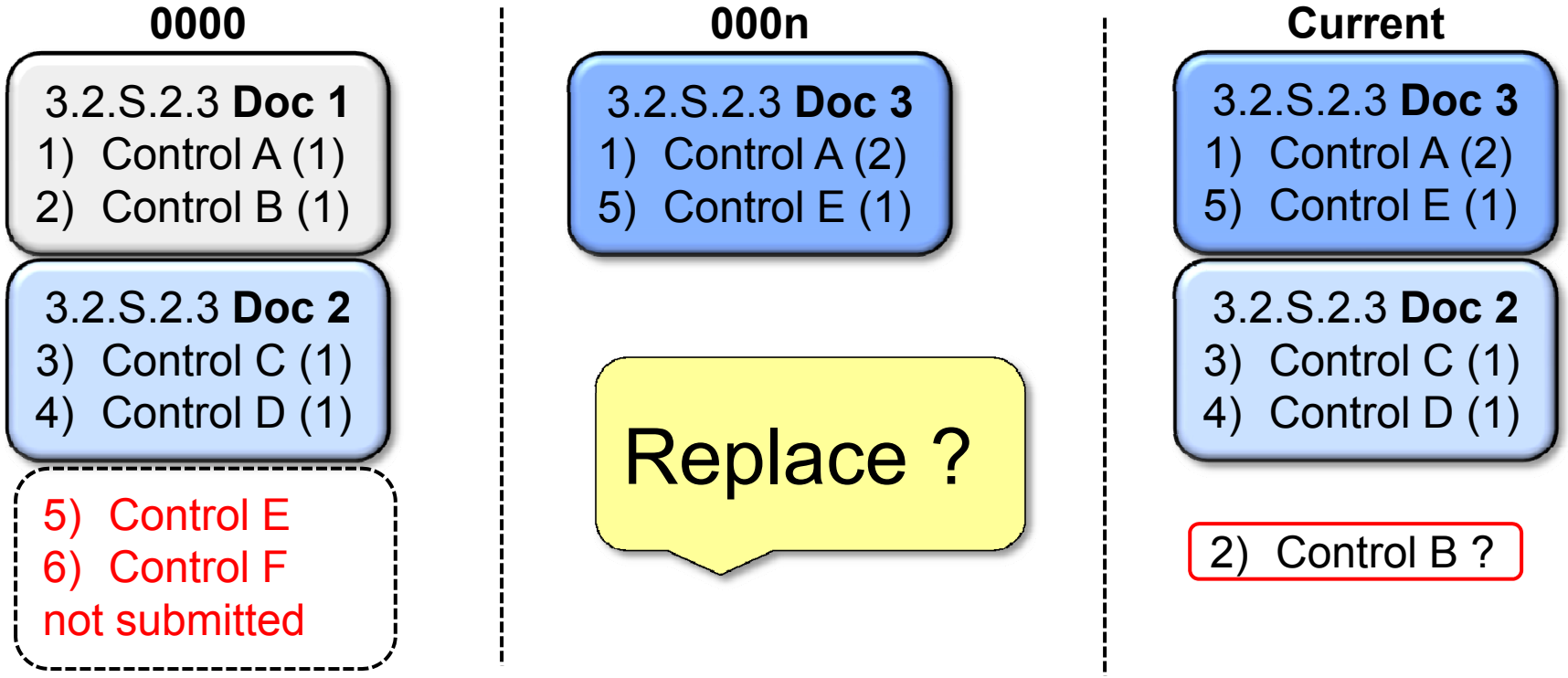
Current

3.2.S.2.3 **Doc 1**
1) Control A (1)
2) Control B (1)

3.2.S.2.3 **Doc 2**
3) Control C (1)
4) Control D (1)

3.2.S.2.3 **Doc 3**
1) Control A (2)
5) Control E (1)

Granularity issues without baseline (cont'd)



Conclusions

- Consider the same things as with eCTD baseline – but redundantly!
- Subsequent eCTD sequences must match the granularity level of the previous ones; select highest level of granularity possible
- No „current view“ of complete dossier:
  - Tracking of dossier content difficult
  - Tracking of regulatory status of individual documents difficult
- Parallel repository for eCTD and legacy / paper documents required *at sponsor and agencies*

Conclusions (cont'd)

- Increased risk of inconsistencies
  - Increased risk of questions / refusals
  - Increased risk of additional response / correction sequences
- Only short-term advantage, more disadvantages in the long-term
- Definitely not recommended for complex multinational procedures

Thank You !

Contact

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