COMAC MEDICAL

Context Of Use – caffeine analysis

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Information provided from the clinical study protocol

- Clinical DDI study
- Population: healthy volunteers and patients with cancer
- Samples collection for caffeine levels: on Day -1 only
- Results from these samples are not used for enrolment decision
- Caffeine levels are not listed in the study endpoints

Additional questions raised to the Sponsor

- How is the caffeine data going to be used in the study?
- The caffeine data will be used to understand what type of coffee drinker (regular or heavy) the participant is and if levels of caffeine could help understand the PK differences we observe in the data
- As consumption of caffeine >200 mg/per day is an exclusion criterion per study protocol, do you have any idea on the expected concentration range of caffeine in the samples? Is there a minimum limit of quantification required?
- Ranges from literature materials are typically 30-15,000 ng/mL or 20-20,000 ng/mL. Since we are not characterizing PK of caffeine and only its plasma concentrations, typical LLOQ values observed in literature would be acceptable.
- If concentrations above the method upper limit of quantification (ULOQ) are obtained, is it sufficient to report them as >ULOQ or you would prefer to have an exact quantification obtained via validated dilution protocol?
- Extrapolated concentrations are OK.

Validation strategy

- Calibration curve (6 levels, with ≥75% pass)
- P&A (1 run; L, M, H n =3 replicates)
- Selectivity (1 source)
- Stability (F/T, long term, bench top)
- Carry over
- Stock solution stability

Samples analysis

- Calibration curve (6 levels, with ≥75% pass)
- QCs (L, M, H n =2 replicates, with ≥50% pass/level) – bracketing the study samples
- IS variability: Study samples with IS signal outside the 3SD control limits will be identified as outliers

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Thank you!