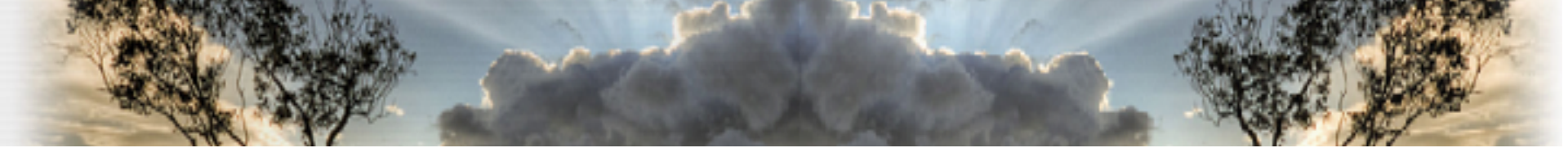

REPEAT ANALYSIS

Boris Gorovits

- Presentation includes collection of comments supplied by the EBF membership although the content may not reflect the position of the entire EBF community

Feedback from EBF and Delegates

Needs clarification that reanalyis calculations should be based on a valid result (i.e. concentration in range, ULOQ or <LLOQ). If not acceptable, there is no valid result (batch QC and/or QC fail, poor chromatography or anomalous ISTD response)

Pre-specifying the poor chromatography (which is a very broad term: Tailing, baseline draft, 'Strange' Baseline, Sharp peaks on the Baseline, 'Poor' Peaks, Poor Performance, Poor Chromatogram, etc.) in an SOP may not cover each and every one of the poor chromatography cases that may occur. Pointing out between brackets "(as predefined in and SOP)" is not necessary in the guidance
Please rephrase to: Poor Chromatography

need clear and unambiguous definition of what a Reanalysis is. Need to differentiate between a) you do not have yet a final, reportable result (e.g. due to run rejection, sample is AQL, …) and therefore need to analyze the sample again and b) you have a final, reportable result but you reanalyse it e.g. by mistake or for TK/PK reasons. Whereas a) and b) should be defined in SOPs, only b) should be discussed in the report.

This requirement causes technical issues: Samples of a rejected run are not considered to be reassayed samples in Watson LIMS. They can not be listed as requested in Table 1

"I disagree"

predose samples could contain detectable concentrations. So they should be removed from the text.

Include the reason - Where the analyte has an observed concentration that is >ULOQ, but yields an observed concentration of greater than 25% below the ULOQ after repeat analysis with dilution

Improper sample injection or malfunction of equipment in case samples can not be reinjected

This text requires clarification. Who identifies whether the samples should be reanalyzed or not? This section mentions that reanalysis is not acceptable for BA/BE studies which in inconsistent with the statement in lines 590-592. Also, later in the document it mentions BE studies and relative BA studies should not have sample reanalysis. We suggest clarifying the text, making it consistent throughout the document.

naïve pre-dose samples. You might expect drug in a pre-dose sample after repeated administration

please rephrase to Rejection of an analytical run because the run failed the acceptance criteria with regard to the precision and accuracy of the calibration standards or of the QCs, rationale: not "and/or" but only "or" because if the standards fail, then QC results are not exploitable

Suggested comment to EMA/EWG

Final recommendation from this presentation, which combines the original recommendation enhanced with the discussions from the panel discussions during the meeting, are captured in the summary slide deck: Recommendations from the EBF Spring FW 2019

Acknowledgment and questions

- The EBF community for survey data and feedback
- Further questions to info@e-b-f.eu before 31 May