Requirements for Reference Standard NCE

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Focus Workshop

(*In collaboration with the AAPS and JBF*)

Industry input into ICH M10: Experimental data as the cornerstone for a science driven bioanalytical guideline

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Problem statement: *Reference standards for NCE*

- Opportunity to harmonise on certificate of analysis requirements
- What level of characterization is required for regulatory work
- Lack of clarity on how to handle updated batch information and assess impact on associated solutions
- Re-test vs expiration date including impact on existing solutions & samples

Outline

- EBF recommendations for the ideal certificate of analysis
  - Including advice on re-test vs expiration

- Recommendations on
  - Use of insufficiently characterised material
  - What to do when batch characterisation data changes
  - Impact of material passing re-test or expiry on derived solutions (and samples)

Minimum Requirements for CofA

- All agencies (FDA, EMA, ANVISA, CFDA, MHWL) agree reference standard should be from authenticated, traceable sources and a Certificate of Analysis (CoA), or equivalent documentation should be provided
- Recommendation
  - **Lot / batch number (source / manufacturer)**
  - **Expiration or retest date**
  - **Purity**
  - **Storage**

Ideal Certificate of Analysis

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General	• Source • Compound name • Product / lot number • Certificate ID • Certificate approval
Identity	• Empirical formula • Structural formula • Molecular weight salt • Molecular weight base • Stereochemical property
Characteristics	• Appearance
Storage Conditions	• Storage temperature • Humidity • Light protection
Retest Date	• Ideally based on stability testing (state if based on testing or not
Purity Information	• Assay as is or potency (including formula)
Final calculation for weighing	• Consider conversion salt / base and purity information

Retest *vs* expiration date recommendation

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- Material with either expiry date or re-test date are acceptable for use
  - Retest – when material should be re-examined to ensure that it is still suitable for use
  - Expiry – assigned to products where stability has been defined
- Preferable to use material where retest date is based on evaluation of data derived from stability studies
  - Acknowledge that this is not always possible for early batches of material
  - Request that CofA should state if retest date is simply “defined” or is based on stability data

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Retest *vs.* expiration date

- Retest – when material should be re-examined to ensure that it is still suitable for use
- This is not an expiry
- <u>Recommendation</u>
  - SOP on how to handle re-testing and continued use of material whilst waiting for formal retesting

Reference standards with insufficiently detailed CofA

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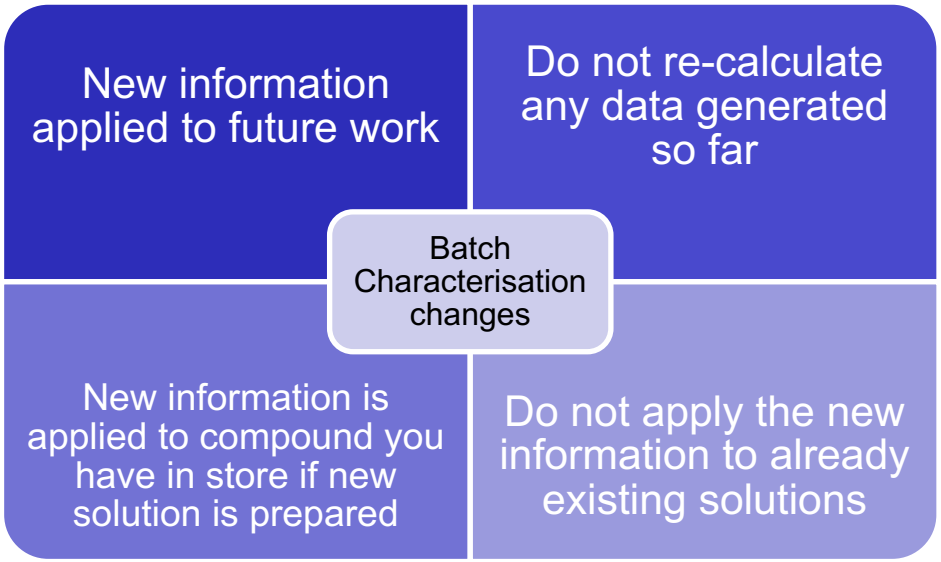
- Recommendation
- Do Not accept an insufficiently detailed CoA in regulated work
- Exception
  - In case of rare material (e.g. metabolite) where an insufficient amount of material is available to allow sufficient characterisation

What to do when CofA information changes

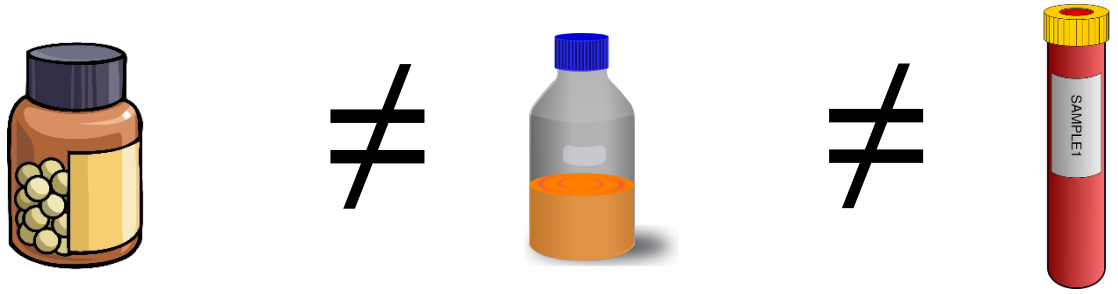
- Recommendations supported by European industry survey data



- If low purity batch used in validation and new batch purity is improved assess the impact on your validated method

Retest and Expiry of NCE

- Retest and Expiry of a compound is for the compound in some physical state (and matrix) under some storage condition



- Therefore
  - Test item expiry does not apply to solutions or samples
- Recommend continued use
  - Stability established for solutions and samples should be adhered to

Acknowledgement

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