RISK ASSESSMENT OF PESTICIDE AND GLP PROGRAM FROM INMETRO/BRAZIL

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The National Institute of Metrology, Standardization and Industrial Quality – Inmetro, through the General Coordination for Accreditation – Cgcre is Brazilian Compliance Monitoring Authority for the Principles of Good Laboratory Practices – GLP, recognizing test facilities that carry out studies/tests with the purpose of the assessment of environmental risk and human health for the record of pesticides, industrial chemical products and other chemical substances.

Cgcre/Dicla is liable for planning, managing, guiding, coordinating and executing the recognition activities of test facilities in compliance with GLP Principles.

The Program of Compliance Monitoring for GLP Principles of Cgcre for the recognition activities of compliance with GLP Principles is based on Guideline 2 of Organization for Economic Cooperation and Development - OCDE (Guideline for Monitoring Authorities in GLP) and follow the normative documents that emphasizes it with other national authorities of allied foreign monitoring, member of the working groups in GLP of OCDE.

Since 1995, Cgcre uses the documents of OCDE that are referenced to the GLP Principles and its additional documents that were translated to Portuguese and available by Cgcre as documents "NIT - Inmetro Technical Guideline." Since then, in Brazil, the GLP Principles of OCDE are base to the Brazilian test facilities to implement GLP Quality System, for the inspectors to check the compliance of test facilities regarding to the principles and to recognition granting by Cgcre.

The program establishment also aims to make possible Brazil, by means of Cgcre, to search for the recognition of OCDE, regarding to the attachment to the Mutual Acceptance of Data – MAD, for the studies accomplished in chemical according to GLP Principles established in the document Guidance 1 of OCDE – GLP Principles.

GLP is necessary to make a study to check if there is any human health and environmental risk when a chemical produced by a manufacturer is going to be trade. The national authorities of regulations in the health and environmental area (IBAMA and ANVISA) are liable for achieve the risk consideration and the record of these chemicals to commercialization in Brazil.

The Program in GLP Recognition is based in legal liability Administrative Rule INMETRO Number 220/09, July 23, 2009, it establishes that Cgcre is the Brazilian Authority of Monitoring of the Compliance with the GLP Principles; Administrative Rule IBAMA Number, October 15, 1996, the Brazilian Institute for the Environment & Renewable Natural Resources – IBAMA, regulatory authority of the environment, bonded to Ministry of Environment, delegates Cgcre, by means of this Administrative rule, the recognition activity of the compliance of the test facilities that carry out studies for the risk assessment of pesticides; Joint Administrative Rule IBAMA-INMETRO, October, 2009, it establishes criteria for the recognition, by Inmetro, of national test facilities that achieve physical-chemical, toxicity and ecotoxicological studies and others to the environmental assessment of the chemical, biochemical and biotechnological required by IBAMA, in accordance with the GLP Principles. This specific joint administrative rule substitutes the Joint Administrative Rule IBAMA-INMETRO Number 66, July 17, 1997.

The normative documentation fostered by Cgcre to the recognition of the compliance of test facilities in accordance with GLP Principles is the Standard NIT-DICLA-035-GLP Principles and its additional normative documents (NIT-DICLA-034, NIT-DICLA-036, NIT-DICLA-037, NIT-DICLA-038, NIT-DICLA-039, NIT-DICLA-040, NIT-DICLA-041, NIT-DICLA-043).

Cgcre dispose on the Inmetro webpage, in the subsite "GLP Monitoring" specific information and documents, this way, the plaintiffs of the recognition in compliance with the GLP Principles can formalize their application.

The systematic that was implemented by Cgcre to operationalize the recognition process of compliance of test facilities in accordance with GLP Principles includes the stages: a) Application of the

recognition by the test facility; b) Pre-inspection; c) Documentation consideration; d) Inspection; e) Decision making and Formalization of Recognition in accordance with GLP Principles.

The Recognition of Compliance with GLP Principles is granted because of the test facility, considering the area of expertise and categories of test items (pesticides and others chemicals), to recognized or required methodologies by the regulatory authorities (IBAMA, ANVISA and MAPA).

The area of expertise are: Physical-chemical Testing; Toxicity Studies; Mutagenicity Studies; Environmental toxicity studies on aquatic and terrestrial organisms; Studies on behaviour in water, soil and air; Bioaccumulation; Residue Studies; Studies on effects on mesocosms and natural ecosystems; Analytical and Clinical Chemistry Testing; Studies with Genetically Modified Organisms.

The inspection in the test facility, that includes study audit, is to check on the facilities of the applicant, by means of objectives evidences, the level o system adhesion of management of test facility toward the GLP Principles established in the standard NIT-DICLA-035 (Principles of Good Laboratory Practices (GLP).

The inspection team shall make one of the following recommendations to Cgcre in the inspection report**:** Recommending the recognition when there isn't nonconformities or abeyances; Recommending the recognition only after eliminated the Nonconformities and abeyances; Do not recommending the recognition because of system failures that make dubitable the capacity of the test facility to develop studies in accordance with GLP Principles.

Inspections and casual studies audits are accomplished every 24 months, and the first one is accomplished 12 months after the recognition granting in order to check compliance with requirements and regulations to the GLP recognition.

Extraordinary Inspections and studies audits can take place at any time due to questions or denunciation of the non-compliance of the GLP Principles or when sought by a regulatory authority (IBAMA, ANVISA and MAPA).

Cgcre/Dicla shall also inform to the regulatory authorities interested in the studies the inspection results and/or study audit that show data manipulation, inconsistence in the compliance to the GLP Principles or any question that might compromise the accomplished studies and/or accomplished by the test facilities.

GLP recognition may at any time be suspended, canceled, or have limited scope, requested by the test facility, by application of the regulatory authority, or by imposition of Cgcre.

The GLP Principles establish criteria for managing test facilities and studies carried out in order to assure the reproduction of these studies at any time, in order to ensure the reliability, the risk assessment and the use with regulatory agencies. When the Principles are not observed, they can impact on the reliability or scientific merit of the data tested, as well as in the capacity of the regulatory authorities to validate or reproduce a study and, consequently, prevent the use of data presented to support the record or license of any product. Thus, the noncompliance with the GLP Principles can compromise the action of regulatory authority on the assessment of risks to the health and environment, preventing proper control and monitoring.

Thus, all the staff involved in the conduction or presentation of studies, such as the sponsor, the test facility manager, the study director or the registrant of chemical products is responsible for the provided data and can be penalized when the nonconformities of the studies influence on the results or in their traceability.

While in Brazil such conduct is a crime, administrative offenses or civil liability, whether by fraud or negligence, the test facility will lose the Certificate of Recognition of the Compliance with the GLP Principles and will be subject to criminal, administrative and civil penalties, filed by the national regulatory agencies which authority involve these studies. As an example, such conducts can be defined in the following legislations: Penal Code, especially articles 171, 184, 299, 316, 330. Sanitary Legislation – Law 6,437 of August, 1997. Environmental Crimes Law – Law 9.605 of February, 1998. Those involved in the test facilities and studies are subject to criminal, administrative or civil penalties, provided in the legislation above, which one way or another contributes to the conduct/procedures which consist in nonconformities with the GLP Principles, highlighted below, without confining other situations which can be typified as: Forgery of the statement on compliance with the GLP Principles; Not maintaining or falsifying the staff records; Error when characterizing the test substance, control or reference substance; Not maintaining sample of test substance for the period defined by authorities or improperly storing them; Failure to record raw data; Adulteration of raw data; To overlook or

deliberately change the study results; Refuse to present essential information such as raw data required by the monitoring authority or relevant regulatory agency.