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Observations following MHRA combined GLP/GCP inspection

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Scope of Audit

- Type and Purpose of Inspection; Joint GLP/GCP Compliance Monitoring Inspection
- Organisation Inspected; ARC Trinova Ltd (now Quotient Sciences)
- Organisation Type; Contract Analytical Laboratory
- Date of Inspection; 10-11 May 2018
- Number of Inspectors; 2
- Inspection Report Date; 8 June 2018

MHRA
Regulating Medicines and Medical Devices

Observation (Data Integrity)

- Inspectors focussed their attention on data transfer (for clinical bioanalysis) from Waters MassLynx to Thermo Watson LIMS

- Watson LIMS (v 7.5 SP1) was validated 2016
- Waters Xevo and MassLynx 4 was installed and validated 2017
- Waters Nugensis installed and validated 2016

- Flat-file transfer between MassLynx and LIMS

Observation (Data Integrity)

- EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (Section 6.12 Data Recording);

- All data should recorded directly, promptly, accurately and legibly
- Implement a quality control procedure to ensure data generated in a lab is accurate and complete
- Any change to data should not obscure previous entry
- If data is generated, recorded, modified, corrected and stored or archived electronically, it is recommended that than an electronic audit trail is maintained, where possible
- The impact of new computerised systems that are interfaced with existing LIMS should be assessed
- Following changes to system (upgrade or patches) the need to re-validate system should be determined. Access to computerised systems should be controlled

Observation (Data Integrity)

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- EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (Section 6.16 Computerised Systems);

- All Computer systems should be developed, validated and maintained to ensure validity, integrity and security of the data
- A responsible person should be identified as administrator
- The components (e.g. hardware and software) which constitute system should be clearly defined
- The impact of new computerised systems that are interfaced with existing LIMS should be assessed
- Following changes to system (upgrade or patches) the need to re-validate system should be determined. Access to computerised systems should be controlled

Observation (Data Integrity)

- Our CAPA and response to MHRA was accepted
- No distinction between GLP/GCP in terms of computer system validation and data integrity

Observation (Clinical Study Management and Conduct)

- ‘The laboratory did not provide a sponsor’s sub-contracted statistical analysis vendor with a updated sample analysis data set from study XXXXXX following finalisation of the validation study’

- LC-MS assay was fully validated
- Haemolysis (>1%) had impact on assay integrity
- Sponsor was informed of this limitation
- No haemolysed samples >1% were received or analysed

- Bioanalysis (ARCINOVA) was sub-contracted via Sponsor
- Statistical analysis (Company XXX) was sub-contracted via Sponsor

- We transferred concentration data to sponsor's sub-contractor for data analysis, but did not inform them directly of assay limitation

Observation (Clinical Study Management and Conduct)

- EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (Section 6.4 trail conduct);

- Appropriate procedures should be implemented to ensure effective and timely communication with the sponsor or their representative, regarding any serious deviations from the work instruction, clinical trial protocol or contract/agreement.
- Timely reporting will ensure that the sponsor or their representative are able to determine the significance and impact of the deviation on the safety and well being of the trial subjects and on the integrity and reliability of the trial data.
- The impact of any deviations from the laboratory's standard operating procedures or documented policies should be assessed and documented.
- Where there is potential for a deviation to impact on the integrity or reliability of the trial data, patient or subject confidentiality, consent or safety, appropriate procedures should be implemented to ensure the issue is reported immediately to the sponsor or their representative and, if appropriate, to the investigator.

Observation (Clinical Study Management and Conduct)

- EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (Section 6.6 sub-contracting);

- If analysis or evaluation of clinical trial samples is sub-contracted to another laboratory, the ability of the sub-contractor to perform the work must be assessed prior to its initiation. Particular attention should be paid to staff training.
- Before placing work with a sub-contractor, the sponsor, or their representative, should be informed and, if necessary, the contract with the sponsor amended.
- A contract or service level agreement should be implemented between the two laboratories prior to the initiation of any work. Any such contract or service level agreement should clearly state roles and delegated tasks and the scope and nature of the work that will be undertaken by the sub-contractor.
- Care should be taken to ensure that contracts do not conflict with the requirements of the clinical trial protocol, work instruction or the contract between the analytical laboratory and the sponsor.

Observation (Clinical Study Management and Conduct)

- ‘The laboratory did not provide a sponsor’s sub-contracted statistical analysis vendor with a updated sample analysis data set from study XXXXXX following finalisation of the validation study’

- Whilst we make reasonable endeavours to ensure data integrity is maintained, we cannot guarantee that a client will not subsequently transfer data to a sub-contractor for data processing without including any data or assay limitations. As a consequence, our bioanalytical Sample Analysis Outline (SAO) has been updated to state that the Sponsor will ‘Notify contracted third parties of any limitations pertaining to the concentration data’

- Our CAPA and response to MHRA was accepted

Audit Close

- During inspection we did not observe any significant distinction between GLP and GCP
- Our responses to MHRA where accepted
- We received MHRA certification for both GLP and GCP compliance programmes

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