Checklist for GCP/GCLP Inspection of Bioequivalence Centre.

1.0 Introduction

The Inspection Guide for Bioavailability/Bioequivalence Centres for establishment of interchangeability is a document that internalizes a consistent approach to the implementation of GCP/GCLP inspections at Bioequivalence Centres in Nigeria.

The document is set in line with the Powers given to the National Agency for Food and Drugs Administration and Control (NAFDAC) as the entity in Nigeria to regulate and control Medicinal Products in Nigeria (ACT CAP N1 LFN 2004), section 12 of ACT CAP F33, 2004 and section 3 of the Clinical Trial regulation 2021 which include providing oversight for GCP inspection.

For the purposes of this Instruction, the following **definitions** are adopted:

Essential (I): item that meets the recommendations of good practices for bioavailability/bioequivalence of medicines, which can have a critical influence on the quality or safety of tests and on the safety of workers in their interaction with products and processes during the test studies.

Necessary (N): item that meets the recommendations of Good Practices for Bioavailability/Bioequivalence of Medicines, which may influence to a less critical degree the quality or safety of the tests and the safety of workers in their interaction with products and processes during testing carrying out studies.

Recommended (R): item that meets the recommendations of good practices for bioavailability/bioequivalence of medicines, which can influence to a non-critical degree the quality or safety of the tests and the safety of workers in their interaction with products and processes during testing carrying out studies; It is

I**nformative** (INF): item that presents descriptive information, which does not affect the quality and safety of the tests and the safety of workers in their interaction with the products and processes during the studies.

1.1 **Application of Checklist-**

The administrative procedure regarding the inspection route in bioavailability/bioequivalence centers must comply with the criteria established for the classification of the items in the route set out in the Regulation.

A. The criteria established for classifying the items in the inspection script are based on the inherent potential risk of each item in relation to the quality and safety of the test and worker safety in their interaction with the activities carried out, to guarantee reliability of the results obtained.

B. The items in the inspection checklist can be answered “yes” or “no”, or in a descriptive form, when appropriate.

C. The item in the Inspection checklist is considered necessary when not complied within one inspection and will be classified as essential in subsequent inspections.

D. The item in the inspection checklist considered recommended when not complied with in one inspection and will be classified as necessary in subsequent inspections but will never be treated as essential.

INSPECTION ROUTE IN BIOAVAILABILITY/BIOEQUIVALENCE CENTERS

I. CLINICAL STAGE

1.1. INSTALLATIONS - GENERAL CONDITIONS		
No.	**Items**	**Specifics**
1.1.1	INF	What is the physical area of the inpatient ward?
1.1.2	INF	Are there sources of pollution or environmental contamination close to the clinical unit?

1.1.3	N	Are the surroundings of the buildings clean?
1.1.4	R	As for the external appearance of the building(s), does it have good conservation (free from cracks, infiltrations, etc.)?
1.1.5	N	Are the floors, walls and ceilings appropriate for the activities carried out in the area?
1.1.6	N	Are the facilities constructed to provide protection against the entry of insects and other animals?
1.1.7	R	Is the lighting appropriate?

1.2. AUXILIARY FACILITIES		
No.	**Items**	**Specifics**
1.2.1	R	Are there enough changing rooms for employees (related to the area and number of employees)?
1.2.2	N	Are they in appropriate hygienic conditions?
1.2.3	R	Are there enough toilets for employees (related to the area and number of employees)?
1.2.4	N	Are they in appropriate hygienic conditions?
1.2.5	R	Is access to employee restrooms independent of hospitalization areas?
1.2.6	N	Is there an electricity generator for emergency cases?
1.3. ADMISSION WARD		
No.	**Items**	**Specifics**
1.3.1	**I**	Is the area exclusive to volunteers during hospitalization periods?

1.3.2	N	Is the lighting in the inpatient ward appropriate?
1.3.3	N	Is ventilation in the inpatient ward appropriate?
1.3.4	INF	How is the distribution of beds, in a multi-bed ward or in apartments?
1.3.5	INF	What is the furniture and equipment in the bed areas?
1.3.6	N	Are there enough toilets?
1.3.7	N	Are the toilets in hygienic conditions and are they provided with hot and/or cold water, soap, and towels or hairdryers?
1.3.8	N	Is there a nursing station?
1.3.9	INF	What is the area of the infirmary?
1.3.10	R	Is there a rest area for the nursing team?
1.3.11	I	Do you have a doctor on duty at the study site during the entire hospitalization period?
1.3.12	R	Is there a rest area for the doctor?
1.3.13	N	Is there an office to evaluate volunteers?
1.3.14	I	Does the clinical unit have an ICU?
1.3.15	INF	Is the ICU system mobile or is it part of the clinical unit?
1.3.16	I	In the case of a mobile ICU, will it be available at the place of hospitalization during the period of greatest risk of serious adverse events (SAEs)?
1.3.17	I	In the case of a mobile ICU, is there a pre-established fixed unit for transferring the volunteer?
1.3.18	INF	What is the distance between the hospitalization ward and the ICU?

1.3.19	INF	Is there a cafeteria?
1.3.20	N	Is there a leisure area for volunteers?
1.3.21	INF	What furniture and equipment are available in the leisure area?

1.4. EQUIPMENT		
No.	**items**	**Specifics**
1.4.1	R	Is the distribution of equipment/instruments rationally ordered?
1.4.2	R	Is there a UPS in emergency equipment?

1.5. OFFICE/NURSING		
No.	**Items**	**Specifics**
1.5.1	**I**	Is there a sphygmomanometer? Conditions?
1.5.2	N	Are they periodically calibrated? What type of calibration?
1.5.3	**I**	Is there a stethoscope? Conditions?
1.5.3	**I**	Are there thermometers? Conditions?

1.6. EMERGENCY CART		
No.	**Items**	**Specifics**
1.6.1	**I**	Do you have an oxygen mask?

1.6.2	**I**	Do you have an Ambu?
1.6.3	**I**	Do you have a laryngoscope?
1.6.4	**I**	*Do you have a cuff* intubation cannula in good condition?
1.6.5	**I**	Do you have disposable syringes?
1.6.6	**I**	Are there emergency medicines? Which?

1.7. SAMPLE PREPARATION ROOM		
No.	**Items.**	**Specifics**
1.7.1	INF	Are samples prepared at the clinical unit or sent to another unit?
1.7.2	R	Is there a room reserved for sample preparation?
1.7.3	N	Is there a centrifuge? Is it refrigerated? Is it calibrated?
1.7.4	N	Is there a cleaning and decontamination procedure for the centrifuge?
1.7.5	R	Is there a freezer?
1.7.6	N	Is there a freezer temperature record? Are the thermometers used calibrated by a laboratory accredited by RBC?
1.7.7	R	Is there a refrigerator?
1.7.8	N	Is there a record of refrigerator temperatures?
1.8. DOCUMENTATION		
No.	**Items**	**Specifics**
1.8.1	N	Is there a specific clinical record for the study covering its particularities?

1.8.2	N	Do the volunteers' clinical records contain all the necessary data (name, age, sex, address, etc.)?
1.8.3	**I**	Are volunteers' personal data handled within medical confidentiality?
1.8.4	INF	Is the data entry system computerized or is it manual in a protocol book?
1.8.5	N	Is there a record to control the medicines dispensed?
1.8.6	**I**	Are/will volunteers' medical records be kept for a minimum of five years?
1.8.7	R	Is there a volunteer database?

1.9. GOOD CLINICAL PRACTICES		
No.	**Items**	**Specifics**
1.9.1	**I**	Are the study protocol and amendments submitted to the Research Ethics Committee?
1.9.2	**I**	Are all Protocols approved by the HREC before they are started?
1.9.3	**I**	Are the studies conducted in accordance with the protocol previously approved by the HREC?
1.9.4	INF	Does the institution have a zip code?
1.9.5	INF	Is the researcher or a member of his team part of the HREC? If so, does he refrain from judging his own research?
1.9.6	**I**	Is the Research Ethics Committee registered with NHREC?
1.9.7	**I**	Is the Informed Consent Form dated and signed before any clinical procedure?

1.9.8	INF	Who is responsible for the process of obtaining the Informed Consent Form?
1.9.9	N	Are studies conducted in accordance with national and international standards (ICH/GCP)?
1.9.10	N	Is all information generated during the clinical study recorded and stored in order to guarantee accurate reporting?
1.9.11	N	Is there a specific field for recording adverse events in clinical records?
1.9.12	N	Are serious adverse events being reported to the HREC and NAFDAC?
1.9.13	**I**	Is the confidentiality of volunteer records properly maintained?
1.9.14	N	Are study medications stored in an appropriate location with temperature and humidity control?
1.9.15	N	Are study medications dispensed in accordance with study guidelines?
1.9.16	N	Is there insurance for volunteers?
1.9.17	N	Is there compensation for volunteers who participate in studies?
1.9.18	R	Is there a study monitoring procedure by the sponsor?
1.9.19	N	Is there a procedure for medical referral of volunteers in whom an illness was detected during pre-study examinations?
1.9.20	N	Is there a commitment to continued medical treatment in case of sequelae caused by adverse drug effects?
1.10. TECHNICAL PERSONNEL		
No.	**Items**	**Specifics**

1.10.1	N	Does the principal investigator have experience conducting clinical studies?
1.10.2	N	Does the team have the support of a medical team?
1.10.3	N	Does the team have support from a nursing team?
1.10.4	N	Is there an employee qualification and training program?
1.10.5	N	Are there records relating to employee training and re-training?
1.10.6	N	Is the team uniformed?
1.10.7	N	Are the uniforms clean and in good condition?
1.10.8	N	Are the number of people in charge of collection of samples sufficient for the number of volunteers hospitalized in each period?
1.10.9	R	In the case of hospitalization of volunteers carried out in a non-hospital unit, is the doctor accompanying the study certified in emergency care?

1.11. PROCEDURES		
No.	**Items**	**Specifics**
1.11.1	INF	What are the types of examinations performed on the volunteers?
1.11.2	INF	What is the validity period of the tests carried out by volunteers?
1.11.3	N	When including volunteers in the study, is the exam validity period of a maximum of three months respected?
1.11.4	INF	What is the admission procedure for volunteers?
1.11.5	INF	Who receives volunteers at the place of internment?

1.11.6	R	Upon admission, does an inventory of the volunteers' belongings carried out to ensure that they are not bringing food, medicines or other items?
1.11.7	R	Do volunteers receive a kit containing a uniform and personal hygiene item for use during hospitalization?
1.11.8	R	Is there a pre-consultation immediately before volunteers are admitted?
1.11.9	N	Are volunteers admitted the day before taking the medication?
1.11.10	INF	Who is responsible for receiving, storing and storing study medications?
1.11.11	N	Is the procedure for preparing and cleaning beds for hospitalization adequate?
1.11.12	INF	Who monitors the intake/administration of medications by volunteers?
1.11.13	**I**	Is the first blood sample taken before taking the medication?
1.11.14	**I**	Are collection times respected as established in the protocol?
1.11.15	INF	What type of material was used in the collection (tubes, syringe, scalps, etc.)?
1.11.16	N	Is there temperature and blood pressure control for volunteers during the hospitalization period?
1.11.17	**I**	Is the menu prepared by a nutritionist according to the specifications of each study?
1.11.18	INF	What is the established procedure for volunteer meals?
1.11.19	**I**	Are post-study clinical and laboratory exams performed on volunteers?
1.11.20	N	Are complications during the volunteers' hospitalization period recorded?

1.11.21	INF	In the case of adverse events, what procedures are adopted?
1.11.22	INF	What is the volunteer discharge procedure?

1.12. STANDARD OPERATING PROCEDURES		
No.	**Items**	**Specifics**
1.12.1	N	Do you have SOP for the recruitment and selection of volunteers?
1.12.2	N	Do you have SOPs for collecting samples during hospitalization?
1.12.3	N	Do you have SOPs for sample identification and preparation?
1.12.4	N	Do you have SOPs for storing and transporting samples?
1.12.5	N	Do you have SOPs for the hospitalization of volunteers?
1.12.6	N	Do you have SOPs for emergency assistance for volunteers?
1.12.7	N	Is there SOP for cleaning and preparing areas for volunteer admission?
1.12.8	N	Do you have SOPs for the disposal of biological and non-biological materials?
1.12.9	N	Do you have SOPs for receiving and controlling study medications?

1.13. STUDY DESIGN		
No.	**Items**	**Specifics**
1.13.1	N	Does the person responsible for statistical analysis has qualifications in the field of statistics?
1.13.2	INF	Does the Center have advice from a statistician?

1.13.3	N	Does the person responsible participate in planning the study? (Decisions about experiment design, sample size, etc.).
1.13.4	N	Are there criteria for defining the design of the experiment? Which?
1.13.5	**I**	Is the method of allocating volunteers to the medication intake sequence randomized? What procedure was adopted?
1.13.6	INF	Software used:

1.14. DATA PROCESSING (e.g. COMPUTERIZED SYSTEMS)		
No.	**Items**	**Specifics**
1.14.1	N	Is there SOP regarding the execution of statistical analysis and/or obtaining pharmacokinetic parameters?
1.14.2	N	Is there a procedure for criticizing data obtained during collection times?
1.14.3	INF	How is data from chromatograms transcribed into worksheets?
1.14.4	INF	What is the procedure adopted in the case of missing samples and/or problems in the chromatograms?
1.14.5	N	Are occurrences arising from previous steps documented?
1.14.6	N	Does the person responsible receive information regarding occurrences arising from previous stages?
1.14.7	INF	How are pharmacokinetic parameters obtained?
1.14.8	INF	How many data transcriptions have been done since the volunteers' analytical run ended?
1.14.9	N	Is there a dated and signed record to check the transcribed data?

1.14.10	INF	Are data transcriptions done manually or through a digital interface?
1.14.11	INF	What are the means for archiving the information generated in the process?

1.15. STATISTICAL ANALYSIS (e.g. COMPUTERIZED SYSTEMS)		
No.	**Items**	**Specifics**
1.15.1	R	Is preliminary (exploratory) analysis of the data performed before proceeding with statistical modeling?
1.15.2	INF	What points were covered in the preliminary analysis? Does it have a graphical presentation?
1.15.3	N	What criteria are adopted to detect atypical or discrepant values?
1.15.4	INF	What measures are taken when atypical observations are detected?
1.15.5	N	Is the data transformed for modeling (ANOVA)?
1.15.6	**I**	In the Analysis of Variance, are the effects of sequence (group), volunteers within the sequence, period and treatment considered?
1.15.7	**I**	Is the ANOVA carried out based on the experimental design adopted in the evaluated study?
1.15.8	INF	Is residual analysis carried out after modeling?
1.15.9	R	Is any methodology used to verify the presence of an interaction effect between period and treatment (residual effect)?
1.15.10	INF	What are the methods used to determine the Confidence Interval?
1.15.11	N	Are the software used in statistical analysis appropriate?

II. BIOANALYTIC STAGE		
2.1. INSTALLATIONS - GENERAL CONDITIONS		
No.	**Items**	**Specifics**
2.1.1	INF	What is the physical area of the laboratory?
2.1.2	INF	Are there sources of pollution or environmental contamination close to the company?
2.1.3	N	Are the surroundings of the buildings clean?
2.1.4	N	Regarding the external appearance, is the building(s) in good condition (free from cracks, infiltrations, etc.)?
2.1.5	N	Are the facilities constructed to provide protection against the entry of insects and other animals?
2.1.6	N	Are floors, walls and ceilings appropriate for the activities carried out in the area?
2.1.7	INF	Is the area exclusive for analyzing biological material?
2.1.8	N	Is access restricted to employees?
2.1.9	N	Is the lighting appropriate?
2.1.10	N	Is the air conditioning adequate? Do you control and record temperature and humidity with a thermometer certified by an accredited laboratory or accreditation body?

2.2. AUXILIARY FACILITIES		
No.	**Items**	**Specifics**

2.2.1	R	Are there enough changing rooms (related to the area and number of employees)?
2.2.2	N	Are they in appropriate hygienic conditions?
2.2.3	R	Are there enough toilets (related to the area and number of employees)?
2.2.4	N	Are they in appropriate hygienic conditions?
2.2.5	R	Is access to restrooms independent of the technical areas of the laboratory?
2.2.6	INF	Is there an electricity generator for emergency cases?

2.3. ORGANIZATION OF THE LABORATORY ENVIRONMENT		
No.	**Items**	**Specifics**
2.3.1	R	Is the physical space adequately distributed to carry out laboratory activities?
2.3.2	R	Is the positioning of the benches, in relation to the cabinets and equipment, operational?
2.3.3	R	Is the positioning of freezers and refrigerators operational?
2.3.4	R	Is the circulation area for technicians good?
2.3.5	R	Is there a suitable place to keep glassware for immediate use?
2.3.6	R	Is access to electricity easy and is there any power back-up in case of main power outage?

2.4. ORGANIZATION OF THE WORKBENCH		
No.	**Items**	**Specifics**
2.4.1	N	Are the benches suitable (in terms of construction material)?
2.4.2	N	Are the benches clean at the time of the visit?
2.4.3	N	Are the SOPs accessible to technicians?
2.4.4	R	Is there support for automatic pipettes?

2.5. GOOD LABORATORY PRACTICES		
No.	**Items**	**Specifics**
2.5.1	N	Is there a Quality System, with designated personnel who ensure that responsibilities are being carried out in accordance with the principles of existing technical standards (GLP, ISO and OECD)?
2.5.2	N	Is the Quality Program disclosed to all employees?
2.5.3	N	Does the laboratory have a quality manager?
2.5.4	INF	Does the quality manager have other duties in the laboratory routine?
2.5.5	N	Does quality management usually carry out internal audits?
2.5.6	N	Is the internal audit frequency at least annual?
2.5.7	N	Are there records of internal audits?
2.5.8	**I**	Does the person responsible for the Bioanalytical Stage have qualifications and experience in relation to the proposed activities?

2.5.9	R	Is there a training program for laboratory employees?
2.5.10	N	Are there records of training and qualifications for each employee?
2.5.11	N	Is the team trained and guided to ensure the correct and complete execution of defined processes and procedures?
2.5.12	N	Are new laboratory procedures only implemented after complete evaluation and approval by Quality Assurance?
2.5.13	N	Does the laboratory have an organizational chart?
2.5.14	**I**	Does the laboratories have Standard Operating Procedures?
2.5.15	N	Are SOPs appropriate and used by different sectors?
2.5.16	N	Does the Laboratory have records in the different sectors?
2.5.17	N	Is there a Quality Manual?
2.5.18	R	Is the Quality Manual easily accessible to the laboratory's technical staff?
2.5.19	N	Does the Quality Manual cover the individual duties of the technical and management staff?
2.5.20	INF	Do you have certification from a competent entity? Which entities?

2.6. STANDARD OPERATING PROCEDURES		
No.	**Items**	**Specifics**
2.6.1	N	Do you have SOPs for transporting and receiving samples?
2.6.2	N	Do you have SOP for sample storage?
2.6.3	N	Do you have SOP for sample identification?

2.6.4	N	Do you have SOP for washing glassware?
2.6.5	N	Do you have SOPs for use, maintenance, and validation of chromatographic systems?
2.6.6	N	Do you have SOP for validating the analytical method?
2.6.7	N	Do you have SOPs for drug stability studies in biological liquids?
2.6.8	N	Do you have SOPs for using and maintaining the PH Metre
2.6.9	N	Do you have SOPs for the use and maintenance of refrigeration systems?
2.6.10	N	Do you have SOPs for use and maintenance of scales?
2.6.11	N	Do you have SOPs for use and maintenance of the water system?
2.6.12	N	Do you have SOP for the sequence of analytical runs?
2.6.13	N	Do you have SOPs for use and maintenance of pipettes?
2.6.14	N	Do you have SOPs for disinfection and disposal of biological and non-biological material?
2.6.15	N	Do you have SOPs to assess the quality of chromatograms?
2.6.16	N	Does it have a SOP establishing criteria for sample reanalysis?
2.6.17	N	Do you have SOPs for preparing solutions and usage patterns?
2.6.18	N	Do you have SOP for the pharmacokinetic analysis of the data obtained?
2.6.19	N	Do you have SOP for storing study documentation?

2.7. EQUIPMENT

No.	Items	Specifics
2.7.1	INF	What equipment are used to analyse the samples?
2.7.2	R	Is there an equipment disinfection procedure?
2.7.3	R	Is the operating manual for each piece of equipment available in the laboratory?
2.7.4	R	Is the distribution of equipment/instruments rationally ordered?
2.7.5	R	Is there an electric current stabilizer?
2.7.6	N	Is there a UPS in the laboratory equipment?

2.8. CHROMATOGRAPHIC SYSTEMS		
No.	**Items**	**Specifics**
2.8.1	**I**	Is chromatography equipment periodically certified/qualified?
2.8.2	INF	What is the frequency?
2.8.3	INF	What is the date of the last Certification/Qualification carried out on chromatography equipment?
2.8.4	N	Was the certification/qualification carried out by a qualified company?
2.8.5	N	Do you have a preventive and corrective maintenance program for this equipment?
2.8.6	N	Is there a record for preventive and corrective maintenance?
2.8.7	N	Is the chromatographic equipment installed properly?
2.8.8	N	Do you have procedures for using, maintaining and storing chromatographic columns?

2.8.9	INF	Are the columns used for more than one study?
2.8.10	**I**	Is the ideal temperature range for equipment operation respected?

2.9. REFRIGERATION/ACLIMATIZATION SYSTEMS		
No.	**Items**	**Specifics**
2.9.1	INF	What is the freezer temperature specification?
2.9.2	N	Is there a record of freezer temperatures?
2.9.3	INF	Do the freezers have identification?
2.9.4	N	Is the storage capacity of freezers respected?
2.9.5	N	Is there a record of refrigerator temperatures?
2.9.6	**I**	Are there alternative procedures in the event of a power outage, in order to preserve the contents of freezers and refrigerators?
2.9.7	N	Do they have thermometers properly installed in the refrigeration systems?
2.9.8	N	Is there a record of the ambient temperature?
2.9.9	N	Do they have a hygrometer and recording of ambient humidity?
2.9.10	R	Do you have a procedure for preventive and corrective maintenance of air conditioning equipment?

2.10. WATER SYSTEM

No.	Items	Specifics
2.10.1	INF	What equipment is used to purify water?
2.10.2	INF	Is there a container for storing purified water?
2.10.3	INF	If so, how long does the water remain stored?
2.10.4	N	Is the water used subject to quality control?
2.10.5	INF	How often?
2.10.6	N	Is there a record for water quality control?
2.10.7	R	Is there a procedure for preventive and corrective maintenance of water purification equipment?
2.10.8	N	Is there a record for maintenance of the water treatment system?

2.11. ANALYTICAL BALANCE		
No.	**Items**	**Specifics**
2.11.1	N	Is the scale certified by an accreditation body or an accredited laboratory (In Nigeria or an international organization)
2.11.2	N	Is the analytical balance installed in accordance with the manufacturer's recommendations?
2.11.3	N	Is there a standard operating procedure for using an analytical balance?
2.11.4	INF	Is there a procedure for preventive and corrective maintenance of the analytical balance?
2.11.5	INF	Is the calibration verification procedure performed daily?
2.11.6	N	Is there a record of the calibrations carried out?

2.12. PEAGMETER?? pH Metre		
No.	**Items**	**Specifics**
2.12.1	**I**	Does the analytical laboratory have a pH Metre?
2.12.2	N	Is there a procedure for using the pH Metre?
2.12.3	R	Is there a procedure for preventive and corrective maintenance of the pH Metre?
2.12.4	N	Do you have a record of the pH Metre calibrations?
2.12.5	N	Is the PH Metre checked at at least two pH points?
2.12.6	N	Are check buffers stored according to the manufacturer's recommendations?

2.13. CENTRIFUGE		
No.	**Items**	**Specifics**
2.13.1	N	Is the centrifuge installed in accordance with the manufacturer's recommendations?
2.13.2	R	Does the centrifuge have a cooling system?
2.13.3	R	Is there a standard procedure for using the centrifuge?
2.13.4	R	Is there a procedure for preventive and corrective maintenance of the centrifuge?
2.13.5	R	Is there a maintenance record for the centrifuge?
2.13.6	N	Is there a procedure for cleaning and decontaminating the centrifuge?

2.14. GLASSWARE AND PIPETTERS		
No.	**Items**	**Specifics**
2.14.1	R	Are tests carried out to check the quality of the glassware washing process?
2.14.2	R	Is the volumetric glassware certified by an accreditation company or an accredited laboratory?
2.14.3	R	Is the volumetric glassware kept in an appropriate location?
2.14.4	INF	What type of material are the *vials* used for the analytical run?
2.14.5	N	Are used *vials* discarded?
2.14.6	N	Are automatic pipettes certified?
2.14.7	R	Do you have a procedure for using automatic pipettes?
2.14.8	INF	Is the maintenance/calibration periodicity of automatic pipettes at least annual?
2.14.9	N	Is there a record of maintenance/calibration of automatic pipettes?
2.14.10	N	Do you have a procedure for cleaning and decontaminating pipettes/micropipettes?
2.14.11	**I**	Are used tips discarded?

2.15. REAGENTS		
No.	**Items**	**Specifics**

2.15.1	**I**	Do the reagents have a batch number, concentration, impurities?
2.15.2	**I**	Are the reagents within their expiration date?
2.15.3	N	Is reagent storage carried out in accordance with the manufacturer's recommendations?
2.15.4	N	Does the laboratory have temperature and humidity records for storage locations?
2.15.5	R	Does the laboratory have stock control?
2.15.6	R	Are the reagents separated by classes (flammable, non-flammable, oxidants, acids and bases)?
2.15.7	N	Does the laboratory have a fume hood for handling toxic reagents?
2.15.8	N	Do they use good labelling on reagent solutions prepared in the laboratory?

2.16. MOBILE PHASE		
No.	**Items**	**Specifics**
2.16.1	INF	What is the purity of the solvents used to prepare the mobile phase?
2.16.2	INF	What is the degree of purity of the additives for preparing the mobile phase (salts, acids, buffers, etc.)?
2.16.3	I	Is the water used to prepare the mobile phase type 1?
2.16.4	R	Is the mobile phase prepared daily?

2.16.5	INF	Is the pH of the mobile phase checked beforehand to carry out the analytical runs?
2.16.6	R	Is the mobile phase filtered?
2.16.7	INF	What means are used to filter the mobile phase?
2.16.8	R	Is the mobile phase degassing process carried out?
2.16.9	INF	What is the procedure for degassing the mobile phase?
2.16.10	INF	What is the cleaning procedure adopted to clean the mobile phase reservoir filter?

2.17. REFERENCE CHEMICAL SUBSTANCES		
No.	**Items**	**Specifics**
2.17.1	INF	Do they use Pharmacopoeia Reference Chemicals?
2.17.2	**I**	Do the Working Chemical Substances (secondary standards) have an analysis report?
2.17.3	INF	Are secondary standards provided by an institution independent of the contracting company?
2.17.4	N	Are reference standards stored in an appropriate location?
2.17.5	R	Is there a record of stock control of reference substances?
2.17.6	N	Is there a procedure for discarding expired standards?

2.18. SAMPLES		
No.	**Items**	**Specifics**
2.18.1	N	Is there a record of receipt of samples?
2.18.2	R	Does the laboratory have a checklist for receiving samples (temperature history, sample identification and data, packaging condition, etc.)?
2.18.3	INF	What is the storage temperature for biological samples?
2.18.4	**I**	Are biological samples stored properly in freezers? Do you control temperature using thermometers certified by INMETRO or an accredited laboratory (RBC)?
2.18.5	**I**	Do the samples have adequate labelling containing all the data necessary for their identification?
2.18.6	INF	Are biological samples aliquoted? What procedure was adopted?
2.18.7	N	In the case of reanalysis of samples, are they duly justified and recorded?
2.18.8	N	In the case of lost samples, are they duly justified and recorded?

2.19. EXTERNAL SAMPLE TRANSPORT		
No.	**Items**	**Specifics**
2.19.1	INF	Is there external transport of biological samples?
2.19.2	INF	Are biological samples pre-processed at their place of origin?
2.19.3	N	Is there prior knowledge of road or air dispatch times and dates?

2.19.4	N	Are thermal boxes with adequate refrigeration material used for the transport time of biological samples?
2.19.5	R	Do biological samples accompany a temperature recording device during the journey?
2.19.6	INF	What is the method used for external transport of samples?
2.19.7	INF	What is the average duration of external sample transport?

2.20. INTERNAL SAMPLE TRANSPORTATION		
No.	**Items**	**Specifics**
2.20.1	INF	How are samples transported internally?

2.21. VALIDATION OF ANALYTICAL METHODS		
NAME OF AUDITED STUDY:		
No.	**Items**	**Specifics**
2.21.1	**I**	Does the laboratory have complete validation records?
2.21.2	**I**	Are accuracy and precision studies carried out within acceptable limits?
2.21.3	N	Are analyses performed to determine the limit of quantification?
2.21.4	N	Is the recovery level of the method determined?

2.22. STABILITY		
No.	**Items**	**Specifics**
2.22.1	**I**	Are stability studies carried out in sample freezing and thawing cycles?
2.22.2	**I**	Are short-term stability studies carried out?
2.22.3	**I**	Do stability studies cover the period between collection and analysis of the last study sample (long-term stability)?
2.22.4	**I**	Is a drug stability study carried out in stock solutions?
2.22.5	**I**	Post-processing stability study is carried out.

2.23. BIOSAFETY - COLLECTIVE PROTECTION		
No.	**Items**	**Specifics**
2.23.1	R	Is there a Biosafety Commission?
2.23.2	R	Are the laboratory's technical staff periodically subject to health examinations?
2.23.3	R	Is there an employee vaccination program?
2.23.4	N	Is there a waste treatment program?
2.23.5	N	Do you carry out decontamination of biological waste produced during laboratory activities?
2.23.6	N	Are care taken for the packaging and final disposal of chemical waste?
2.23.7	R	Are suitable containers used to dispose of broken glassware?

2.23.8	N	Do they have an emergency shower and eyewash?
2.23.9	N	Are fire extinguishers, sand/granulated absorbent available?
2.23.10	N	Are accident prevention and notification carried out?
2.23.11	R	Is there educational signage to prevent the risk?
2.23.12	N	Is there information on how to act in an emergency, such as: telephone numbers for hospitals, emergency rooms and fire departments?
2.23.13	R	Are boxes available with first aid materials in case of accidents?

2.24. INDIVIDUAL PROTECTION		
No.	**Items**	**Specifics**
2.24.1	N	Does the laboratory provide and instruct employees to use PPE (Personal Protective Equipment)?
2.24.2	N	Do employees wear long coats with long sleeves?
2.24.3	N	Do employees use disposable gloves?
2.24.4	N	Do employees wear protective glasses or face shields?
2.24.5	R	Do employees wear masks?
2.24.6	N	Do employees wear closed shoes or protective sneakers?
2.24.7	N	Do employees wear clothing that protects their legs (long pants)?
2.24.8	R	Is washing uniforms used by employees the responsibility of the laboratory?

2.25. DOCUMENTATION (Part of COMPUTERIZED SYSTEMS)		
No.	**Items**	**Specifics**
2.25.1	INF	What are the archiving methods for study chromatograms and other documents?
2.25.2	R	Is access to study documentation facilitated?
2.25.3	**I**	Is study documentation archived for a minimum period of 10 years?

Acknowledgements: Full citation

1. ICH M13-EWG

2. EMA

3. FDA

4. ANVISA