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Number 8 (Revised)**

**Consensus Document
THE ROLE AND RESPONSIBILITIES OF THE STUDY DIRECTOR
IN GLP STUDIES**

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REVISED CONSENSUS DOCUMENT

OECD SERIES
ON
PRINCIPLES OF GOOD LABORATORY PRACTICE AND COMPLIANCE MONITORING

Number 8 (revised)

GLP Consensus Document

**THE ROLE AND RESPONSIBILITIES OF THE
STUDY DIRECTOR IN GLP STUDIES**

Environment Directorate

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

Paris 1999

FOREWORD

In the framework of the third OECD Consensus Workshop on Good Laboratory Practice held 5th to 8th October 1992 in Interlaken, Switzerland, a working group of experts discussed the interpretation of the GLP Principles as applied to the role and responsibilities of the Study Director. This working group was chaired by Dr. David F. Moore of the United Kingdom GLP Compliance Monitoring Authority; the Rapporteur was Dr. Heinz Reust (Swiss Federal Office of Public Health). Participants in the Working Group were from both national GLP compliance monitoring authorities and from testing laboratories in the following countries: Austria, Canada, Federation of Russia, Finland, Germany, Japan, Netherlands, Switzerland, United Kingdom and United States.

The draft document developed by the working group was circulated to Member countries for comments. The text was revised, based on comments received, and reviewed by the OECD Panel on Good Laboratory Practice at its fifth meeting in March 1993, which amended the text and forwarded it to the Joint Meeting of the Chemicals Group and Management Committee of the Special Programme on the Control of Chemicals. At its 20th Session, the Joint Meeting endorsed the document with minor editorial changes and recommended that it be derestricted under the authority of the Secretary-General.

In light of the adoption of the Revised OECD Principles of GLP in 1997, this Consensus Document was reviewed by the Working Group on GLP and revised to make it consistent with modifications made to the Principles. It was endorsed by the Working Group in April 1999 and, subsequently by the Joint Meeting of the Chemicals Committee and Working Party on Chemicals, Pesticides and Biotechnology in August 1999. . It too is declassified under the authority of the Secretary-General.

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GLP CONSENSUS DOCUMENT

THE ROLE AND RESPONSIBILITIES OF THE STUDY DIRECTOR IN GLP STUDIES

The Role of the Study Director

The Study Director represents the single point of study control with ultimate responsibility for the overall scientific conduct of the study. This is the prime role of the Study Director, and all duties and responsibilities as outlined in the GLP Principles stem from it. Experience has shown that unless responsibility for the proper conduct of a study is assigned to one person, there is a potential for personnel to receive conflicting instructions, which can result in poor implementation of the study plan. There can be only one Study Director for a study at any given time. Although some of the duties of the Study Director can be delegated, as in the case of a subcontracted study, the ultimate responsibility of the Study Director as the single central point of control cannot.

In this regard, the Study Director serves to assure that the scientific, administrative and regulatory aspects of the study are controlled. The Study Director accomplishes this by coordinating the inputs of management, scientific/technical staff and the Quality Assurance programme.

In multi-site studies which involve work at more than one test site and the Study Director cannot exercise immediate supervision, study procedures may be controlled by an appropriately trained, qualified and experienced member of the staff, called the Principal Investigator. He is responsible for the conduct of certain defined phases of the study in accordance with the applicable Principles of Good Laboratory Practice, acting on behalf of the Study Director.

Scientifically, the Study Director is usually the scientist responsible for study plan design and approval, as well as overseeing data collection, analysis and reporting. The Study Director is responsible for drawing the final overall conclusions from the study. As the lead scientist, the Study Director must coordinate with other study scientists, and/or Principal Investigator(s) keeping informed of their findings during the study and receiving and evaluating their respective individual reports for inclusion in the final study report.

Administratively, the Study Director must request and coordinate resources provided by management, such as personnel, equipment and facilities, to ensure they are adequate and available as scheduled for the proper conduct of the study.

Compliance with regulations is also the responsibility of the Study Director. In this role the Study Director is responsible for ensuring that the study is carried out in accordance with the Principles of GLP, which require the Study Director's signature on the final study report to confirm compliance with the GLP Principles.

Management Responsibilities

Management of a testing facility is responsible for ensuring that the facility operates in compliance with GLP Principles. This responsibility includes the appointment and effective organisation of an adequate

number of appropriately qualified and experienced staff throughout the facility, including Study Directors, and, in the event of multi-site studies, Principal Investigator(s), if needed.

Appointment of Study Directors

Management should maintain a policy document defining the procedures adopted for selection and appointment of Study Directors, their deputies, and Principal Investigator(s) if required by national programmes.

When appointing a Study Director to a study, management should be aware of that person's current or anticipated workloads. The master schedule, which includes information on the type and timing of studies allocated to each Study Director, can be used to assess the volume of work being performed by individuals within the testing facility and is a useful management tool when allocating studies.

Replacement of a Study Director and/or Principal Investigator should be done according to established procedures and should be documented.

Training of Study Directors

Management should ensure that there is documentation of training in all aspects of the Study Director's work. A training programme should ensure that Study Directors have a thorough understanding of GLP Principles and an appropriate knowledge of testing facility procedures. This may include an awareness and working knowledge of other guidelines and regulations pertinent to the testing facility and the particular study type, for example, the OECD Test Guidelines. Training may include work experience under the supervision of competent staff. Observation periods or work experience within each discipline involved in a study can provide a useful basic understanding of relevant practical aspects and scientific principles, and assist in the formation of communication links. Attendance at in-house and external seminars and courses, membership in professional societies and access to appropriate literature may allow Study Directors to maintain current awareness of developments within their scientific field. Professional development should be continuous and subject to periodic review. All training should be documented and records should be retained for the period specified by the appropriate authorities.

Documented records of such a programme should reflect the progression of training and provide a clear indication of the type of study that an individual is considered competent to direct. Further training or retraining may be necessary from time to time, for example, following the introduction of new technology, procedures or regulatory requirements.

Responsibilities of the Study Director

The Study Director is the individual who has overall responsibility for the scientific conduct of a study and can confirm the compliance of the study with the OECD Principles of Good Laboratory Practice.

Study Initiation

The Study Director has to approve the study plan which is prepared before study initiation by dated signature. This document should clearly define the objectives and the whole conduct of the study and how they are to be achieved. Any amendments to the study plan have to be approved as mentioned above. For a

multi-site study the study plan should identify and define the role of any Principal Investigator(s) and any test facilities and test sites involved in the conduct of the study.

The Study Director should take responsibility for the study by dated signature of the study plan, at which stage the study plan becomes the official working document for that study (study initiation date). If appropriate, the Study Director should also ensure that the study plan has been signed by the sponsor and the management, if required by national programmes.

Before the study initiation date the Study Director should make the study plan available to Quality Assurance (QA) staff for verifying that it contains all information required for compliance with the GLP Principles.

Before the experimental starting date of the study, the Study Director should assure that copies of the study plan are supplied to all personnel involved in the study; this should include Quality Assurance (QA) staff.

Before any work on the study is undertaken, the Study Director should ascertain that management have committed adequate resources to perform the study, and that adequate test materials and test systems are available.

Study Conduct

The Study Director has responsibility for the overall conduct of the study and should ensure that the procedures laid down in the study plan including amendments are followed and all data generated during the study are fully documented. Specific technical responsibilities may be delegated to competent staff, and need to be documented.

The Study Director's involvement during the course of the study should include overseeing the study procedures and data to ensure that the procedures laid down in the study plan are being followed and that there is compliance with the relevant Standard Operating Procedures, and should include computer-generated data. In order to demonstrate this, the type and frequency of the reviews should be documented in the study records.

As all decisions that may affect the integrity of the study should ultimately be approved by the Study Director, it is important that he remains aware of the progress of the study. This is of particular importance following temporary absence from the study and can only be achieved by maintaining effective communication with all the scientific, technical and administrative personnel involved, and for a multi-site study with Principal Investigator(s). Of necessity, lines of communication should ensure that deviations from the study plan can be rapidly transmitted and that issues arising are documented.

If data are recorded on paper, the Study Director should ensure that the data generated are fully and accurately documented and that they have been generated in compliance with GLP Principles. For data recorded electronically onto a computerised system, the Study Director's responsibilities are the same as for paper systems. In addition, the Study Director should also ensure that computerised systems are suitable for their intended purpose, have been validated, and are fit for use in the study.

Final Report

The final report of a study should be produced as a detailed scientific document outlining the purpose of the study, describing the methods and materials used, summarising and analysing data generated, and stating the conclusions drawn.

If the Study Director is satisfied that the report is a complete, true and accurate representation of the study and its results, then and only then, should the Study Director sign and date the final report to indicate acceptance of responsibility for the validity of the data. The extent of compliance with the GLP Principles should be indicated. He should also assure himself that there is a QA statement and that any deviations from the study plan have been noted.

Archives

On completion (including termination) of a study the Study Director is responsible for ensuring that the study plan, final report, raw data and related material are archived in a timely manner. The final report should include a statement indicating where all the samples of test and reference items, specimens, raw data, study plan, final report and other related documentation are to be stored. Once data are transferred to the archives, the responsibility for it lies with management.

Sub-contracting

Where parts of any study are contracted out, the Study Director (and QA staff) should have knowledge of the GLP compliance status of that facility. If a contract facility is not GLP compliant, the Study Director must indicate this in the final report.

Study Plan Amendments and Deviations

Study Plan Amendment

A study plan amendment should be issued to document an intended change in study design after the study initiation date and before the event occurs. An amendment may also be issued as a result of unexpected occurrences during the study that will require significant action. Amendments should indicate the reason for the change and be sequentially numbered, dated, signed and distributed to all recipients of the original study plan by the Study Director.

Study Deviations

Whereas an amendment is an intended change to the study plan, a deviation is an unintended change which occurs during the execution of the study. Study information such as a deviation from the study plan should be noted in the study documentation. Such notes may be initiated by other personnel involved in the study, but should be acknowledged, described, explained and dated in a timely fashion by the Study Director-and/or Principal Investigator(s) and maintained with the study raw data. The Study Director should approve any corrective action taken. The Study Director should consider whether to consult with other scientists to determine the impact of any such information on the study, and should report (and discuss where necessary) these deviations in the final report.

Qualifications of the Study Director

Qualifications for a Study Director will be dictated by the requirements of each individual study. Setting the criteria is the responsibility of the management. Furthermore, management has the responsibility for selection, monitoring and support of the Study Director to ensure that studies are carried out in compliance with the GLP Principles. Any minimal qualifications established by management for the position of Study Director should be documented in the appropriate personnel records. In addition to a strong technical background, the coordinating role of the Study Director requires an individual with strengths in communication and problem solving and managerial skills.

Interface with the Study

The Study Director has the overall responsibility for the conduct of a study. The term "responsibility for the overall conduct of the study and for its final report" may be interpreted in a broad sense for those studies where the Study Director may be geographically remote from parts of the actual experimental work. With multiple levels of management, study personnel and QA staff, it is critical that there are clear lines of authority and communication, and assigned responsibilities, so that the Study Director can effectively carry out his GLP responsibilities. This should be documented in writing. Test facility management should ensure that for multi-site studies clear lines of communication exist between the Study Director, Principal Investigator(s), the Quality Assurance Programme(s) and the study personnel

For studies that have delegated responsibilities to a Principal Investigator(s), the Study Director will rely on that individual to assure that relevant phase(s) of the study are conducted in accordance with the study plan, relevant SOPs and with GLP Principles. The Principal Investigator should contact the Study Director when event(s) occur that may affect the objectives defined in the study plan. All communications should be documented.

Communication between the Study Director and QA is required at all stages of the study.

This communication may involve:

- an active involvement with QA, for example, review of study plans in a timely manner, involvement in the review of new and revised Standard Operating Procedures, attendance of QA personnel at study initiation meetings and in resolving potential problems related to GLP.
- responding to inspection and audit reports promptly, indicating corrective action and, if necessary, liaising with QA staff and scientific and technical personnel to facilitate responses to inspection/audit findings.

Replacement of the Study Director

The Study Director has the responsibility for the overall conduct of a study according to the GLP Principles and he has to ascertain that in every phase of a study these principles are fully complied with, that the study plan is followed faithfully and that all observations are fully documented. Theoretically, this

responsibility can only be fulfilled if the Study Director is present all the time during the whole study. This is not always feasible in practice and there will be periods of absence which might make replacement necessary. While the circumstances under which a Study Director would be replaced are not defined in the GLP Principles, they should be addressed to the degree feasible by the facility's SOPs. These SOPs should also address the procedures and documentation necessary to replace a Study Director.

The decision for replacement or temporary delegation is the responsibility of management. All such decisions should be documented in writing. There are two circumstances where replacement might be considered, both of which are of importance only in longer-term studies, since the continuing presence of a Study Director during a short study may be assumed. In the event of termination of employment of a Study Director, the need for replacing this key person is obvious. In this case, one of the responsibilities of the replacement Study Director is, with the assistance of Quality Assurance personnel, to assure himself as soon as practicable of the GLP compliance in the study as conducted to date. The replacement of a Study Director and the reasons for it must be documented and authorised by management. It is also recommended that the results of any interim GLP review should be documented in case deficiencies or deviations have been found.

The second circumstance is when a Study Director is temporarily absent because of holidays, scientific meeting, illness or accident. An absence of short duration might not necessitate the formal replacement of the Study Director if it is possible to communicate with him if problems or emergencies arise. If critical study phases are expected to fall into the period of absence, they may either be moved to a more suitable time (with study plan amendment, if necessary), or a replacement of the Study Director may be considered, either by formally nominating a replacement Study Director or by temporary delegation of responsibilities to competent staff for this specific phase of the study. Should the unavailability of the Study Director be of longer duration, a replacement should be named rather than delegation to competent staff.

The returning Study Director must ascertain as soon as practicable whether or not deviations from GLP Principles have occurred, irrespective of whether or not he was formally replaced during his absence. Deviations from GLP Principles during his absence should be documented by the returning Study Director.

Legal Status of the Study Director

The Study Director, by virtue of his signature in the final report confirming compliance with the GLP Principles, assumes responsibility for the performance of the study in compliance with GLP Principles and for the accurate representation of the raw data in the final report. However, the legal liability of the Study Director is established by national legislation and legal processes, and not by the OECD Principles of GLP.