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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
WHOPIR
Palatability Study

Part 1	**General information**
Organization details	
Company information	
Name and Address of Clinical site	Alimosho General Hospital Iganda, Lagos Nigeria
Corporate address of Organization	N/A
GPS coordinates	6.56253° N 3.25171° E
WHO product numbers covered by the inspection/ Product names/ Study numbers/ Study titles	**WHO application no: DI014** A prospective, open-label, multicenter, 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) 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@swiphanigeria.com Website: www.swiphanigeria.com
Inspection details	
Dates of inspection	27 to 28 June 2022
Type of inspection	Initial
Introduction	
Summary of the activities	The palatability study was conducted at the Paediatric Ward of Alimosho General Hospital. The ward was a part of the Clinical Services Department under the supervision of the Medical Director.

General information about the company and site	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 Limite 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 Limited. 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. 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: - **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	The inspection included one clinical study to evaluate the acceptability of Zinc Sulphate Dispersible Tablets in children with acute diarrhea. The following scope and study-related activities were reviewed: 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. A review of the clinical study data was conducted, along with a comparison of the source data to the study reports.
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.

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

	PI	principal investigator
	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**

General section

1. **Organization and management**

The PI, Dr. Edem Duke, explained the organization of the hospital, as well as the study-related activities of the clinical trial.

The following groups had responsibilities to the trial:
- The principal investigator and co-investigator with relevant qualifications conducted the study activities;
- The pharmacist was responsible for the receipt, storage, and dispensing of the IMP;
- The study coordinator was liable to carry out follow-up visits:
- Two trial monitors;
- Sponsor.

A clinical trial agreement for conducting the study of Zinc sulphate acceptability/palatability was signed between Alimosho General Hospital @ Dr Duke and sponsor Swiss Pharma Nigeria Limited on 6 Jul 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.

The hospital was led by the Hospital management committee/MD/CEO and consisted of 12 different departments, including Clinical services, pharmacy, nursing laboratory, etc. A copy of a general organogram was available to show the relationship between the organization's departments. The study took place in the Clinical services department, Paediatrics Ward.

The recruitment only occurred in the daytime, between 8 am and 4 pm. Every day, up to 150 children could be admitted to the hospital.

2. Quality management

The sponsor was responsible for implementing a quality assurance system 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 concerning Quality Management were addressed in the respective CAPA plan.

3. Archive facilities

There was no specific place to archive the study documentation. At the time of conduct of the study, consisting of ICF, CRF, questionnaire, and subject inspection responses on day five and day 10, was available and kept under the supervision of the PI, next to the study room. The documentation was stored in the cupboard, and the PI had the key to those cupboards during the study. Later, the study documentation was conveyed to the Head of Department office, and at the time of inspection, the documentation was kept under the custody of the PI.

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 and CRFs assignment.

Subject files and other supporting data were kept for inspection purposes.

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 inspection team's request.

In the respective CAPA plan, observations made about the Archive facility were attended to.

4. Premises

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

The study site located at the Paediatric ward consisted of the following units:

- A study exam room/doctor's office with a cupboard for archiving the study documentation. The door had a lock and was kept locked when unoccupied.
- A physical exam area was located in the reception area, where they had the scale, thermometers, and stethoscope.
- Pharmacy office

The premises were equipped with smoke detectors.

The sponsor did not sufficiently support the clinical trial, which compromised the correct performance of the study and the accuracy of documentation. Appropriate storage facilities were not available to keep the IMPs and protect the study documentation. Calibrated equipment to be used for the physical exams was not provided.

Pharmacy

A room was assigned to the IMP's reception, storage, and dispensing at the time of study in the reception area of the hospital's Paediatric ward. This room was converted into a pharmacy area after the study. According to the pharmacist, at the time of the study, only the IMP was kept at this facility in the cupboards with locks. The access to the room was restricted by keys.

Volunteers should go to the hospital pharmacy to receive their other medications prescribed for their ailment, based on the prescription provided by the study investigator, which was also recorded in the volunteers' medical journal. Prescriptions were sent to an off-site archiving facility. They were unavailable at the time of inspection; hence the information could not be verified.

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 PI had not participated in any clinical trial before.

Using the activity codes, a site delegation of responsibility log was provided to specify the study staff responsibilities.

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

A study protocol was authorized on 6 July 2020, and a Manual of Operation 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 mother/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 measure 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 at this clinical site on 3 November 2020, the last patient on 13 January 2021, and the enrolment of the last patient was completed on 22 January 2021.

The PI had accepted in writing the responsibility for the project's scientific conduct and providing the required progress reports. Dr Edem Duke Samuel signed an agreement to conduct the study according to the respective responsibility on 13 October 2020.

Subject screening and enrolment logs were provided in paper form with information about the screening date, name of the subject and hospital ID, study ID, etc. Screening failures and the respective reasons were mentioned on the list. Of 134 screened children, 12 children were not eligible to be recruited for the study. One hundred twenty children were enrolled in the study.

The clinical trial was carried out under conditions that ensured safety for the subjects.

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

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 who was the study coordinator at the time of submission. He was not involved in the study activities at the time of conducting the trial.

The study completion was notified to the HREC by Dr B Mutiu, the study coordinator. The letter was dated 8 February 2021.

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 damage was established due to the administration of Zinc sulphate Tablet used for the study. The details of compensation and indemnification were explained in the agreement with Leadway Assurance Company Limited covering the period of 26 June 2020 until 25 June 2021. The number of participants was also determined to be 300.

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

INFORMED CONSENT FORMS (WHO GCP 4.5)

The investigator was responsible for giving adequate information to subjects about the trial. Information about the study was provided in 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 the Ethics committee and ICF were addressed in the respective CAPA plan.

9. Monitoring

Two trial monitors on behalf of the sponsor carried out the monitoring visits, including site pre-visit, study monitoring visits on 13 and 25 November 2020, and a close out meeting.

The monitors were required to ensure that the trial was conducted according to the standards of the International Conference on Harmonization (ICH). The trial monitors concentrated on the progress of the trials and adherence to the protocol. Completed tasks were verified.

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

10. Investigators

Refer to section 5; “Personnel”

11. Receiving, storage and handling of investigational drug products

The pharmacist kept a drug inventory log. Information about the IMP receipt, the quantity received, the patient number, released staff signature, monitor comment, and monitor signature was documented. Expiry date and lot number were also recorded. The shipment documentation was provided with a specific serial number. The sponsor representative delivered the IMP, and the receipt was confirmed by the pharmacist on the specific form and dated. The IMP was delivered in 5 shipments, from 3 November 2020 until 6 January 2021.

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

The study investigator updated accountability records of the investigational product according to the protocol. The investigation product was dispensed in a blister pack containing ten 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 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 preventing diarrhea disease and look for any adverse reactions. The final endpoint was Day 10, in which the mother/caregiver brought the completed palatability assessment form and the blister pack of the drug irrespective of whether it was completely used or not.

The sponsor was responsible for the packaging and investigational labelling of the pharmaceutical products. 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;
- That the investigational product was used only following the protocol, which implied use only for subjects included in the trial and that the IMP was distributed by the designated staff responsible, and that the usage was documented in such a way as to ensure appropriate dosage;
- That 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 pharmacy and kept with the CRF.

Observations made in relation to IMP handling 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/enrolments visit and follow-up, end of the study visit, inclusion criteria, exclusion criteria, and the questionnaire. The questionnaires were a 5-point scale to classify the palatability response options.

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

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

A GPS detail was provided to the sponsor at each home visit by the visitor to verify the existence 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 that 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, and the IMP package with used blisters.

The observations made regarding the completion of the CRFs were addressed in the respective CAPA plan.

13. Volunteers, recruitment methods

The investigators were responsible for ensuring the unbiased selection and an adequate number of suitable subjects according to the protocol. Six physicians were assigned the responsibility to obtain a sufficient number of subjects.

The study physician screened all children within the defined age group for study eligibility criteria. Mothers / 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. A list of screening and a list of recruitment logs were provided. Name, ID number, date of birth, treatment pack number, and the name of the person who obtained consent were recorded on the recruitment log. Information about name, hospital number, date of birth, whether diarrhea was present or not, and eligibility and reason for illegibility were recorded on the screening log. 134 volunteers were screened. Out of 134 volunteers, 122 children were eligible, and 120 children were enrolled.

Upon signing a written informed consent, after providing information about the study and its interventions, possible benefits and risks, and 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 based on inclusion and exclusion criteria for subject selection, and screening procedures were described in the clinical trial protocol. The screening procedures were performed in the outpatient unit of the Clinical service, the Paediatric department. Randomly selected screening forms were reviewed to verify the process.

Observations made in relation to Recruitment 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 provided a form for “Suspected unexpected serious adverse reaction”, to be used in the case of SUSAR.

Observations made in relation to Safety 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 sponsors 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 study.

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

CRF forms 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 Diarrhoea
3: Adherence of product in children with diarrhoea between 18 months
4: Palatability of Zinc sulphate dispersible tablets in children with diarrhoea
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 CSR for the Source Data Verification.

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

Part 3	Conclusion - Inspection outcome

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 ***Alimosho General Hospita***l, located at ***Iganda, 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

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. Guidance for organizations performing in vivo bioequivalence studies. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 9.
   Short name: WHO BE guidance or ***TRS996 Annex 9***

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

4. Guideline for good clinical practice E6(R2). EMA/CHMP/ICH/135/1995
   Short name: ICH GCP E6

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

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

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

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***

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***

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

11. 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

12. 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

13. 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

14. 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

15. Ethical principles for medical research involving human subjects, 52nd WMA General assembly, Edinburgh Scotland, October 2000.
Short name: Declaration of Helsinki

16. Good manufacturing practices: guidelines on validation, WHO Technical Report Series, No. 1019, 2019
Short name: WHO TRS No. 1019, Annex 3