Fit for Purpose Validation in Practice at GSK

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Clinical Assay Validation to support FTIH

- FFP/SV is our “first intent” for assays to support FTIH (SAD/MAD) studies
- These studies are by default supported in-house
- Exception where FTIH = FTIP (e.g. oncology)
- Approach adopted since Sep 2016
- Around 25 assets supported with SV/FFP assays
- No regulatory questions to date
  - Studies not submitted as part of a filing
  - Upcoming GCP inspection by MHRA 4Q18/1Q19

Pre-Clinical Assay Validation to support GLP TK Studies

- SV/FFP assay used to support an early development cyno GLP TK study (3Q17) where BioA was in-house
- An *a priori* SOP deviation was prepared to cover the validation
  - Process has since been refined such that SOP allows SV/FFP documented via a validation plan
- Engagement with internal stakeholders – no issues
- During study support it was necessary to “top up” the validation with dilution QCs, processed sample re-injectability

MHRA Findings related to FFP Validation use to support Cyno TK study

"There were issues with management and reporting of the bioanalytical phase of study [redacted] relating to communication with the Study Director and transparency of phase report……

…The analytical method [redacted], which supported the bioanalytical phase of the study was not validated in accordance with Test Facility procedures and this was not communicated to the [redacted] Study Director.

….. It is acknowledged that a deviation from SOP-[redacted] was documented on 07 April 2017. However, the information and rationale for this deviation were not provided to the Study Director to allow them to assess its impact on the study…

…In addition to responding to this deficiency GlaxoSmithKline are required to communicate the information relating to the method validation and the on-study assessments to the Study Director to allow an impact assessment to be made…."

- **Feedback during the inspection (and at the close out meeting) was that adoption of SV/FFP approach to support early GLP TK studies was acceptable**
- **Deficiency related to communication to the SD and <u>NOT</u> the use of FFP/SV**

Post Inspection “Fall-Out”

- Further stake-holder engagement and “education”
- No concerns from stakeholders
- Worries within global BA group regarding requirement to seek SD “approval” for using SV/FFP and the implications of communicating all “in-study” validation experiments to the SD (who is likely at a CRO and not a bioanalyst)
- Decision made to do full (BMV) validations to support future GLP TK studies
- We continue to adopt SV/FFP assays for clinical FTIH studies