Note

- These are excerpts from the discussion at JBF ICH-M10 workshop 2023. Please note that these do not represent the official position of JBF.

Chromatography

NA for CHROM

- **Did not discuss** these topic on JBF M10WS 2023
  - C1: Hybrid assays & ICH M10
  - C3: Focus on urine and metabolites
  - C5: Stock and working solutions stability
  - C6: Surrogate/rare/preclinical matrix for CHROM
  - PC-01: Tissues - how are you interpreting the requirements?
  - PC-02: Choosing the right regression model
  - PC-04: Carry over assessment during samples analysis
  - PC-05: New metabolites = new (full) validation?

Chromatography

C2: Whole blood stability for Chrom

- **Implement whole blood stability in non-clinical? ➡ Yes and No**
  - Why **NOT** implement whole blood stability?
    - **3Rs** reason
    - **Short time** until centrifugation in nonclinical study site (but not always short time)

- **How to assess whole blood stability?**
  - **How many conc levels?** ➡ Major opinion: **2 conc.** (There were no companies who evaluate at 1 conc.)
  - **Accuracy or Residual ratio?** ➡ Major opinion: **Residual ratio** (There were no companies who evaluate as whole blood conc [All companies evaluate as plasma conc.].)

Chromatography

C4: Dilution QCs during validation & sample analysis

- **Include dilution QCs in sample analysis runs? ➡ Yes**
  - In the validation study, we can validate **"dilution ratio"** and **"how to prepare dilution QC"**. On the other hand, in the study sample analysis, we can check ensuring **"dilution operation"**.
- **Are they solely to cover dilutions outside of the validated bracket of dilution factors? ➡ No**
  - As described above, we can check ensuring **"dilution operation"**.
- **How many dilution levels should we evaluate when we use more than 3 levels of dilution factors? ➡ Only lowest and highest levels** (as described in ICH M10)

Chromatography

PC-03: Matrix effect - special population, haemolysed and lipaemic

- **Evaluate haemolysed or lipaemic matrices? ➡ Yes**
  - **Haemolysed** matrices: Evaluate **typically both in non-clinical and clinical**
  - **Lipaemic** matrices:
    For **clinical**, evaluate **typically**.
    For **non-clinical**, evaluate **in cases of hyberlipidemia models**, etc.
- **Patient and special population**
  - **What timing** will these be included?
    - **When the patients recruited** in clinical trial (can use **pre-dosing samples**).
    - **Hepatically or renally impaired** patient‘s matrices are **commercially available**. ⇒ **Can include validation study.** (only a few companies evaluated in validation study)
    - In case of **changing indication**, target patients may change. ⇒ **Postpone until Phase 3.**
  - What will we do **when the results failed?**
    - If there is time, consider **revalidation** and **reanalysis of study samples**.
    - In some cases, it may be possible **using dilution** for study sample analysis.