

**Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
WHOPIR
Palatability Study**

Part 1	General information
Organization details	
Company information	
Name and Address of Clinical Research Site (Inspected site)	Maternal and Child Center Amuwo Odofin 1st Avenue Festac Lagos, Lagos Nigeria
Corporate address of Organization	N/A
GPS coordinates	6.461962305733836 N 3.3021116440418887 E
WHO product numbers covered by the inspection/ Product names/ Study numbers/ Study titles	WHO application no: DI014 A prospective, open-label, multicentre, Phase 3 study. Children of age 3-59 months with an acute diarrhea episode were prescribed Zinc sulphate dispersible tablets and oral rehydration salts (ORS) as per WHO guidelines
Sponsor & Applicant	Swiss Pharma Nigeria Limited 5, Dopemu Road, Agege - Lagos, Nigeria P.O. Box 463 Ikeja Mob: +234 (0) 8116691826 Email: ogana.emmanuel@swiphannigeria.com Website: www.swiphannigeria.com
Inspection details	
Dates of inspection	29 to 30 June 2022
Type of inspection	Initial

Amuwo Odofin Maternal and Child Center Hospital, Lagos, Nigeria, Clinical site-CRO

29 to 30 June 2022

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Introduction	
Summary of the activities	The study was conducted in the Pediatric Ward of the department. The ward was a part of the Medical Department under the supervision of the Medical Director.
General information about the company and site	<p>Swiss Pharma Nigeria Limited (Swipha), acting as the sponsor of the study, is a subsidiary of Servier group, i.e., a French Pharmaceutical Company. In 1976, Roche Nigeria Limited was incorporated by F. Hoffmann-La Roche, Switzerland, to produce and market medicines supplying Nigeria and West Africa. In 1999, Roche Nigeria Limited became Swiss Pharma, Nigeria Ltd. The Swiss Pharma brand was launched as a premium branded generic offering affordable products covering mainly Anti-malaria, CNS, Anti-infectives, Anti-diabetes, and Cardiovascular. Servier group / Biogaran acquired Swiss Pharma in 2017 to launch the presence of a French pharmaceutical company to extend their range of products to Nigerians.</p> <p>The sponsor had made a contract with three clinical sites in Nigerian hospitals to conduct the Zinc sulphate dispersible tablets study to verify the palatability of the product:</p> <ul style="list-style-type: none"> - Alimosho General Hospital - Maternal and Child Center - Adeoyo Maternity Teaching Hospital (Paediatric Ward)
History	The site was not previously audited/inspected.
Brief report of inspection activities undertaken	<p>The inspection included one clinical study to evaluate the acceptability of Zinc Sulphate Dispersible Tablets in children with acute diarrhea.</p> <p>The following scope and study-related activities were reviewed:</p> <p>The company's history, clinical study performance, monitoring of study, informed consent process, ethics committee approvals and correspondence, archiving procedure, IMP accountability, dispensation and storage, equipment calibration, study-staff training, and a tour of the facility.</p> <p>A review of the clinical study data was conducted, along with a comparison of the source data to the study reports.</p>

Scope and limitations	
Out of scope	Not applicable During the inspection, it was considered that the study was conducted to verify the acceptability and adherence of a well-established product in children with diarrhoea.
Restriction	Due to the PI's other commitments, the inspection team was requested to complete the inspection on 30 June 2022. Hence, a more intensive inspection was carried out and a closing meeting was held on that day at 3 pm.

Abbreviations		
	ADR	adverse drug reaction
AE	adverse event	
ALCOA	attributable, legible, contemporaneous, original and accurate	
BE	bioequivalence	
BDL	below detection limit	
CAPA	corrective actions and preventive actions	
CC	calibration curve	
CPU	clinical pharmacology unit	
CRA	clinical research associate(e)	
CRF	(electronic) case report form	
CRO	contract research organization	
CTM	clinical trial manager	
CoA	certificate of analysis	
CSR	clinical study report	
DQ	design qualification	
ECG	electrocardiogram	
ERC	ethics review committee	
GAMP	good automated manufacturing practice	
GCP	good clinical practice	
GLP	good laboratory practice	
GMP	good manufacturing practice	
HPLC	high-performance liquid chromatograph	
LC-MS/MS	liquid chromatography–mass spectrometry	
IB	investigator's brochure	
ICF	informed consent form	
ICH	International Conference on Harmonization	
(I)EC	(Independent) Ethics Committee	
IMP	investigational medicinal product	

	IQ	installation qualification
	LIMS	laboratory information management system
	LLOQ	lowest limit of quantification
	LOD	limit of detection
	MS	mass spectrophotometer
	MVR	monitoring visit report
	NRA	national regulatory agency
	OPD	outpatient department
	OQ	operational qualification
	PIS	patient information sheet
	PQ	performance qualification
	PQS	pharmaceutical quality system
	QA	quality assurance
	QC	quality control
	QRM	quality risk management
	RRC	research review committee
	SAE	serious adverse event
	SAR	serious adverse reaction
	SOP	standard operating procedure
	SUSAR	suspected unexpected serious adverse reaction
	ULOQ	upper limit of quantification
	URS	user requirements specifications

Part 2	Summary of the findings and comments
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General section

1. Organization and management

The PI, Dr Oyejoke Oyapero gave an overview of the activities of the site and the management of the clinical trial.

The following groups had responsibilities to the trial:

- The principal investigator and co-investigator with relevant qualifications ran the study activities;
- The pharmacist was responsible for the receipt, storage, and dispensing of the IMP;
- The research assistant was liable to make follow-up visits:
- Two trial monitors;
- Sponsor.

A clinical trial agreement for conducting the study of Zinc sulphate acceptability/palatability was signed between Amuwo Odofin Maternal and Child Center Hospital @ Dr Oyejoke Oyapero and sponsor Swiss Pharma Nigeria Limited on 1 July 2020. The investigator and institution's responsibility, clinical trial governance, the obligation of parties, indemnification, insurance, subject injury, data protection, intellectual property, confidentiality etc., were specified in the contract.

The Principal Investigator was responsible for adequate and safe medical care of the subjects during the trial and for ensuring that appropriate medical care and relevant follow-up procedures were maintained.

A general organogram was available to show the relation between the departments in the organization. The hospital consisted of eight different departments, including the Medical department, pharmacy, nursing, laboratory, etc which was led by the Medical Director I/C and Hospital management Committee.

2. Quality management

The sponsor was responsible for implementing a system of quality assurance in order to ensure that the trial was performed, and the data were generated, recorded, and reported in compliance with the protocol, Good Clinical Practice, and applicable requirements.

Study related data and documents were available for review during the inspection.

Observations made in relation to Quality Management were addressed in the respective CAPA plan.

3. Archive facilities

The study documentation was kept in a cupboard in the PI's office under her supervision.

The investigator kept the subject identification codes with the rest of the study documentation to permit any medical follow-up which might be warranted. The national requirements were not specified.

It was possible to identify each trial subject by name against subject and product container identification codes, treatment assignment, and the CRFs.

The sponsor retained the protocol, documentation, approvals, and other essential documents related to the trial, including monitoring reports that had been carried out. The available data and documents were provided upon the inspectors' request.

The sponsor was requested to make appropriate arrangements for the retention of all essential documentation, including source data pertaining to the clinical trial in a form which could be retrieved for future reference.

Observations made in relation to the Archive facility were addressed in the respective CAPA plan.

4. Premises

During the second day of inspection, a tour of the facility was conducted and led by the PI.

The study site located on the ground floor consisted of the following units:

- Two physical exam rooms. The door had a lock and was kept locked when unoccupied. The Nursing unit provided the equipment.
- Pharmacy office

The premises were equipped with smoke detectors and fire extinguishers.

Pharmacy

There was a pharmacy office for reception, storage and dispensing of the IMP in the reception area on the ground floor of the hospital.

Observations made in relation to Premises were addressed in the respective CAPA plan.

5. Personnel

A sufficient number of medical staff with the appropriate qualifications and training to support the trial and to be able to respond effectively to all reasonably foreseeable emergencies were available. The site PI had not participated in any clinical trial before.

Using specified activity codes, a site delegation of responsibility log was provided to specify the study staff activities. Only PI and one of the Research assistants were available at the time of inspection. The rest of the study staff were either relocated or off the site.

Training documentation was provided for staff involved in the study, and the training details were documented on the training log by the monitor. The PI trained the remaining staff before the initiation of the study.

Records of training and assessment of knowledge of GCP and other relevant areas were maintained for the investigators. The investigators' GCP certificates and CVs were available and reviewed.

The hospital had facilities, including a laboratory, equipment, and adequate medical and clerical staff in the emergency room to support the trial and deal with reasonably foreseeable emergencies. The investigator had sufficient time to conduct and complete the trial.

Observations made in relation to Personnel were addressed in the respective CAPA plan.

Clinical section

6. Clinical phase

The study protocol was authorized on 6 July 2020, and a Manual of Procedures was later available, i.e., 11 August 2020.

The study's primary objective was to evaluate the acceptability of the zinc product in managing childhood diarrhea. The secondary objective was to assess palatability.

The following endpoints were defined in the protocol:

Primary endpoint: The treatment would be considered to have good acceptability if 80% of the prescribed treatment was taken by at least 70% of the children.

Secondary endpoint: Taste palatability, i.e., a subjective evaluation measured based on a caregiver's report of their child's behavior when the medicine was administered.

Palatability

The mothers/caregivers were asked about the perception of the taste of the zinc product given to the child compared to other medicines. A 5-point scale was used to classify response options. The choices were:

- 5 - Very well tolerated, much better than the response to other medicines.
- 4 - Well tolerated, somewhat better than the response to other medicines.
- 3 - Tolerated, response comparable to other medicines.
- 2 - Poorly tolerated; the second dose was retained after initial vomiting.
- 1 - Not tolerated; the second dose was also vomited by the subjects.

The scoring system used during the study was different from the scoring as defined in the protocol, and it corresponded with the information on the leaflet provided together with the IMP.

This measurement was the overall response during the treatment period. Individual daily recorded responses were helpful in arriving at the overall response value on the 5-point scale.

Adherence

Adherence was the primary endpoint for the study. Adherence was evaluated in relation to the dose given, frequency of daily administration, duration of treatment, and preparation (dispersion) of the tablets.

The first patient was recruited & enrolled on 15 October 2020, and the enrolment of the last patient was completed on 21 January 2021.

A protocol agreement form was signed by PI on 13 October 2020, stating that the study would be conducted in accordance with ICH E6, GCP principles, and local requirements. It was also confirmed that the investigators and co-investigators were aware of their responsibilities to conduct the study.

Subject screening and enrolment logs were provided on paper templates with information about screening numbers and patients' names, patients' hospital numbers, DOB, presence of diarrhea, eligibility, and reason for non-eligibility. The enrolment log had also information about the recruitment date, treatment pack number, and name of the person who obtained the ICF. Reviewing randomly selected study specific ICFs verified that an ICF was provided for all the enrolled volunteers, but not for the subjects with screening failure outcomes.

The clinical trial was carried out in a facility equipped with Emergency exits, fire detectors and fire extinguishers.

The PI had provided information to the staff involved in the trial, and the participation of the volunteers in the study was recorded in their respective medical journals., together with a copy of ICF.

Investigator Brochure (IB) was provided. The sponsor provided a package leaflet with each package of IMP.

94 volunteers were enrolled in the study, and four volunteers were lost to follow-up during the trial.

Observations made in relation to the Clinical phase were addressed in the respective CAPA plan.

7. Clinical/Pathology lab

Not applicable.

8. Ethics

Prior to the commencement of the study, the investigator ensured that the proposed clinical protocol was reviewed and accepted in writing by the Institutional Review Boards IRB Focal Person, Health Research and Ethics committee; Lagos State University College of Medicine / Teaching Hospital; Ikeja, Lagos State (HREC LASUTH). The approval applied to dates from 21 November 2018, to 20 February 2019. An extension was provided for 25 September 2020 to 24 September 2021.

Submission to and acceptance by the ethics committee were in writing and dated. An application was completed for “Application for ethical approval”. The application was dated 23 October 2018 by Dr Bamidele Mutiu.

The completion of the study was notified to the HREC by Dr B Mutiu who was the study coordinator. The letter was dated 8 February 2021. He was not involved in the conducting of the study due to business reasons.

The Sponsor should reimburse the Institution for all reasonable expenses incurred as a result of an injury or illness caused as a direct result of a Clinical Trial Subject's participation in the Clinical Trial if such injury was established due to the administration of Zinc sulphate Tablet used for the study. The details of compensation and indemnification were explained in the respective agreement with Leadway Assurance Company Limited covering period of 26 June 2020 until 25 June 2021. The number of participants were also determined to be 300.

The composition of EC at the time of protocol assessment was provided upon the Inspectors' request on 28 June 2022. The documentation was reviewed and found the EC independent from the study activities.

INFORMED CONSENT FORMS

The investigator was responsible for giving adequate information to subjects about the trial. Information about the study was given in the oral form. Since the ICF was available only in the English version, only mothers/caregivers with the capability of understanding English were recruited for the study.

Observations made in relation to Ethics were addressed in the respective CAPA plan.

9. Monitoring

Two trial monitors on behalf of the sponsor carried out the monitoring visits. A monitoring site visit log was available, starting from 12 November 2020, ending 27 January 2021, consisting of five visits. The monitors belonged to an organization named CLRCC. Mr Emmanuel, the sponsor representative, visited the site on 12 November 2020 with the monitors.

The monitors were responsible for ensuring that the trial was conducted according to the standards set out in the International Conference on Harmonization (ICH). The Trial Monitors concentrated on the progress of the trials and adherence to protocols.

Site close-out was completed on 27 January 2021, and the report was issued on 17 February 2021.

During the visits to the clinical trial site, the monitor should check that

- all study products for the trial were used within the limits defined by the protocol.
- inventory records of study products were in order, and there were sufficient supplies.
- the expiry dates were not exceeded.
- that the storage conditions for study products were adequate.
- procedures for and records of returned and/or unused study products were followed.

Observations made in relation to the Monitoring were addressed in the respective CAPA plan.

10. Investigators

Refer to section 5; Personnel

11. Receiving, storage and handling of investigational drug products

A drug inventory log was kept by the pharmacist. Information about the receipt of the drug, number received, the patient number, the name of person who had dispensed the IMP, staff signature, monitor comment, and monitor signature was documented. Expiry date and lot number were also recorded on the IMP label. The shipment documentation was provided with a specific serial number. The supply was provided by Swiss Pharma Nigeria ltd. on 15 October and 6 November 2020 to MCC containing 100 blisters in small plastic bags, labelled with IMP information. The receipt was confirmed and dated by the study pharmacist.

The certificate of analysis of the investigational product was prepared and provided by the sponsor. The IMP specifications were verified.

The investigation product was dispensed in a blister pack containing 10 tablets. The mothers/caregivers were expected to show the blister packs to the Home Visit Team and bring them along during follow-up (even if all tablets were used) to evaluate adherence at the follow-up visit. The study investigator updated accountability records of the investigational product according to protocol.

The IMP was administered at home and the mothers/caregivers performed the evaluation. A home visit was done on Day 5 of the study to assess the patients' response to clinical management, counsel on the prevention of diarrhea disease, and looked for any adverse reaction. The final endpoint was Day 10 in which the mother/caregiver brought the filled palatability assessment form and the blister pack of the drug to the site irrespective of whether it was completely used or not.

Records were kept of information about the shipment, delivery, and receipt. The department of the local hospital assumed the responsibility for storage, delivery, return, and keeping records of the investigational product.

The sponsor was responsible for the packaging and investigational labelling of the pharmaceutical products used. Study products were labelled in compliance with the protocol. Investigational label information was accurate and in a language that was understandable to the subject.

The investigator was responsible for ensuring:

- Proper and safe handling of the investigational during the clinical trial in cooperation with the study pharmacist;
- the investigational product was used only following the protocol, which implied use only for subjects included in the trial, that it was distributed by designated staff, and that this use was documented in such a way as to ensure appropriate dosage;
- the dosage and instructions for use were correct, and every subject involved understood them properly.

The sponsor was responsible for:

- Supplying the IMP in accordance with the principles of Good Manufacturing Practice.
- Ensuring that the package of the investigational product was of a size suitable for the trial and adequate for the trial subjects.
- Keeping sufficient samples from each batch used in the trial as a reference for control tests and data validation, as required in national regulations.
- Providing information about the expiry date (month/year) on the packaging label.

Unused investigational products dispensed to the volunteers were returned per the protocol to the site and kept with the CRF.

Observations made in relation to the handling of IMP were addressed in the respective CAPA plan.

12. Case report forms

The site had paper-based medical documentation. The source data was compared with the Clinical Study Report data listings and the data entered in the CRFs.

Source data verification included all source data for randomly selected subjects. Both screening/enrolment visit and follow-up, end of the study visit, inclusion criteria, exclusion criteria and a questionnaire which was a 5-point scale to classify the palatability response options were reviewed.

Physical exam included signs of dehydration, skin turgor testing, general conditions, weights, temperature, pulse, tachycardia, and tachypnea. It was emphasized that the child should return to the facility if the condition was exacerbated.

The subjects' medical records were also reviewed for respective subject.

A GPS detail was provided to the sponsor at each home visit by the visitor to verify the execution of the visit. The presence of volunteers at the time of screening could also be confirmed by the patient registration card/payment receipt attached to their medical records. Tracking number, name of the patient, name of the ward, i.e., "Paediatric ward", folder no. and tracked and admin date were recorded on the hospital fee payment receipt.

CRF included demographic data, inclusion criteria, exclusion criteria, an inspection response form to be completed by the research team on Day 5 and Day 10, a 5-point scale questionnaire, and the IMP package with empty blisters.

CRF related observations were addressed in the respective CAPA plan.

13. Volunteers, recruitment methods

The investigator was responsible for ensuring the unbiased selection and an adequate number of suitable subjects according to the protocol.

The study physician screened all children within the defined age group for study eligibility criteria. Parents / attending caregivers of those fulfilling the eligibility in the application of the inclusion and the exclusion criteria were invited to provide their consent for enrolment of their children in the study.

Upon signing a written informed consent, after providing information about the study, the respective instruction, and the voluntary nature of participation, along with the right to withdraw children at any time after the initial consent without providing any reason, children were enrolled by the study physician.

Study subjects were included recruited based on inclusion and exclusion criteria for subject selection, and the screening procedures were described in the clinical trial protocol. The screening procedures were performed in the Paediatric ward of the hospital. Randomly selected screening forms were reviewed to verify the process.

Eligible study subjects received the Zinc tablet from the pharmacist, as well as the verbal instruction, the 5-point score form and ORS. The dosing administration took place at home by the volunteers' caregivers.

Recruitment observations related observations were addressed in the respective CAPA plan.

14. Safety, adverse events, adverse event reporting

The method by which adverse events would be monitored was stated in the study protocol.

There was no incidence of AE. However, vomiting from the drug was observed but was not considered an AE. The incidence was used in the assessment of study endpoints.

Swiss Pharma (the sponsor) provided a form for “Suspected unexpected serious adverse reaction to be used in the case of SUSAR.

Observations related to AE reporting were addressed in the respective CAPA plan.

15. Data processing and documentation

The study data, i.e., ICF, CRF, GPS details of the home visits and questionnaire, were uploaded using designated cloud storage which belonged to the Swiss Pharm share-point provided by the sponsor. The study documentation was scanned and uploaded in the Share point.

The essential documentation was kept in the ISF and was provided upon the Inspectors' request.

The designated cloud storage data system was accessible only by the investigators, data analysts, and sponsor to be used for the project. At the time of inspection, three staff members of Swiss Pharma had access to the cloud storage data system and the only user with permission to share a link was the Regulatory Affairs Manager. The site Principal Investigators had "Read-only" access to the respective folder, with the possibility to upload study documentation, only at the time of the conduct of the study.

A copy of GPS coordinates related to the Day 5 visit was also uploaded for each respective subject to verify the home visit.

CRFs and questionnaires were in handwriting and scanned, so the data could not be edited/modified.

The data analyst transferred the data on the CRF provided by the investigators into an Excel sheet. The Excel sheet was reviewed and compared with the study data for randomly selected volunteers during the inspection. The availability of source documentation in the cloud storage system was also randomly confirmed.

Observations made in relation to Data progressing and documentation were addressed in the respective CAPA plan.

16. Study report

Information about the Study Protocol, Consent Form and Case Report Form was appended to the report, and the following tables were provided:

- 1: Summary of key features of the study population
- 2: Adherence of product in children with diarrhea
- 3: Adherence of product in children with diarrhea between 18 months
- 4: Palatability of Zinc sulphate dispersible tablets in children with diarrhea
- 5: Cumulative palatability Score
- 5.1: Palatability Score

- 6: Association between palatability and dosage of dispersible zinc tablets taken among the younger children aged < 18 months
- 7: Association between selected sociodemographic variables and Palatability
- 8: Association between selected sociodemographic variables and Acceptability
- 9: Missed Doses

The inspectors used the CSR for the Source Data Verification.

The deficiency related to the Study report was addressed in the respective CAPA plan.

Part 3	Conclusion - Inspection outcome
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Based on the areas inspected, the people met, and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, as well as the corrective actions taken and planned, the palatability study of Zinc sulphate dispersible tablets was considered to have been conducted at an acceptable level of compliance with WHO GCP guideline at *Maternal and Child Center - Amuwo Odofin*, located at *1st Avenue, Festac, Lagos; Nigeria*.

All the non-compliances observed during the inspection that were listed in the complete report as well as those reflected in the WHOPIR, were addressed by the CRO, to a satisfactory level, prior to the publication of the WHOPIR.

This WHOPIR for the palatability study of Zinc sulphate dispersible tablets will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of guidelines referenced in the inspection report
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1. Guidelines for good clinical practice for trials on pharmaceutical products. WHO Technical Report Series, No. 850, 1995 (pp. 97–137).
Short name: WHO GCP Annex 3
2. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4.
Short name: WHO TRS No. 1033, Annex 4
<https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations>

3. Good clinical laboratory practice (GCLP), WHO on behalf of the Special Programme for Research and Training in Tropical Diseases. Geneva, 2009
Short name: WHO GCLP
<https://www.who.int/tdr/publications/documents/gclp-web.pdf>
4. Guideline for good clinical practice E6(R2). EMA/CHMP/ICH/135/1995
Short name: ICH GCP E6
https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-6-r2-guideline-good-clinical-practice-step-5_en.pdf
5. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
Short name: WHO TRS 1010, Annex 9
https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1
6. Handbook – Good Laboratory Practice (GLP): quality practices for regulated non-clinical research and development – Annex I: The OECD Principles on GLP, 2nd ed., 2009.
Short name: OECD GLP
<http://www.who.int/tdr/publications/documents/glp-handbook.pdf>
7. Standards and operational guidance for ethics review of health-related research with human participants. Guidance Document. Geneva, World Health Organization, 2011.
Short name: WHO Ethics Committee Guidance
<https://www.who.int/ethics/publications/9789241502948/en/>
8. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report. Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9.
Short name: WHO storage and transport guidance or TRS 961 Annex 9
https://apps.who.int/iris/bitstream/handle/10665/44079/WHO_TRS_961_eng.pdf;jsessionid=B7F180F317E8BE2DB4289C7BF9A561FF?sequence=1
9. Guidelines for the preparation of a contract research organization master file, WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 7.
Short name: WHO CROMF Guidelines or TRS No. 957, Annex 7
https://www.who.int/medicines/areas/quality_safety/quality_assurance/GuidelinesPreparationContractResearchOrgMasterfileTRS957Annex7.pdf?ua=1

10. Glove use information leaflet, Patient Safety, Save lives clean your hands. Geneva, World Health Organization, 2009 (revised).

Short name: Glove use information leaflet

http://www.who.int/gpsc/5may/Glove_Use_Information_Leaflet.pdf

11. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability

Republication of Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, WHO Technical Report Series, No. 992, Annex 7 with a new Appendix 2

WHO Technical Report Series, No. 1003, 2017, Annex 6

Short name: WHO multisource guidance

https://www.who.int/medicines/areas/quality_safety/quality_assurance/trs1003_annex6.pdf

12. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4.

Short name: WHO TRS 1025, Annex 4

<https://www.who.int/publications-detail/978-92-4-000182-4>

13. Model guidance for the storage and transport of time- and temperature-sensitive pharmaceutical products. WHO Technical Report Series, No.961, 2011, Annex 9.

Short name: WHO TRS No. 961, Annex 9

https://www.who.int/medicines/areas/quality_safety/quality_assurance/ModelGuidanceForStorageTransportTRS961Annex9.pdf?ua=1

14. Ethical principles for medical research involving human subjects, 52nd WMA General assembly, Edinburgh Scotland, October 2000.

Short name: Declaration of Helsinki

[https://www.who.int/bulletin/archives/79\(4\)373.pdf](https://www.who.int/bulletin/archives/79(4)373.pdf)

15. Good manufacturing practices: guidelines on validation, WHO Technical Report Series, No. 1019, 2019

Short name: WHO TRS No. 1019, Annex 3

https://www.who.int/medicines/areas/quality_safety/quality_assurance/WHO_TRS_1019_Annex3.pdf?ua=1