NATIONAL PROGRAM FOR THE MONITORING OF GOOD LABORATORY PRACTICES - ONAC

ONAC
ORGANISMO NACIONAL DE ACREDITACIÓN DE COLOMBIA

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1. OBJECTIVE

The purpose of this document is to describe the organization and operation of the National Monitoring Program for the verification of compliance with Good Laboratory Practices (GLP) of the Organization for Economic Co-operation and Development (OECD), so that the test facilities that perform non-clinical safety studies for regulatory purposes, obtain recognition of the compliance with GLP and effectively join the program.

2. SCOPE

This Program applies to all testing facilities that conduct non-clinical safety studies for regulatory purposes, that wish to apply to be incorporated into the Registry of GLP facilities of the Program, once they have obtained recognition of compliance with Good Laboratory Practices. Likewise, it applies to all test facilities already registered and recognized that want to maintain their recognition.

3. DEFINITIONS AND REFERENCE DOCUMENTS

Mutual Acceptance of Data. (MAD): the Council of the OECD adopted a Decision C (81)30/1981/FINAL in 1981 - on mutual acceptance of data (MAD) - indicating that the test data generated in any member country or fully adherent country, in accordance with the OECD Test Guidelines and Principles of Good Laboratory Practices (GLP), are accepted in full member countries or adherent countries for evaluation purposes and other uses related to the protection of human health and the environment.

Actions to eliminate deviations: actions taken to eliminate the cause of a deviation from the GLP Principles.

Study audit: comparison of the original data and the records associated with the partial and final reports, in order to determine if the original data have been notified accurately, and if the tests were carried out according to the study plan and the Standard Operational Procedures (SOPs), as well as to obtain additional information that has not been provided in the report, and establish whether some practices were used to obtain the data that could invalidate the results of the study.

National Monitoring Authority: body established by a member country responsible for monitoring the compliance with the GLP of the test facilities within its territory, and for the performance of other functions related to GLP, as determined at the national level.

Regulatory Authority: National Organization with legal responsibility on aspects related to the control of chemical materials.

Good Laboratory Practices (GLP): Good Laboratory Practices (GLP) constitute a quality assurance system related to the organization of non-clinical safety studies related to health and the environment and, also, to the conditions under which these studies are planned, executed, controlled, recorded, archived and reported.

Original data: they represent the set of reports and original documents of the test facility, or of verified copies that are in accordance with said documents, and that are derived from the observations and the original work carried out within the study framework. The original data may also include, for example, photographs, microfilm or microfiche copies, supporting computer data, automatic data records or any other means of data storage, which is considered capable of guaranteeing the storage of information with the greatest security for a certain duration.

Deviation from the GLP Principles: non-compliance with the GLP Principles, detected as a result of the inspection visit or study audit. The deviation can be classified as minor or major.

Test Facility Management: includes the person or persons who have authority and official responsibility for the organization and operation of the test facility, in accordance with the Principles of Good Laboratory Practices.

Test Site Management: includes the person(s) (if previously appointed) responsible for ensuring that the study phase(s) for which they are responsible are developed in accordance with the Principles of Good Laboratory Practices.

Study Director: is the person responsible for the general direction of the non-clinical safety study, concerning health and the environment.

3. DEFINITIONS AND REFERENCE DOCUMENTS

Test Facility: includes the people, premises and operational units necessary for the execution of a non-clinical safety study related to health and the environment. For studies carried out in multiple sites (multi-site), or carried out in more than one site, the test facility includes the location at which the Study Director is located, and all the test sites involved, which can be considered individual or collectively as test facilities.

State of Compliance with the GLP: a test facility's level of compliance with the Principles of Good Laboratory Practices evaluated through the (National) Monitoring Authority of Good Laboratory Practices.

Non-clinical safety study relating to health and the environment: hereinafter simply referred to as "study", consists of an experience or a set of experiences during the course of which a test item has been examined in the laboratory or in the environment, in order to obtain data on its properties and/or security, destined to be submitted to the competent regulatory authorities.

Simulated study: study where there will not be a GLP study request by a real sponsor, but where a commercially available material is used. The study must be planned, executed, audited, recorded, reported and archived as a real study.

Inspector team: group of inspectors appointed by the Monitoring Authority that performs the inspection of the test facilities and study audits. The group can be formed by the **Coordinating Inspector**, Inspectors and Technical Experts, as the case may be.

Expert: person appointed to provide specific knowledge or expertise on the type of studies subject to the inspection.

Principal Investigator: is the person who, in the case of a study in multiple locations, exercises the responsibilities perfectly defined for the phases of the study that are delegated to him, on behalf of the Study Director. The Study Director cannot delegate his or her responsibility to the Principal Investigator(s) regarding the general direction of the study, since it mainly is about approving the study plan, with all its amendments, and the final report, and ensuring respect for all the relevant Principles of Good Laboratory Practices.

Inspector: person who carries out inspections of test facilities and study audits on behalf of the (National) GLP Monitoring Authority.

Coordinating Inspector (or Lead Inspector): inspector in charge of organizing and directing an inspection, as stipulated in the Compliance Program of the GLP Monitoring Authority.

Follow-up Inspection: On-site visit to verify that the test facility implemented the actions for the elimination of the deviations to GLP Principles.

Test Facility inspection: on-site examination of the procedures and practices of the test facility, to assess the degree of compliance with the GLP Principles. During inspections, the organizational structure and operating procedures of the test facility are evaluated, the key technical personnel are interviewed, as well as the quality and integrity of the data generated by the test facility are evaluated and communicated.

Resolve: The resolution of detected deviations.

Compliance Monitoring of the GLP: periodic inspections of the test facilities and/or study audits with the purpose of verifying adherence to the Principles of Good Laboratory Practices.

Suspended Recognition: it is considered a temporary state of "non-compliance" of the test facility, where it is not currently able to comply with the GLP Principles, but it has every intention of attending to the deviations found and reintegrating into compliance. In a state of suspended recognition, it is considered that a test facility still belongs to the program but cannot issue statements of compliance of the studies in progress or to be carried out until ONAC has lifted the suspension. This status can be applied to the entire facility or some of its areas of recognized competences.

Routine Inspection: annual or biannual on-site visit (after the 2nd routine inspection) to verify that the test facility continues to comply with the OECD GLP Principles.

3. DEFINITIONS AND REFERENCE DOCUMENTS

Withdrawn Recognition: it is considered a permanent state in which the test facility has been formally withdrawn from the OECD GLP Monitoring Program of ONAC.

(National) GLP Compliance Program: a particular scheme established by a member country to monitor the compliance with the GLP in test facilities within its territory, by means of inspections and study audits.

Sponsor: is the person who orders, sponsors or submits a non-clinical safety study related to health and the environment.

Pre-Inspection: The objective is to familiarize the Inspector with the test facility that has requested the inspection service with respect to the management structure, the physical design of the buildings and the variety of studies. This activity is carried out through the study of the documentation sent by the facility, including the application, the Standard Operating Procedures (SOPs), and other relevant documentation.

Quality assurance program: corresponds to a precise system, which integrates all the corresponding personnel, and which is independent of the study management, and which is also intended to ensure that the current Principles of Good Laboratory Practices have been correctly respected to the Test Facility Management.

Standard Operating Procedures: correspond to the methods and procedures supported by documents that describe the way to execute the tests or tasks, and whose detail does not normally appear in the study plan or in the guidelines for the tests.

Study plan: a document that defines the study objectives and the experimental devices necessary for its development, including any amendment that may occur.

Test site: includes the site(s) on which one or more phases of a given study are carried out.

ABBREVIATIONS

ONAC - National Accreditation Body of Colombia (for its acronym in Spanish).
OECD – The Organization for Economic Co-operation and Development.
GLP - Good Laboratory Practices.
MAD - Mutual Acceptance of Data.
SOP - Standard Operational Procedures

REFERENCE DOCUMENTS AND DEFINITION

• OECD Principles
No 1: OECD Principles on Good Laboratory Practice

• GLP Consensus documents
No 4: Quality Assurance and Good Laboratory Practices
No 5: Compliance of Laboratory Suppliers with the Principles of Good Laboratory Practices
No 6: The Application of the Principles of Good Laboratory Practices to Field Studies
No 7: The Application of the Principles of Good Laboratory Practices to Short Term Studies
No 8: The Role and Responsibilities of the Study Director in GLP Studies
No 13: The Application of the OECD Principles of GLP the Organization and Management of Multi-Site Studies.

• Guidance Documents for Compliance Monitoring Authorities
No 2: Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practices
No 3: Revised Guidance for the Conduct of Laboratory Inspection and Study Audit
No 9: Guidance for the Preparation of GLP Inspection Reports

• Advisory Documents of the Working Group on GLP
No 11: The Role and Responsibilities of the Sponsor in the Application of the Principles of GLP
No 12: Requesting and Carrying Out Inspections and Study Audits in Another Country
No 14: The Application of the Principles of GLP in vitro Studies

3. DEFINITIONS AND REFERENCE DOCUMENTS

No 15: Establishment and Control of Archives that Operate in Compliance with the Principles of GLP
No 16: Guidance on the GLP Requirements for Peer Review of Histopathology
No 17: Application of GLP Principles to Computerized Systems

• Decree 1595 of 2015 "By which rules are issued regarding the National Quality Subsystem and modifies chapter 7 and section 1 of chapter 8 of title 1 of part 2 of book 2 of the Sole Regulatory Decree of the Trade Sector, Industry and Tourism, Decree 1074 of 2015, and other provisions are dictated "

4. GENERAL CONSIDERATIONS

4.1 General Aspects

The legislation applicable to product control is based, within the OECD member countries, on an approach aimed at the prevention of risks by which tests and evaluation of chemical materials are considered in order to determine their hazardous potentials. These evaluations should be supported by the quality of the test data. The Principles of Good Laboratory Practice (GLP) have been developed to promote the quality and validity of the test data used to establish the safety of chemical materials.

These Principles constitute a management concept that encompasses the organizational processes and the conditions under which the studies are planned, implemented, controlled, recorded and reported. These principles must be met by the test facilities that carry out non-clinical safety studies on pharmaceutical products, cosmetics, pesticides, veterinary medicines, additives for human and animal feeding; and industrial chemical products, to be presented to the Regulatory Authority for the purpose of determining their effects on human health and the environment.

ONAC's GLP Monitoring Program establishes the guidelines for the monitoring compliance with Good Laboratory Practices, of the test facilities that perform non-clinical studies, to be presented to the Regulatory Authority in order to obtain the registration or authorization of product commercialization. ONAC's GLP Monitoring Program aims to verify if the test facilities have implemented the GLP Principles for conducting studies and if the quality and integrity of the resulting data is adequate.

4.2 Organization and Legal Framework (Description of ONAC and its structure)

The National Accreditation Body of Colombia - ONAC is a non-profit corporation, of mixed nature and participation, governed by private law. It was set up by means of the constitution of the assembly of the November 20 of 2007, under Colombian laws, within the framework of the Civil Code and the norms on science and technology. The National Accreditation Body of Colombia (ONAC) was constituted, with a record of the existence and legal representation of the Chamber of Commerce of Bogotá S00031036 and with NIT 900.190.680-7.

On the other hand, within the framework of the process of adhering Colombia to the OECD, initiated in September 2013, the National Accreditation Body of Colombia - ONAC has been designated as the National GLP Monitoring Authority through the Decree No. 1595 of the Ministry of Commerce, Industry and Tourism of Colombia of August 5 of 2015. The aforementioned Decree establishes that ONAC must "Exercise as a Monitoring Authority of Good Laboratory Practices of the Organization for Economic Co-operation and Development - OECD", chapter 7, section 7, art 2.2.1.7.7.6 - inc 15.

ONAC is the National Accreditation Body of Colombia that accredits the technical competence of the compliance assessment bodies. It also exercises the role of the National Monitoring Authority of the Principles of Good Laboratory Practices of the Organization for Economic Co-operation and Development (OECD) in accordance with the designation contained in chapter 26 of the Decree 1074 of 2015, and the other standards that these principles modify, replace or complement. Additionally, in Resolution 2581 of 2017; adopting the Principles of Good Laboratory Practices (GLP) of the Organization for Economic Co-operation and Development (OECD), and the voluntary application of this system for susceptible products or materials of registration in the country that require non-clinical safety studies, issued by the Ministry of Commerce, Industry and Tourism; Article 5 presents the obligations of ONAC in its capacity as National Monitoring Authority of the OECD GLP Principles, and monitoring through inspection of test facilities conducting non-clinical safety studies under the OECD GLP Principles.

ONAC establishes its legal conditions in the statutes, and the certificate of existence and legal representation. ONAC keeps the records of its associates in the Associates Records Book No. 000445 of the Chamber of Commerce of Bogotá, and the Data Base of Associates of ONAC, information kept by the Administrative Management.

4. GENERAL CONSIDERATIONS

The associates constitute the General Assembly, which, in accordance with the Statutes, elects the Board of Directors composed of representatives of the sectors with direct interests in accreditation, indirect interests in accreditation, and designated members of the Colombian Government. The Executive Director of ONAC is appointed by the Board of Directors, which in turn is constituted as ONAC's top management.

ONAC has established its organizational structure with responsibility and authority documented in the job profiles and the procedures derived from each process. Specifically, the Development and Improvement Management oversees the development of the OECD GLP Program, and the OECD GLP Program Coordinator oversees the execution of the same, which in this case is the Research and Projects Coordination.

ONAC, as the National Monitoring Authority, is responsible for and has the authority to make related decisions regarding the recognition of test facilities compliance with Good Laboratory Practices of the OECD. The decisions include granting, maintaining, expanding, reducing, suspending and withdrawing the OECD GLP Recognition.

The Colombian GLP Monitoring Program adopts document No. 1 "OECD Principles on Good Laboratory Practices" (reviewed in 1997) to carry out the inspections and study audits.

Likewise, the Monitoring Program complies with the relevant documents of the OECD, established in the following documents:

• OECD/GD(95)66 "Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practices". Environmental Monograph No. 110 (Document No. 2 of the Environment Directorate of the Organization for Economic Co-operation and Development - OECD).

• OECD/GD (95)67 "Revised Guidance for Carrying Out Laboratory Inspection and Study Audits". Environmental Monograph No. 111 (Document No. 3 of the Environment Directorate of the Organization for Economic Co-operation and Development - OECD).

• OECD/GD (95)114 "Guidelines for the Preparation of GLP Inspection Reports" Environmental Monograph No. 9 (Document No. 9 of the Environment Directorate of the Organization for Economic Co-operation and Development - OECD).

ENV/JM/MONO (2000)3 "The Request and Conduct of Inspections and Study Audits in Another Country" (Document N° 12 of the Environment Directorate of the Organization for Economic Co-operation and Development - OECD).

4.3 Personnel. Qualification and Training

ONAC, the GLP Monitoring Authority, is responsible for ensuring that an appropriate team of inspectors, who has the necessary competence to carry out the Inspections and Study Audits, is appointed. The number of inspectors varies according to the scope requested by the test facility (degree of complexity of the inspection, the types of studies requested and the type of product). The inspectors perform the inspections according to the procedures and documents described in this Program. All Inspectors have a deep understanding of the OECD GLP Principles and the requirements necessary to comply with these principles, and are qualified with practical experience in chemistry, pharmaceutical chemistry, chemical engineering, biology and other relevant disciplines that are part of this Program.

ONAC's group of inspectors consists of: an inspector who is part of the permanent personnel and four inspectors hired by ONAC. In the latter case, ONAC, as the GLP Monitoring Authority, is ultimately responsible for determining the state of compliance with the GLP by the test facility.

The profile for an Inspector to be qualified by ONAC to perform the OECD GLP Recognition activities of Test Facilities is:

• University Professional in scientific disciplines related to the sciences of interest of the GLP, such as chemistry, pharmaceutical chemistry, chemical engineering, biology, among others.

• Have a minimum of 5 years of work experience in activities related to the studies covered by the scope of the GLP Monitoring Program.

• Be aware of the national legislation on GLP and the relevant OECD regulations.

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• Have completed a GLP Inspector's course:
- Dictated by the OECD or,
- Taught by inspectors or experts qualified as Inspectors of OECD Member countries or full adherent countries, or
- Taught by ONAC inspectors with more experience.

• Have participated in an inspection and simulated study audit in the role of GLP Inspector, and in a real inspection and study audit. In both cases, a qualified GLP Inspector must issue a performance report, which will be submitted to the OECD GLP Coordinator who decides whether the person is qualified as a GLP Inspector.

Although, for the initial qualification, inspectors are not required to participate as observers in inspections and study audits carried out by other GLP Compliance Monitoring Authorities belonging to the MAD agreement, participation in said activities is desirable, as it will complement his or hers training and provide ongoing training to the Inspectors.

In some cases, GLP Inspectors may contract the assistance of technical experts for specific disciplines involved in inspections and study audits that follow the principles of the OECD Good Laboratory Practices.

The profile that technical experts must comply with:

• University Professional in the specific discipline involved in the process of inspection and study audit.

• Have a minimum of 3 years of practical experience in the area in which the process of inspection and study audit is developed.

The inspector trainings will be carried out at two levels:

Level 1- It is the initial training for the new inspectors, including training on the national legislation and the respective OECD regulations, introductory training in GLP, and the gradual participation in the work of the inspection team.

Level 2 - Continuous training for all inspectors, including, for example, participation in OECD courses for GLP, workshops given by inspectors or experts qualified as Inspectors belonging to OECD Member countries or fully adherent countries, workshops on specific topics on GLP requirements, and, optionally, exchange of experiences with other Monitoring Authorities of OECD Member countries.

This information is detailed in the PR-5.4-06-FLP **"Procedure on the Competence of the Inspectors for the Program of Good Laboratory Practices" - GLP, and associated formats**.

At the beginning of the program, ONAC qualified five of the professionals who participated in the trainings and workshops as inspectors. They demonstrated a good performance, clear incorporation of the concepts and that they had training in audit techniques from an evaluation. They carried out an inspection accompanied by an observer, a GLP expert with inspector training, from an OECD Member country or fully adherent country belonging to the MAD agreement, in order to obtain feedback from the latter, on how the activity had been carried out and the performance of the inspectors. Additionally, the GLP expert with inspector training, will be able to observe the performance of some of these inspectors during their first inspection.

The inspectors participate in internal harmonization activities, organized by the National Monitoring Authority annually. The inspector team will not audit the scientific-technical aspects of the studies, since the evaluation of these aspects is only attributed to the regulator.

On the other hand, ONAC promotes the exchange with members of other Monitoring Authorities to promote international harmonization in the interpretation and Compliance Monitoring with the GLP Principles, and in this regard, the possibility of receiving interested members from other Monitoring Authorities is contemplated to observe inspections conducted by ONAC's inspectors. In such cases, the consent of the Test Facility that will be inspected will be requested.

4.4 Confidentiality

In the execution of its functions, ONAC has access to scientific and commercially valuable information, and can even request or withdraw sensitive documentation from the test facilities or include details of it in the final inspection report. This highlights the need for confidentiality on ONAC's behalf.

4. GENERAL CONSIDERATIONS

The following is considered to be confidential:

• The request for monitoring by the applying test facility.

• ONAC ensures confidentiality not only in relation to its inspectors, but also to all personnel who have access to the files of the test facility, the documentation thereof and the decisions taken in relation to the condition of compliance with the GLP. Personnel and inspectors must sign the **FR-5.4-01-GLP "Statement of Conflict of Interest for personnel linked to the GLP-OECD Recognition Program**", as well as to abide by the ethical and conduct norms contained in the **"Code of Ethical Action"** and the **FR-5.4-02-GLP "Agreement of confidentiality for external personnel",** undertaking to respect the confidentiality and reservation of all current or previous information related to the facilities inspected or in the process of inspection; and to guide their activities and actions in accordance with the provisions in the Code of Good Governance.

• ONAC ensures restricted access to commercially sensitive information, studies requested or withdrawn from the site, and inspection reports to only the ONAC Management; inspectors, in the case of inspections in which they have participated; ONAC personnel involved in the GLP Compliance Monitoring Program; and, when appropriate, the corresponding Regulatory Authorities. Copies of documents from the test facilities will only be available at the request of the Regulatory Authority and with the explicit authorization of the corresponding test facility. ONAC ensures that the studies submitted to monitoring, or the companies that sponsor such studies, are kept confidential by the inspectors and experts, and that they have no economic or other interests with the inspected facilities.

• In relation to the archiving of the documents related to the test facilities, ONAC is based on Law 594 of 2000, which dictates the General Law of Archives and other provisions, and in which a 10-year maintenance period for documents is established. Additionally, ONAC's archives have an exclusive section for GLP documentation, with restricted access, previously authorized and duly registered.

• ONAC communicates the names of the designated inspectors to the testing facility. If the facility considers that a problem of confidentiality or potential conflict of interest could arise in relation to any member of the inspection team, it may request a replacement of the same in writing. including the respective justification.

• In the case of the participation of observers from other GLP Monitoring Authorities in the inspections, authorization will be previously requested from the test facility. Observers must sign the necessary documents regarding confidentiality.

• In case of participation of Regulatory Authorities or OECD personnel during the inspection, these participations will be notified to the test facility in sufficient time.

The following information is not confidential:

• During inspections or study audits, when ONAC identifies situations that compromise the integrity and validity of studies concerning compliance with GLP, it will notify such situations to the OECD and to all the members of the GLP Working Group and the corresponding regulatory authority. Also, it will inform about suspensions or cancellations of the test facilities.

• The name of the inspected test facility that meets all the requirements and that integrates the facility's registry in accordance with GLP.

• The certificate of Compliance with Good Laboratory Practices.

• The dates on which the inspections have been carried out.

• Information on the National Monitoring Program on Compliance with the GLP of the OECD, published on ONAC's website, accessible to the public.

5. ONAC's NATIONAL MONITORING PROGRAM

5.1 Scope of ONAC's National Monitoring Program

Decree No. 1595 of the Ministry of Commerce, Industry and Tourism of Colombia of August 5, 2015, establishes that ONAC must "Exercise as the Monitoring Authority of Good Laboratory Practices of the Organization for Economic Co-operation and Development - OECD".

The Ministry of Commerce, Industry and Tourism has published the Resolution 2581 of 2017, in which it adopts the Principles of Good Laboratory Practices (GLP) of the Organization for Economic Co-operation and Development (OECD), and the voluntary application of this system for products or materials susceptible to registration in the country that require non-clinical safety studies, and which establishes in Article 4, that the Intersectoral Quality Commission will be the body through which the incorporation of the GLP Principles of the OECD will be established for the regulations issued by the regulatory bodies related to the areas of study established in the paragraph of article 2 of the resolution. The foregoing is subject to the request of the interested regulatory entities.

The purpose of the study of the materials contained in the products is to obtain data about their properties, their harmlessness with respect to human health and/or the environment, which will be evaluated by the regulator.

ONAC's GLP Monitoring Program comprises the areas of competence in accordance with the Appendix to Annex III [C (89)87(Final)]/Revised in C(95)8(Final) of the Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practices (Document nº 2 Guide for the Monitoring Authorities of the Good Practices of Laboratory, of the Environmental Management of the OECD):

1. Physical-chemical tests;
2. Toxicity studies;
3. Mutagenicity studies;
4. Environmental toxicity studies on aquatic and terrestrial organisms;
5. Studies on behavior in water, soil and air; bioaccumulation;
6. Residue studies;
7. Studies on effects on mesocosms and natural ecosystems;
8. Analytical and clinical chemistry testing;
9. Other studies

ONAC does not include other types of studies that do not comply with the indicated types and purposes in the scope of the program.

5.2 Request by the Test Facilities

The test facilities interested in entering the GLP Monitoring Program must submit **the "Inspection Request Form for the Recognition of Compliance with Good Laboratory Practices" (FR-3.2-01-BPL)**, available to the public on the website www.onac.org.co, to ONAC.

The scope requested by the test facility to obtain compliance with the GLP must be clearly established. The facilities should detail:

- The product tested (cosmetics, pesticides, industrial chemicals, etc.)
- The areas of competence:
    a. Physical-chemical tests;
    b. Toxicity studies;
    c. Mutagenicity studies;
    d. Environmental toxicity studies on aquatic and terrestrial organisms;
    e. Studies on behavior in water, soil and air; bioaccumulation;
    f. Residue studies;
    g. Studies on effects on mesocosms and natural ecosystems;
    h. Analytical and clinical chemistry testing;
    i. Other studies
- The test (e.g. acute oral toxicity in rats),
- The experimental system (e.g., laboratory animals, plant crops, soil, microorganism cultures, etc.)
- Personnel;
- Team members;
- The facilities;

5. ONAC's NATIONAL MONITORING PROGRAM

At the time of making the request, the test facility must have at least one completed study (real or simulated) and a study in progress (real or simulated) at the time of the inspection visit. The studies (real or simulated) must belong to the different areas of competence declared in the scope of the request.

5.3 Procedure for carrying out inspections of the facilities and/or study audits to verify the compliance with the GLP

The Inspection activity is carried out according to the OECD/GD (95)67Revised Guidelines for Carrying Out Laboratory Inspections and Study Audits - Document nº 3 Guide for the Monitoring Authorities of the Good Practices of Laboratory, of the series of the OECD Principles of GLP and Compliance Monitoring, and involves the following stages (times are set out in the Annex to this document):

5.3.1 Master Schedule of Inspections and/or GLP Study Audits

ONAC manages a **Master Schedule of Inspections and/or GLP Study Audits (FR-3.3-15-GLP**). This form consists of an annual programming of execution and execution control of the inspections and/or study audits carried out or to be carried out at a later time. When changes are made, they are justified. In the Master Schedule, the test facility, inspection period, members of the inspection team, the areas of competence and comments (where applicable) are recorded.

This document is managed electronically and is the responsibility of the GLP Program Coordinator.

5.3.2 Activity prior to the inspection visit and/or study audit

Once the official request is received, ONAC acknowledges the receipt of the same and reviews the documentation provided in order to verify if the activity can be subject to the GLP Recognition, and if it is complete and adequate. If the documentation is not complete or adequate, the testing facility will be asked to complete it and resolve the problems detected.

The evaluation process continues when the received documentation is complete and adequate. The minimum documentation required to initiate the GLP Recognition process is:

- Certificate of existence and legal representation of the applying legal entity
- Title of property and/or lease agreement and/or title that proves the right to use the headquarters of the test facility.
- Architecture plan of the test facility.
- The test facility's Quality Manual, or a procedure in which the facility and its activities are described.
- Organizational chart that reflects the internal organization of the test facility (both for GLP studies and outside of these) identifying the departments related to the execution of the studies requested, as well as the organization chart of the larger organization to which it belongs, if applicable.
- Master Schedule of documents of the test facility, including a copy of general procedures, and a copy of standard operating procedures.
- Current master schedule of studies.
- Copy of certificates issued by suppliers of biological test systems, when applicable.
- Calibration/verification program.
- Copy of calibration/maintenance certificates for measuring and testing equipment.
- The test facility's job descriptions and the personnel's CVs requested in number 4.
- Copy of the study plans with their respective raw data and final reports, of the non-clinical studies carried out by the test facility.

The program coordinator designates an inspection team, which is notified to the test facility along with the scheduling of the on-site visit **(FR-3.2-02-GLP Notification of the inspection to monitor compliance with the OECD GLP)**, for performing the pre-inspection consisting of the study of the documentation sent by the facility, including the application, the Standard Operating Procedures (SOPs) and relevant documentation, in order to have a frame of reference regarding compliance with the Principles of Good Laboratory Practices of the OECD by the requesting test facility.

As part of the study of the documentation, ONAC will request copies of some study plans with their respective final reports of the studies carried out by the facility. If necessary, the inspection team may request additional information.

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The Inspection Team prepares the Documentation Study Report where the detected deviations are listed **(FR-3.3-08-BPL Inspection Report)**, indicating its classification, and submits it to the coordination. Based on the nature and/or number of deviations detected, it is possible that the ONAC requires the test facility to act on the deviations and respond to the written report with a proposal and evidence of the actions taken to resolve them. **(FR-3.3-12-GLP Plan for the elimination of deviations from the GLP Principles).**

The documentation review allows:

• For ONAC, to assure that the test facility has a system that is GLP compliant and adequately prepared for an inspection;

• For GLP inspectors, the opportunity to prepare adequately for the inspection; to understand how the GLP systems of each facility work and to minimize the amount of time necessary to read the procedures at the place.

• For applying test facilities, to get feedback on how well prepared they are, and what areas of their GLP operation may require additional development;

ON SITE VISIT: INSPECTION AND/OR STUDY AUDIT

The procedure to carry out the inspections at the test facilities and the study audits verifying that the compliance with the GLP Principles is aligned with document OECD/GD(95)67 "Revised Guidance for Carrying Out Laboratory Inspection and Study Audits "(Document No. 3 of the Environmental Management of the Organization for Economic Co-operation and Development - OECD).

5.3.2.1 Preparation of the on-site visit

Before carrying out the inspection and/or the study audits, the inspectors will examine all the existing information on the test facility, including the request, the documentation study report, previous inspection reports (if applicable). In particular, inspectors should consider recorded deviations from inspections and/or previous study audits (when applicable).

ONAC's Program Coordinator establishes the dates to carry out the inspection which are incorporated in **the FR-3.3-15-GLP Master Program for Inspections and/or GLP Study Audits**. The number of inspection days will depend on the size of the facility, the number of study directors and the number of studies that must be audited according to the applied sampling. ONAC communicates the date and duration of the visit to the test facility and sends the **FR 3.3-13-GLP Plan for Compliance Monitoring with the Good Laboratory Practices** with the appropriate amount of time in advance of the agreed visit date.

5.3.2.2 On-Site Visit

On the agreed upon date with the test facility, the designated inspection team conducts an inspection visit to the requesting facility whose purpose is to determine the extent to which the facility and the studies comply with the OECD Principles of Good Laboratory Practice.

The inspectors will not enter test facilities against the will of the facility. However, circumstances may arise, for example, due to requirements by the National Regulatory Authorities or GLP Compliance Monitoring in other countries, where access to facilities and data is necessary. The test facilities are obliged to provide access to all the test facilities to the inspectors responsible for the inspection and/or study audits, as well as to provide them with the information and documentation necessary to carry out their task. This may include the application, prior to the inspection of copies of study plans, raw data and final reports, as well as the withdrawal of the same at the end of the inspection. If the test facility refuses to comply with this requirement, ONAC will proceed to suspend their compliance with the GLP and will notify such situation to the corresponding Competent Authority and to the GLP Secretary of the OECD.

The inspection will normally take place in 3 stages:

1. Opening meeting

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The meeting is held between the inspection team and the test facility's personnel at the beginning of the visit. The presence of the Management Representative is important at the opening meeting, allowing also to make a presentation of the organization and activities that it carries out.

The following items should be covered during the opening meeting of the visit:

- Presentation of the inspection team and test facility's personnel;
- Nature and purpose of the inspection;
- Confirmation of the scope of the GLP Recognition;
- General description of the inspection activities carried out to date, for example, review of the documentation;
- Confirmation of the inspection plan and the availability of the test facility's personnel to assist the inspectors;
- Review/confirmation of the master schedule and selection of studies for the audit;
- The health and safety requirements of the testing facilities in relation to inspection equipment;
- Registration of attendance **(FR-3.3-17-GLP Attendance registration for the opening and closing meetings of the inspection)** of the people who attended the opening meeting.

During the inspection of the facilities, the inspectors must be accompanied, at least, by one of the members of the quality assurance unit, and/or key personnel who have sufficient authority to assure the inspectors access to all the documents, personnel and activities that are required to be inspected. They can also request a suitable place to examine the documentation.

2. The undertaking of the inspection and/or Study Audits

To begin the inspection, the facility is requested to list current documents and an updated copy of the Master Study List, to select the studies to be audited. The studies that the inspector team requests to be removed from the archive to conduct the study audits must be available in reasonable time or the team may simply remove them as part of the inspection of the archive and its management.

GLP inspections should include two types of inspection:

- The OECD GLP inspection of independent laboratories of any study e.g., the inspection/particular audit of the test facility, the quality assurance system of the GLP organization, the management and the personnel, the function of the quality assurance area; the handling of test and reference products, the equipment management, devices and reagents; the inspection of facilities and the environment; the management of experimental systems, the management of standard work procedures (SOPs); the generation of study plans and reports and data registry, and the function of the archive.

- Study audits examine the application of the GLP system at the time the study is being carried out, and in the context of the requirements of the Study Plan. In addition, they are applicable to completed studies to evaluate the consistency between the study plan, the SOPs, the raw or original data, and the final report.

During the days scheduled to carry out the inspection, the inspectors proceed to the careful review of the facilities and/or study audits that are subject to the inspection, according to the GLP Principles, which covers the activities indicated below:

- Organization and personnel;
- Quality control program;
- Facilities;
- Care, lodging and confinement of biological testing systems;
- Apparatus, materials, reagents and specimens;
- Test systems;
- Test and reference material;
- Standard Operating Procedures;
- Study execution;
- Study results report;
- Storage and retention of records;

The inspectors must use the **GLP Principles Inspection Checklist (FR-3.3-10-GLP)** to perform this activity.

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The inspection team does not perform a scientific evaluation of the study data, nor of the scientific design or the adequacy of the test systems used. However, the study plan must be developed by appropriately qualified technical/scientific personnel with proven experience in all aspects of the study, and ONAC inspectors will verify such training.

If serious deviations from the GLP Principles are observed during the inspection and/or Study Audits, it/they can be interrupted. The guidelines for conducting inspections and study audits are described in **INS-3.3-01-GLP Inspection and/or Study Audits of a Test Facility.**

The deviations found in the inspection are classified as:

- Major deviation: Deficiency that endangers the good functioning of the GLP Quality System or the integrity of the study data.
- Minor deviation: Deficiency that has not yet seriously impacted the functioning of the GLP Quality System or the integrity of the study data.

The inspection team may make improvement observations, considered recommendations, for the compliance with the OECD GLP Principles. These observations are not a deviation from the requirements for registration and the test facilities are not required to take corrective measures.

Upon completion of the inspection, the Inspector Team meets in private to discuss the strengths, deviations, recommendations and the ability of the Test Facility to conduct the requested studies, in accordance with the GLP Principles, the Monitoring Program and ONAC's criteria. The GLP Inspector records the deviations detected in the format **FR-3.3-07-GLP Findings of the inspection activities.** In case there are no deviations from the inspection visit and/or Study Audits, the Inspector Team must indicate so in the same format.

3. Closing meeting

At the closing meeting, the Inspector Team reports the conclusions, including the GLP deviations detected, the observations, strengths and weaknesses of the GLP System, which will be discussed before the end of the closing meeting.

The participants of the closing meeting should at least consist of key personnel and all facility personnel that the management considers should be present. At the end of the meeting, the GLP Inspector gives the Facility Representative a copy of the FR-3.3-07-GLP Findings of the inspection and/or study audits, which must be signed by both the Inspector Team and the Authorized Facility Representative.

When appropriate, the lead inspector records the list of documents (procedures, studies, communications, etc.) whose copies are removed from the entity. Two copies of this record are made, which must be signed by the lead inspector and the facility representative.

If the deviations detected during an inspection and/or study audit are such that the verification of the actions for the removal of deviations do not require an on-site inspection, ONAC will follow up on the actions through the proposals and evidences sent by the facility to resolve the deviations.

The test facility's file and copies of removed or received documents will be preserved in conditions that assure its recovery. ONAC establishes a 10-year period of document storage, in accordance to the Law 594 of 2000, which dictates the General Law of Archives and other provisions. Additionally, ONAC's archives have an exclusive section for the GLP documentation, with restricted access, previously authorized and duly registered.

5.3.2.3 Inspection Results

The inspection and/or study audits carried out by the inspection team may result in the following situations:
- If no deviations emerge from the inspection visit and/or study audits, the GLP Inspector and the inspection team prepares the Final Report. **(FR-3.3-08-BPL Inspection Report)**, enclosing it to the GLP Compliance Monitoring Plan, the GLP Opening and Closing Meeting format, and the Deviations from the GLP Principles Report.

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- When during the inspection, minor or mayor deviations from the OECD GLP Principles are identified, the inspection team prepares a preliminary report **(FR-3.3-08-GLP Inspection Report)** that is sent to the test facility. The facility must answer to this report enclosing the objective evidence from the implementation of the corrective actions.

- When during the inspection, minor or mayor deviations from the OECD GLP Principles are identified, a preliminary report is prepared, and in the case that the solution to the deviations require an on-site verification, a Follow-up Inspection is planned.

5.4 Inspection Report

The inspector group prepares a final report **(FR-3.3-08-GLP Inspection Report)** with the results and information gathered during the inspection, including the response by the test facility to the identified deviations, to be presented to the OCDE GLP Program Coordinator. The Inspection Report/ Study Audits are prepared in accordance with the requirements of Document No. 9 of the OECD Environmental Directorate "Guide for the preparation of GLP inspection reports", and will contain the following information as a minimum:

- Name of the Authorized Representative of the Facility.
- Date of pre-inspection (documentation evaluation).
- Date of the inspection and/or study audits.
- Name of the members of the Inspector Team.
- Type of inspection (inspection of the test facility, study audits, etc.).
- Date of the last inspection, status in relation to compliance with the GLP and any significant changes made by the test facility since the last inspection.
- Deviations observed in the documentation study.
- Deviations observed regarding the GLP and responses of the Test Facility.
- Strengths.
- Recommendations.
- Conclusions.
- Information related to the closing meeting, participants, etc.
- Report date
- Recommendation for the granting of the compliance declaration.
- Signatures of the GLP Inspector and the Inspector Team.
- Annexes, for example, copies of documents referenced in the report, as appropriate.

Other sections of the report include an introduction, a descriptive part, a final synthesis, an opinion on the status of compliance with the GLP and the annexes (depending on the case). All this information should provide an accurate idea of the way in which the Test Facility respects the GLP Principles and the quality of each study that has been audited.

The descriptive part should include:

- Narrative of the observations and the activities carried out during the inspection. The information must reflect each of the requirements of the GLP Principles: Organization and Personnel, Quality Assurance Unit, Facilities, etc.

- Regarding the studies (ongoing and completed) selected for audits: the following must be recorded in the report: details of the same, code, material, sponsor, name of the ED, methods, audits of the UAC, and description of the data or portion of data (partial audit) examined. Indicate the deviations observed.

5.5 Pending Status

In the period between the inspection and/or study audit and the final decision, the facility is considered as "PENDING". This is a period of maximum 6 months, in which the facility may resolve the deviations detected. Through its inspection team, ONAC will decide, based on the case by case results of an inspection, if during the "pending" period, the Study Director(s) can continue issuing final reports with the Declaration of Compliance with the GLP Principles, or on the contrary, it will not be able to do so until the deviations are resolved.

5.6 Decision on the recognition of the OECD GLP

The inspection alone does not result in a formal approval of the studies carried out by the facilities. Compliance with the BPL Principles of a test facility is guaranteed by the declaration of compliance with the GLP granted by ONAC.

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The inspection team carries out its recommendation regarding the declaration of compliance with the Principles of Good Laboratory Practices, in the **(FR-3.3-08-GLP Inspection Report)** final inspection report. The ONAC Executive Management makes the final decision on the test facility's compliance with the GLP according to the result of the inspection.

ONAC can adopt one of the following decisions:

- If the decision is favorable, it will proceed to issue the corresponding Certificate of Compliance with the Good Laboratory Practices by the Executive Manager of ONAC, which will be communicated to the competent authorities, for their information and timely effects.

- If the decision is not favorable, ONAC issues a declaration of Non-Compliance with the GLP that will be included in the final report **(FR-3.3-08-GLP Inspection Report)**, giving details of the failures found. The final report will be sent to the test facility. In addition, ONAC will inform the OECD and members of the GLP Working Group, as well as inform the competent authorities of Colombia about the test facility's status of Non-Compliance with the GLP.

  If the described situation is detected in a routine inspection or a follow-up inspection, in addition to informing the competent authorities of Colombia and the OECD Member countries, the test facility will be removed from ONAC's list of test facilities with the certificate of compliance with the GLP, not belonging to the GLP Compliance Monitoring Program and proceeding to the archive.

  In this case, the facility will be informed that until the detected deficiencies have been corrected, and evidence of its solution is sent, it is not appropriate to submit a new application according to the form FR-3.2-01 GLP.

- When major deviations are identified during a study audits for which the test facility or test site cannot take corrective actions, ONAC, as the GLP Monitoring Authority, will consider that such study(s) are Non-Compliant with the GLP Principles and will make the corresponding statement in this regard.

  In this case, ONAC will also inform about the status of Non-Conformity with the GLP of the study or affected studies informing the GLP Secretariat of the OECD and the corresponding national regulatory authority.

  Through the corresponding Study Director, the test facility is obliged to make an amendment, that contains the final report of the study or studies affected detailing the deviations found therein, to the Declaration of Compliance with the GLP as soon as possible.

  It is worth mentioning that, a situation of No Compliance of a Study or Studies does not necessarily mean that the GLP quality system of the facility is affected.

5.7 Recognition Certificate of Good Laboratory Practices of the OECD

After a favorable decision, and once the test facility has paid the corresponding costs, ONAC issues a Certificate of Recognition of Good Laboratory Practices of the OECD, which attests the granting of the recognition in favor of the facility signed by the Executive Director of ONAC.

The following are stated in the certificate, as a minimum:

- The name of the test facility and the certification number granted.
- Types of test products.
- Recognized test areas.
- Reference to the validity.

This document will be considered the property of ONAC and, as such, should not be modified if it is not by the Monitoring Authority itself.

ONAC will publish the list of test facilities that are in compliance with the OCDE GLP on its website, including the main information collected in the certificates.

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The cancellation of a certificate of compliance with GLP may be considered when changes, in the legal or ownership situation of the test facility, have occurred without notification, or greater deviations (without resolution) of the Principles of Good Laboratory Practices are detected during the inspection process.

In the case of cancellation of the Certificate of Compliance with the GLP, ONAC:

- Will formally communicate this circumstance to the test facility.
- Communicate the cancellation of the certificate and withdrawal of recognition to the competent authorities.
- Remove the facility from the list of test facilities with certificates of compliance with GLP, no longer belonging to the Compliance Monitoring Program with the OECD GLP.

5.8 Follow-up Inspection: Re-inspection

If deviations to the GLP Principles have been identified during the Inspection and/or Study Audits of the Test Facility, and for its closure it is necessary to carry out an on-site verification; then a re-inspection must be scheduled, which must be done before the 6 months period expires counted from the date of the Inspection.

The Testing Facility receives the plan for follow-up (FR-3.3-13-GLP Plan for monitoring compliance with the good laboratory practices). The visit includes three phases, an opening meeting where the purpose of the visit is explained, the verification of the corrective actions and the closing meeting where the results of the re-inspection are communicated orally, and a written record is made in the final report **(FR-3.3-08-BPL Inspection Report)**.

5.9 Special Inspections

Special inspections are carried out at the request of the National Regulatory Authority or Regulation Authorities of other OECD Member countries, either because there are doubts in the presentation of certain studies, or because there are indications of non-compliance with the application principles of the GLP, jeopardizing the integrity of compliance with the OECDE GLP of the test facilities.

ONAC can also perform special inspections when:

1. There are reasons to presume a deterioration in the activity of the facility.
2. If this had undergone a significant reorganization (changes of Study Directors, Quality Assurance Responsibility, etc.)
3. Due to a change of owner or company name.
4. Due to the receipt of complaints where the test facility is involved.
5. By extension of the scope of the facility.
6. Any other circumstance that makes this type of inspection necessary.

The test facility will be informed in writing of the need to carry out a special inspection and/or study audit to verify that the registration requirements continue to be met. The special inspection follows the same procedure described in 5.3.

5.10 Maintenance of the compliance with the OECD GLP

Once the test facility has recognition in the GLP OECD, routine inspections are performed to verify its compliance. After twelve (12) months of the initial inspection, the recognized test facility will undergo a new inspection and study audit since the registration was granted, in accordance with the provisions of section 5.3 of this document.

Maintenance inspections are performed in order to ensure that:

- The test facility continues to operate in accordance with the requirements established in the National GLP Monitoring Program and the applicable documentation.

- The test facility has implemented the pertinent corrective actions for the deviations that arose in the last inspection.

- Follow up on any change in the organization, procedures and resources of the test facility that does not affect the performance of studies according to the GLP and applicable regulations.
- The test facility performs the activities according to what is indicated in the Certificate of Conformity with the GLP, verifying the studies carried out or in execution.

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After the initial inspection, the test facility must request, at least 3 months in advance, on-site inspection visits so that the National Monitoring Authority verifies that the facility continues to comply with the OECD GLP Principles. The first and second routine inspections will be annual, from there, if there is no problem, the routine inspections will be biannual with annual documentary checks, where it will be reviewed if changes were made in the facility's GLP system (personnel changes, for example), the master schedule of studies; and based on these, some studies will be requested for its audit.

If it is verified, during a routine inspection, that the test facility has not carried out studies for a period of 2 years and does not plan to carry it out new studies for a period of approximately 1 year, the Acknowledgment will be withdrawn and this fact will be communicated to the competent authorities, the OECD and the members of the GLP Working Group.

5.11 Extension or Reduction of the OECD GLP Recognition

5.11.1 Extension or reduction of competence areas

The test facility may formally request an extension or reduction of the scope of compliance with the GLP.

5.11.1.1 Extension

If the Test Facility wishes to extend its scope to new competence areas, it must submit the **FR-3.2-01-GLP** Inspection Request Form for the Recognition of Compliance with the Good Laboratory Practices, detailing the requested extension and the tests involved in the studies. The inspection and/or study audit visits will be limited only to those specific aspects related to the requested, confirming the compliance with the GLP, as established in 5.3.

During the extensions of the competence areas, the **FR-3.3-11-GLP Listing of the tests associated with the GLP studies carried out by the facility continues will be updated.**

In case the declaration of compliance is granted to the area of competence extension requested by the facility, the Certificate of Recognition in OECD GLP is updated, maintaining the stipulated dates for the regular inspection visits. Likewise, the information published on the ONAC website is updated.

5.11.1.2 Reduction

The test facility must submit a formal statement to ONAC, detailing the areas of competence for which it requests the reduction. Once the reduction in the area of competence has been accepted, ONAC updates the Certificate of Recognition in OECD GLP, maintaining the stipulated dates for the regular inspection visits. Likewise, the information published on the ONAC website is updated, and it informs the competent authorities, the OECD and the members of the GLP Working Group about the reduction.

5.11.2 Extension or reduction of the tests associated with the competence areas

The test facility may formally request an extension or reduction of the tests associated with the areas of competence of the GLP studies carried out by the facility.

5.11.2.1 Extension

To incorporate a new test associated with the GLP studies carried out by the facility, the facility must present the request for compliance monitoring with good laboratory practices (GLP). ONAC verifies that the inclusion of the requested test corresponds to an area of competence covered by the recognition of the facility and proceeds to evaluate the need for carrying out an on-site inspection. If, according to the documentation evaluated, an on-site inspection is not considered necessary, then this test will be included in the GLP recognition scope.
If, on the other hand, due to the complexity of the study, or because the applied methodology differs substantially from that involved in the recognized studies of the facility, or that a specific competence is required for its development, the on-site inspection is necessary, as established in 5.3.

5.11.2.2 Reduction

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The test facility must submit a formal statement to ONAC, detailing the tests for which it requests the reduction. The reduced tests are eliminated from the **FR-3.3-11-GLP** List of tests associated with the GLP studies carried out by the facility.

5.12 Suspension and withdrawal of the OECD GLP Recognition

The Compliance with the OECD GLP of the test facilities in the OECD GLP can be suspended or withdrawn, voluntarily by decision of the entity, or by decision of ONAC; as a result of an inspection process of the facility. For the ONAC National Monitoring Program, the test facilities may be in one of the following states:

- Recognized facility (Compliant)
- Suspended facility (Non-compliant)
- Withdrawn facility (Non-compliant)

5.12.1 Suspension of the OCDE GLP Recognition

5.12.1.1 Voluntary suspension

The test facility may request the suspension of part of the scope or the total scope of the OECD GLP Recognition in writing at any time. The facility must specify in detail the reason why it makes this decision. Once the request is accepted, ONAC proceeds to update the information published on the website, and informs the competent authorities, the OECD and the members of the GLP Working Group about the suspension.

5.12.1.2 Suspension as a decision of the National Monitoring Authority

During an on-site inspection, if the BPL inspector discovers that the testing entity is not meeting, or cannot comply with, the GLP requirements, and that the studies performed have been, or will be, compromised as to their validity and integrity; then the GLP inspector will issue a recommendation to the Executive Management, so that the testing entity does not continue to be recognized. If the test facility is not able to meet the inspection criteria, the decision to suspend the registration is recommended to the ONAC Executive Board.

The lead inspector must consider the status of the studies carried out under the registration now suspended, since the last inspection and/or study audits of this type of studies. The test facility's master study schedule must be reviewed, and ONAC can request the performance of the study audits of all the studies carried out, during time the test facility was recognized for the respective test.

ONAC proceeds to update the information published on the website, and informs the competent authorities, the OECD and the members of the GLP Working Group about the suspension. Suspended test facilities can recover their registration once they have demonstrated that they meet the criteria for GLP Recognition.

5.12.2 Withdrawal of the OECD GLP Recognition

5.12.2.1 Voluntary withdrawal

The test facility may request the withdrawal of the OECD GLP Recognition in writing at any time. The facility must specify in detail the reason why it makes this decision. Once the request is accepted, ONAC proceeds to update the information published on the website, and informs the competent authorities, the OECD and the members of the GLP Working Group about the withdrawal.

5.12.2.2 Withdrawal as decision by the National Monitoring Authority

ONAC considers that there are situations in which the recognition for a test facility is withdrawn: (a) Non-compliance with the GLP, (b) failure to comply with the obligations of the test facility. In case b, it is probable that a suspension period will take effect first, allowing for a complete examination of the facts and circumstances, and allowing the test facility to present its case. Only the Executive Management can authorize a withdrawal of the recognition of a test facility and notify the decision in writing.

ONAC proceeds to update the information published on the website and informs the competent authorities, the OECD and the members of the GLP Working Group about the withdrawal of the recognition. Withdrawn test facilities will have to

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reapply for the recognition to re-enter the program, going through the initial inspection process. When the facility that has been withdrawn wishes to join the program again, it must have evidence of the satisfactory solution of the reasons that originated the cancellation (case a)). Without prejudice to this and depending on the background, ONAC will establish the grace period for the facility to request an inspection again, in order to demonstrate its compliance with the GLP, and thus be included in the registry of facilities in the GLP monitoring program of ONAC.

5.13 Obligations of the Test Facilities

The facilities must always comply with the following obligations:
• Comply with the general requirements established by ONAC in the current OECD GLP Compliance Monitoring Program;
• Declare compliance with the GLP only with respect to the scope for which the facility obtained the compliance or recognition;
• Send the documentation requested by ONAC in a timely manner;
• Inform ONAC on the changes it intends to carry out in relation to:
- its legal-, property-, commercial- or organizational situation;
- its organization and management, for example key personnel;
- facilities or other resources, when relevant;
- extension of the types of studies carried out and/or recognized test areas;
The notification must be made within a period of 5 working days after the change was made.

• As well as any other fundamental change that occurred in the initial conditions from which recognition is granted (authorizations, among others);
• Notify ONAC convincingly, with 60 (sixty) calendar days in advance, of its resignation to the GLP Compliance Monitoring Program;
• Allow free access to its facilities and cooperate with the members of the inspection team duly authorized by ONAC in carrying out the inspection and verification entrusted to them on the agreed dates;
• Allow them to review the documents and records generated. In the case of test facilities that carry out studies under contract, the facility management must ensure that the promoters of the studies are aware of this obligation;
• Pay the costs corresponding to the activities carried out by ONAC;
• Comply with the commitments acquired in the response sent to ONAC after the inspections.

5.14 Complaints and Appeals

5.14.1 Complaints

Any problem or difference of opinion between the inspectors and the test facility can normally be resolved during the inspection or the study audit. However, when these problems persist and an agreement cannot be reached during the inspection process, the facility may submit a written complaint against the results of the Inspection and/or Study Audits, clearly specifying the disagreements, which must be properly supported with adequate evidence. These complaints will be dealt with in the first instance by the OECD GLP Program Coordinator, who could request advice from independent internal or external experts. The final decision is communicated to the test facility.

For complaints related to the operation of the National Monitoring Authority or a recognized test facility, see the PR-4.4-01 ONAC complaint handling procedure.

5.14.2 Appeals

In the case of disagreements with the decisions regarding compliance, suspension or withdrawal, the appeal must be addressed in writing to ONAC's Executive Manager with a copy to the GLP Program Coordinator, at most within 15 calendar days from the date of the decision subject to the appeal. Disagreements must be properly supported with adequate evidence.

Appeals are received by the OECD GLP Program Coordinator, who appoints an Appeals Committee made up of independent members who have not intervened at any stage of the process. At least one of them must have knowledge of the GLP Principles. The OECD GLP Program Coordinator initiates a full review of the facts and requests information from all available sources. The appeal and related information are forwarded to the Appeals Committee, which will decide within 30 calendar days of receiving the appeal in ONAC. The decision on the appeal is presented to the GLP Program Coordinator, who communicates it to the Test Facility within the following 5 business days.

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5.15 Exchange of information with other OECD Members

With respect to the exchange of information and in compliance with its obligations to the other members of the OECD Working Group, ONAC publishes the National GLP Monitoring Program and all related documentation on its webpage. The National GLP Monitoring Program covers all the information required in Annex III [C (89)87(Final)]/Revised in C (95)(Final) of the Revised Guidelines for Compliance Monitoring Procedures with Good Laboratory Practices (Document No. 2 Guide for Verification Authorities of Good Laboratory Practices, of the OECD Environmental Directorate).

Annually, a report is drawn up on the inspections carried out. This report contains:

- Identification of inspected test facilities
- Inspection date
- Nature of the inspection: it indicates if it is a complete GLP inspection or if only a study audit was conducted. It also indicates whether the inspection was routine or not, and if any other authority participated in i
- Areas of competence of the inspected test facility
- Status of Compliance with GLP (compliant, non-compliant or pending, indicating the reasons)
- Date of granting of compliance
- Comments, as the case may be.

The Annual Summary is prepared each year on the previous information so that it constitutes a record that summarizes all ONAC's activities from the beginning of the inspections.

On the other hand, ONAC informs the OECD GLP Working Group about any relevant change in the National GLP Monitoring Program through the OECD Questionnaire.

Additionally, as already mentioned above, when ONAC detects major deviations to the GLP Principles, whose nature could have affected the compliance of specific studies or the operation of the facility's GLP Management System that could not be resolved; ONAC will inform the OECD GLP Secretariat as soon as possible through the format for Notifications by the Monitoring Authorities on situations of non-compliance with GLP.

On the other hand, ONAC will provide detailed information on the status and scope of the recognition of the facilities included in its program, when requested by another Monitoring Authority included in the MAD.

5.16 Archive

In ONAC's central archive, a specific section has been set up for the information regarding the inspections and/or study audits made at the test facilities in accordance with the OECD GLP. The following records and documents shall be kept for a period of 10 years:

- Records of qualifications, training and experience, and descriptions of the tasks of the inspectors/experts.
- Documents sent by the test facility for the preparation of inspections and/or study audits.
- Correspondence with the test facilities related to the inspections and study audits.
- Copies of documents or material obtained during an inspection.
- Copies of all GLP Recognition Certificates.
- Relevant correspondence with other Monitoring Authorities or Regulation Authorities.
- Historical archive of ONAC's replaced documents.
- Historical archive of the Master Program of Inspections of the Good Laboratory Practices.
- All records of inspections and/or study audits.
- Any information that may be considered relevant.

6. RECORDS (Evidence Document)

Code	Name	Physical Storage	Magnetic storage
FR-5.4-01-GLP	DECLARATION OF CONFLICT OF INTEREST FOR PERSONNEL LINKED TO THE OECD LABORATORY PRACTICE RECOGNITION PROGRAM	X	
FR-.5.4-02-GLP	CONFIDENTIALITY AGREEMENT FOR EXTERNAL PERSONNEL LINKED TO INSPECTIONS FOR RECOGNITION IN GOOD LABORATORY PRACTICES OF THE OECD	X	

6. RECORDS (Evidence Document)

Code	Name	Physical Storage	Magnetic storage
FR-3.2-01-GLP	INSPECTION APPLICATION FORM FOR THE RECOGNITION OF COMPLIANCE WITH GOOD LABORATORY PRACTICES (GLP)	X	X
FR-3.3-07-GLP	REGISTRATION OF INSPECTION ACTIVITIES FINDINGS	X	X
FR-3.3-08-GLP	INSPECTION REPORT	X	X
FR-3.3-10- GLP	LIST OF GLP INSPECTION VERIFICATION	X	X
FR-3.3-11- GLP	LIST OF FACILITIES ASSOCIATED WITH GLP STUDIES CARRIED OUT BY THE FACILITY		X
FR-3.3-12- GLP	PLAN FOR DEVIATION SOLUTIONS	X	X
FR-3.3-13 - GLP	PLAN FOR THE COMPLIANCE MONITORING WITH GOOD LABORATORY PRACTICES	X	X
FR-3.3-15 - GLP	MASTER PROGRAM OF INSPECTIONS AND/OR GLP STUDY AUDITS	X	X
FR-3.3-17 - GLP	ASSISTANCE REGISTRATION FOR OPENING AND CLOSING MEETINGS OF THE INSPECTION	X	X

7. CHANGE CONTROL

Version	Date of Approval	Summary of Changes
01	2017-04-28	First edition of the document
02	2019-02-04	Harmonization of new resolution of the Ministry of Commerce, Industry and Tourism General review according to the modifications of the documents associated with the recognition service in the OECD GLP.

8. ANNEX

Activity/Responsible	NATIONAL MONITORING AUTHORITY ONAC	INSPECTOR	TEST FACILITY
Application Review	8 business days (from official receipt)		
Completeness or clarification of the information contained in the application			15 business days (from the response by ONAC)
Service Quote	10 business days (from the acceptance of the request)		
Service payment			30 calendar days (from the acceptance of the quote)
Appointment of Inspectors and Programming Inspection and/or Study Audits	15 business days (from the payment of the service)		
Acceptance of inspectors			5 business days (from notification of designation)
Notice to the inspectors of the acceptance	3 business days (from acceptance)		
Pre-Inspection Programming (Documentation review)		15 business days (once the inspectors have been notified of acceptance)	
Preparation of the Pre-inspection report (documentation review)		7 calendar days (from the completion of the pre-inspection)	
Review of pre-inspection report (documentation review)	5 business days (from receipt of the pre-inspection report)		

Activity/Responsible	NATIONAL MONITORING AUTHORITY ONAC	INSPECTOR	TEST FACILITY
Adjustments to the Report (as applicable)		5 business days (from the completion of the review report)	
Preparation of the Inspection Plan		7 calendar days (from the completion of the pre-inspection)	
Sending the Inspection Plan to the Test Facility	5 business days (before inspection)		
Inspection Report and/or Study Audits		15 calendar days (after inspection)	
Complete Report Review	5 business days (from receipt of the report)		
Adjustments to the Report (as applicable)		5 business days (from the completion of the review report)	
Sending Complete report to the test facility (Pre-inspection Report + Inspection Report and/or Study Audits)	3 business days		
Delivery of proposal to resolve deviations from the GLP Principles			First proposal: 60 calendar days, from sending the report Second proposal: 30 calendar days
Review of the proposal to resolve deviations from the GLP Principles		7 calendar days	
Delivery of Inspection Report including the proposed actions for resolving deviations		30 calendar days	
Final Report Review	5 business days (from receipt of the report)		
Adjustments to the Report (as applicable)		5 business days (from the completion of the review report)	
Sending Final Report and Decision	5 business days		