



# GLP Consultative Committee Meeting Minutes

<b>Date</b>	19 May 2021
<b>Venue</b>	Teleconference
<b>Chair</b>	Medicines and Healthcare product Regulatory Agency (MHRA)
<b>Attendees</b>	MHRA Research Quality Association (RQA) United Kingdom Accreditation Service (UKAS) Health Sciences Records and Archives Association (HSRAA) Scottish Lifesciences Association (SLA) Veterinary Medicines Directorate (VMD) CEFAS Environment Agency (EA) Health and Safety Executive (HSE) Public Health England (PHE)
<b>Apologies</b>	None
<b>Minutes</b>	MHRA
<b>Copies to</b>	All attendees, MHRA GLP Website

## [MHRA updates](#)

### COVID-19

The MHRA provided an update on the work of the inspectorate during 2020/21, detailing the prioritisation of COVID-19 based activities including support for approval of vaccines and treatments as well as continuing to maintain regulatory oversight of laboratories. In relation to the COVID-19 work the Good Laboratory Practise Monitoring Authority (GLPMA) have supported the vaccine review process and provided advice where required.

### Inspections

The approach to regulatory inspections had been adjusted throughout the pandemic based on restrictions and guidance from the UK Government. The GLPMA have developed remote inspection approaches including implementing the use of Microsoft Teams and remote data review techniques.



In 2020/21 the GLPMA conducted 58 inspections across the GXP's which increased from 46 inspections in 2019/20. The typical time spent per inspection was compared with pre-pandemic activities and the averages between pre-pandemic and pandemic levels were deemed consistent by the GLPMA.

The GLPMA acknowledged the collaborative approach to regulatory oversight provided by the facilities inspected.

#### Inspection metrics

The GLPMA confirmed that two critical findings had been raised from remote inspections during the pandemic for the following:

Test & Reference Control - The test item used outside of its expiry date and there was no supporting information available on identity of the compound

Study Management & Conduct - Lack of transparency in reporting after the study director issued an amendment but had incorrectly removed key information.

#### Fabricated reports

The GLPMA made industry aware of a situation raised during the past year, in which an international regulatory receiving authority had received fabricated study reports purporting to be from a test facility within the UK. The reports had been generated using copies of reports from the UK facility and data had been inserted. The GLPMA asked facilities to assess the levels of security and control they have over their reports and make them aware if any concerns are identified.

#### Miscellaneous

The GLPMA have initiated a process to look at improvements to systems around metrics generation and information management to ensure they remained fit for purpose.

Within the inspectorate there had been no significant changes to roles and responsibilities, however within the laboratories group a new inspector is undergoing GLP training.

#### [International and engagement activities](#)

##### OECD GLP Working Party update

The GLPMA provided an update on the OECD activities during the past year. This included a summary of the GLP Working Party meeting in April 2021, as well as updates on the development of guidance documents. In summary these were:

- Confirmation of the publication of the sponsor interference guidance document and of updated Q&A.



- Updates on the OECD data integrity document and quality assurance document.

It was confirmed that OECD GLP Working Party are continuing to support feedback from industry. The GLPMA will inform stakeholders when the next engagement opportunity is confirmed.

The RQA queried what would happen to the MHRA Data Integrity document following publication of the OECD guidance. The GLPMA confirmed that the OECD document would take priority for GLP facilities however a review of the two would be performed to ensure any areas that required clarification.

#### Stakeholder engagement

The GLPMA confirmed that the pandemic has resulted in limited engagement opportunities.

The 2020 MHRA Laboratories Symposium was held in February, prior to lockdown. The GLPMA had planned to hold an event in 2021 but this has been postponed provisionally until March 2022 however this will be confirmed in due course. The GLPMA have continued to present at conferences remotely and will continue to do so.

A review of GLPMA guidance documents has started with the intention to publish later in the year.

#### Questions and answers

Question 1: Can the GLPMA confirm whether it is inappropriate for UK Test Facilities to reference EC Directives in Study Plans and Final Reports (GLP Compliance Statement and / or body of the report)

**GLPMA Response:** Following the end of the transition period it would no longer be appropriate for facilities within GB to include references to the EC directives as these are no longer applicable. Facilities within Northern Ireland are still required to adhere to EC legislation therefore the inclusions will be required for facilities located there.

Question 2: For supply of biopharmaceutical test items (for example MABs) for use in GLP studies would it be acceptable to routinely perform characterisation to an internal quality standard rather than GLP or GMP? If not acceptable on a routine basis, would it be considered appropriate in limited circumstances and if so are there any examples of such circumstances.

**GLPMA response:** This topic is covered in OECD Series On Principles Of Good Laboratory Practice And Compliance Monitoring “Advisory Document of the Working Group on Good Laboratory Practice on the Management, Characterisation and Use of Test Items” document 19.

Section 2.6 outlines why characterization is necessary, and it is acknowledged that not all GLP required information will be applicable to all test items. The characterisation of the test



item may be carried out by the sponsor, a supplier or the test facility. If characterisation is performed by the sponsor or a supplier, Test Facility Management should ensure that documented procedures are in place to verify the integrity and quality of the information provided. The final study report should describe who is responsible for test item characterisation and who performed it. The report should also provide other relevant information such as the quality system under which the characterisation was performed.

Specific guidance for monoclonal antibodies can be found in section 7.5.2:

*“If the test item is a biochemical, for example an antibody, a peptide, a protein, a viral vector or an enzyme, the need for information to verify biological activity should always be considered, including the determination method and its quantification (potency) as part of the characterisation process. If no information is provided to demonstrate the biological activity of the test item, the reasons why the test item is still considered suitable for use in the study should be clearly outlined in the study plan and in the final study report.”*

Any omissions to the required characterisation data, or storage stability information should be detailed in the study director statement and include an impact assessment.

Question 3: The use of digital pathology to undertake peer reviews is increasing. The location of the pathologist becomes more important for claims of compliance. How would the MHRA inspectorate and regulatory reviewers view routine GLP exceptions for pathology peer review of GLP studies?

GLPMA response: OECD Series On Principles Of Good Laboratory Practice And Compliance Monitoring monograph 16 “Advisory Document of the Working Group on Good Laboratory Practice - Guidance on the GLP Requirements for Peer Review of Histopathology” states *“Although there is no absolute requirement in the GLP principles to conduct peer review, most receiving authorities expect that some level of peer review will be performed. The peer review process can lead to changes in the interpretation of histopathology findings that in turn may influence the outcome and conclusion of the study. Consequently, there is an expectation that the peer review should be conducted in compliance with GLP. However, it is recognised that for the peer review to be of scientific value it has to be conducted by a person with the appropriate specialist experience and expertise; consequently that may necessitate the use of acknowledged experts in particular fields who do not work within a GLP test facility. When a decision is made to perform pathology peer review in a non GLP facility it should be justified and recorded within the study plan and final report.”*

From a GLPMA perspective provided the compliance statement was reflective of the situation no objections would be raised. It was also stated that it is expected that a procedure would be in place to manage differences of opinion between pathologists.

Question 4: Can the MHRA provide further guidance on expectations regarding the retention of electronic media, particularly with respect to the practicalities of maintaining legacy



validated computer systems (both in terms of hardware and software) for extended periods of time (maintaining obsolete software, maintaining licenses for decommissioned systems, maintaining trained people for unused legacy systems etc)?

**GLPMA response:** The approach to be taken is likely to vary depending on the requirements of the electronic system itself.

*The 'GXP' Data Integrity Guidance and Definitions document states 'When legacy systems can no longer be supported, consideration should be given to the importance of the data, and if required to maintaining the software for data accessibility purposes. This may be achieved by maintaining software in a virtual environment. Where this is not possible, data should be migrated before archiving in a controlled, tested, and verified way to a system that can continue to be accessed. Migration to an alternative file format that retains as much as possible of the verified copy attributes of the data may be necessary with increasing age of the legacy data.'*

*Where migration with full original record functionality is not technically possible, selection from the options available would have to be based on risk and importance of data over time. The migration file format should be selected taking into account the balance of risk between long-term accessibility versus the possibility of reduced dynamic data functionality (e.g. data interrogation, trending, re-processing etc.). It is recognised that the need to maintain accessibility may require migration to a file format that loses some attributes and/or dynamic data functionality. It is the TFM's responsibility to assess the impact of such losses and maintain the link between the readable audit trail or electronic signatures and the audited data to an acceptable level'.*

With regards to training for staff on unused legacy systems the requirements necessary to be able to access and review data should be determined as part of the software retirement process and clear instructions generated to enable future users to access the data if required. It would not be expected that users had expert knowledge of unused legacy systems but had sufficient information and guidance available to facilitate the retrieval and use of these systems.

Question 5: While conducting a study, what is the consensus with respect to claims of GLP compliance when sample stability (e.g. bioanalytical samples) is not known, or stability testing is on-going under a separate study. Can this affect GLP compliance and thus should it be reflected in the compliance statement, or is discussion of impact in the report test sufficient?

**GLPMA response:** This has been agreed within the OECD working group and has been published within the FAQs (Number 5 under Study Management

#### **Should method validation be completed prior to the initiation of a GLP study?**

There is no requirement to finalise the validation of all methods that will be used to conduct a GLP study before the initiation of the study. However, there is an expectation that methods are fully validated before the results of the study are considered to be valid. (posted on 21 January 2016)



The GLPMA have raised critical findings for finalising studies without suitable stability or where on-going stability does not cover the reported results. This is because the lack of stability undermines the validity of the data and consequently the SDs claim of compliance.

Question 6: Please can the GLPMA provide an update on the general position regarding remote / hybrid and on-premises audits going forward. Members of the Scottish Life Sciences Association have noticed creepage in the duration and completion of remote audits (a general issue, not specific to the MHRA). On-premises audits usually conclude with the closing meeting but it has been noticed that more information has been requested after the closing meeting. It is understood that there are always situations where additional information may be necessary but best practice is to keep to the timescale and scope set initially. It would be interesting to hear the MHRA's experience and their intentions for the future.

GLPMA response: The purpose of requests made following any inspection closing meeting are usually to assist in writing the inspection report or to clarify a deficiency already raised to ensure the facility can appropriately address the deficiency identified. With respect to future inspections a hybrid approach (remote & onsite) may be adopted but an assessment will be made in conjunction with the test facility on the approach to be used.

Question 7: What is the MHRA interpretation on exploratory samples from GLP studies (as discussed in OECD 21). Do the results from exploratory samples need to be reported if clearly not needed/relevant to interpretation and conclusions of the GLP study?

GLPMA response: The reference to exploratory research and exploratory samples in OECD Series On Principles Of Good Laboratory Practice And Compliance Monitoring "OECD Position Paper Regarding Possible Influence of Sponsors on Conclusions of GLP Studies" number 21 is in relation to additional sample analysis at the request of the sponsor. In these situations, where exploratory sample collection is performed within a GLP study, details of the work to be conducted should be outlined in the study plan and the collection of samples should be referenced in the report but specific data and conclusions resulting from analysis of these samples are not required in the report. An assessment should however be made in the report on the impact of the exploratory work on the conduct/compliance of the remaining study. The key message is to be transparent regarding the work that has been done and the impact of the outcome of that work on the compliance status of the study.

#### AOB

HSRRA wished to thank the SLA for the question raised regarding retention of electronic data.

The SLA questioned what the MHRA position would be on the use of a non-GLP facility where a GLP facility exists. The GLPMA confirmed that the use of non-GLP facilities can



only be considered in exceptional circumstances and would need to be judged on a case by case basis. Sponsors would need to contact the GLPMA to discuss the matter further.

RQA queried whether there had been any progress with the admittance of China into the OECD Mutual Acceptance of Data system. The GLPMA confirmed that there were no updates on this topic to provide since the previous meeting.

**Meeting closure.**