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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**MacLeods Pharmaceuticals Limited**
Corporate address of manufacturer	3rd Floor, Atlanta Arcade, Marol Church Road, Andheri (E), Mumbai
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Plot No 25-27, Survey No.366, Premiere Industrial Estate, Kachigam, Daman -396210, India (U.T.)
Unit / block / workshop number	Unit-2, Phase I (injectables)
Inspection details	
Dates of inspection	3-7 June 2019
Type of inspection	Routine GMP inspection of the facility for Bulk Artesunate Sterile Powder (sterile API) and that for the Powder for Injection FPP only.
Introduction	
Brief description of the manufacturing activities	The site houses eight buildings. Phase I was constructed in year 1999, 2000, and the area has been renovated in 2009-2010, 2016-2017 and most recently in 2019 with the introduction of RABs and remodeling of the filling suite for the powder filling line. Bulk sterile API lyophilization was located on the ground floor of phase-I (416.52 m2) and is currently dedicated by design to the manufacture of bulk sterile Artesunate API. Dry Powder injectables FPP Manufacturing was located on first floor of Phase -l (432 m2). Building 1 consisted the Phase- I manufacturing, warehousing for RM and the QC laboratory. Building 7 consisted of the control sample room, document storage and tertiary PM stores. Building 4 consisted of receipt, quarantine, sampling and approved areas for raw material area, building number 8 also housed the QA offices, document storage area, canteen, training hall.
General information about the company and site	Macleods Pharmaceuticals Limited manufactures and markets a wide range of pharmaceutical formulations. It is primarily engaged in manufacturing of both, 1st and 2nd line anti-Tuberculosis formulations/ Anti-Retrovirals, several of which are within the PQ programme as well as Antibiotics/ Anti-Diabetics/ NSAIDs/ Anti-arthritic/ Anti-Osteoporotics/ Asthma & Pulmonary Diseases/ Cardiovascular/ Proton Pump inhibitors/ Gastro-Enterology/ CNS Agents sold in both domestic and export markets. Several

	sites supply to stringent markets. The company also manufactures several APIs. The corporate headquarters is located at Andheri, Mumbai. The corporation employs a total of approximately 13 500 employees including marketing personnel. It has eight facilities in India: o Pharmaceutical Formulation (Unit I), Palghar (Maharashtra). o Pharmaceutical Formulation (Unit II), Daman (Union Territory). o Pharmaceutical Formulation (Unit III), Daman (Union Territory). o Research & Development (R&D) Centre, Andheri (Mumbai). o Active Pharmaceutical ingredient (Unit V), Sarigam (Gujarat). o Pharmaceutical Formulation (Unit VI), Nalagarh (Himachal Pradesh). o Pharmaceutical Formulation (Unit VII), Daman (Union Territory). o Pharmaceutical Formulation (Unit IX), Sikkim.
History	The sterile site of Macleods was last inspected by WHO PQ in April 2016. In addition, the sterile site has been inspected by the following authorities: 1. PPB Kenya, December 2018 2. MOH, Malaysia, April 2018 3. MOH, Russia, August 2017 4. NAFDAC, Nigeria, August 2016 5. MCC South Africa, November 2012
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	o Quality Assurance o Qualification and validation o Complaints o Vendors evaluation o Contracts o Premises o Equipment o Documentation o Production o Quality control
Restrictions	Only the injection manufacturing facilities pertaining to Prequalified and under PQ products were inspected. All other activities on the site were excluded from the scope of this inspection
Out of scope	Only products under PQ program were included in the scope of this inspection.
WHO products covered by the inspection	TB211 - Capreomycin (sulfate) Powder for solution for injection 1000mg TB337 - Capreomycin (sulfate) Powder for solution for injection 500mg TB212 - Kanamycin (sulfate) Powder for solution for injection 500mg TB213 - Kanamycin (sulfate) Powder for solution for injection 1000mg TB214 - Streptomycin (sulfate) Powder for solution for injection 1000mg MA152 - Artesunate + Sodium Bicarbonate + Sodium Chloride Powder and solvent for solution for injection 60mg + 50mg/ml + 9mg/ml – *under assessment by PQ*

Abbreviations	Meaning
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance

QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	**Summary of the findings and comments**

1. Pharmaceutical quality system

In general, a PQS was implemented. Production and control operations were independently managed and specified in written form and GMP requirements were generally being followed. Managerial responsibilities were specified in job-descriptions. Product and processes were monitored, and the results taken into account in batch release and regular reviews of the quality of pharmaceutical products were conducted. Periodic management reviews were performed. Statistical tools were in use in some monitoring activities e.g. PQRs, but there was no comprehensive general SOP discussing the statistical tools that were available and when they should be usefully implemented and when the use of certain tools e.g. use of CpK (i.e. on small data sets) would be inappropriate. The company stated that it had purchased Mini-Tab software which would be implementing thein the next 2-3 months.

Product quality review (PQR)

The SOP for PQR was discussed. It is a site-specific procedure which was prepared based on the CQA guideline. The PQRs were prepared based on a rolling covering a 12- month period with the review period for different products being spread throughout year to smooth the work load in the QA unit. The SOP required the review to be completed within 2 months of the end of the review period. There was also a provision to prepare an addendum to the PQR report in case of any discrepancy was observed for the batches resulted in non-compliance after finalization of the PQR.

Quality risk management

The SOP "Quality risk management" was discussed. The SOP, utilizing FMEA and HCCP tools was applicable for risk management for all processes/systems and Corrective actions and preventive actions. Risk analysis was used for:

- Validations and all levels
- Change control/deviation execution
- Incident reporting and investigation
- Investigation for any failure/non-conformance

- Handling market complaints
- Development of product specification and critical process parameters
- Out of specifications (OOS)/ out of trends (OOT)/out of calibration investigations

Change controls

The SOP "Change control" was discussed. The SOP was applicable for:

- SOPs, specifications and other documents
- Batch manufacturing records (BMR)/batch packaging records (BPR)
- Formats
- Validation
- Vendors
- New product manufacturing
- Facilities

The SOP requires classification and contains forms for risk assessment and authorization of relative parties impacted by the change. The SOP is well designed to handle relatively straightforward and uncomplicated changes.

Deviations

The SOP "Handling of deviation" was reviewed. Deviations were classified as planned and unplanned deviations. According to the SOP formal risk analysis (RA) should be done for each deviation. Based on RPN numbers calculations and risk should be categorized as low/medium/high. For medium and high risk, full scale RA should be performed as per RA SOP. Based on the nature of deviation (critical, major and minor) corrective and preventive actions (CAPA) should be proposed. Timeline for closing the deviations was specified 30 days.

The issues noted from this section have already been addressed and will be verified during future inspections.

2. Good manufacturing practices for pharmaceutical products

Manufacturing processes were generally clearly defined and systematically reviewed. Qualifications and validations were performed where required and documents were produced where requested. Necessary resources were provided, and records were made during manufacture. Significant deviations were recorded and investigated, root causes were investigated and determined in most examples reviewed. Procedures were in-place for tracking corrective and preventive actions and their implementation. A system was available to recall any batch of product from sale or supply and complaints about marketed products were examined, the causes of quality defects were required to be investigated, and appropriate measures taken in respect of the defective products.

The company was asked whether it had performed a comprehensive gap analysis of its facilities, operations and controls against the draft revised sterile products GMP. It stated that it had yet to formally perform such an assessment and the inspectors strongly recommended the company not to delay in the performance of such a review.

3. Sanitation and hygiene

The company had a standard operating procedure as the basis for its approach to personal hygiene and sanitation in its production facilities. Areas were cleaned frequently in accordance with an approved written program and SOPs. Microbial monitoring was regularly performed.

4. Qualification and validation

The key elements of a qualification and validation program were defined and documented in the validation policy and validation master plan.

Aseptic process validation – media simulations
The SOP of aseptic process simulation was discussed. The company performs its media simulations in three parts:

a) The liquid preparation to simulate the dissolution of non-sterile Artesunate and its passage to the filter for the precipitated sterile bulk. It was noted that in this step dehydrated soybean casein dissolved in water, prepared in Grade-C environment and the media then transferred through pipeline to the filtration vessel and from there to the Nuttsche filter.

b) The drying of the wet crystallization mass and drying process in the Lyophilizer and subsequent milling and harvesting in the 20L containers together with sampling is performed with granular dried SCDM media. It was noted that the company has not shown that the solid media used to simulate the powder handling of the process is capable of removing contamination off production surfaces were that to be present. Recovery studies to define the sensitivity of the techniques in use should be performed however it is noted that the approach being performed is one of the typical approaches to the performance of such simulations. It was also noted that the media used is not formally part of the cleaning validation matrix although the company takes additional cleaning steps to try to ensure the removal of media from equipment after the completion of the studies.

c) The dry powder filling operation.
All vial sizes are covered during two media fills (7.5ml and 15ml during one media fill and 10ml during second media fill). This step is also performed by filling SCDM followed by adding water to the filled vial before stoppering and sealing. The filling media fill performed for 24 hours.

Area periodic requalification and certification
It was stated that calibration and cleaning/replacement of filters are performed during non-production days. Airflow mapping was performed by outside party and training was provided before allowing the technicians involved to enter aseptic areas. Requalification was being performed according to ISO 14644 6 monthly.

The issues noted from this section have already been addressed and will be verified during future inspections.

5. Complaints

There were no complaints received for any of the injectable products manufactured at Phase-I, Unit-2, Kachigam, Daman since 2016. It was noted that procedure on complaints was revised since the last WHO PQ inspection based on guidance received from the corporate QA.

6. Product recalls

There was no recall initiated for any of the injectable products manufactured at Phase-I, Unit-2, Kachigam, Daman since 2016. It was noted that procedure on product recall had been revised since the last WHO PQ inspection based on guidance received from the corporate QA.

7. Contract production, analysis and other activities

Manufacturing operations were not contracted out. Animal based laboratory tests (rabbit pyrogen testing and abnormal toxicity) were contracted out. It was stated that the labs had been qualified and audited. The audit reports and agreements for these contractors were not reviewed on this occasion.

8. Self-inspection, quality audits and suppliers' audits and approval

Not inspected due to time constraints.

9. Personnel

The manufacturer had an adequate number of personnel with the necessary qualifications and practical experience. Responsible staff, specific duties were recorded in written job descriptions. Personnel met were aware of the principles of GMP and received initial and continuing training, including hygiene instructions, relevant to their needs. Steps were taken to prevent unauthorized people from entering production, storage and QC areas.

Department	No. of Employees
Quality Assurance	119 **
Quality Control	187 **
Production	56 *
Warehouse	27 **
Engineering	66 **
Administration	6 **

* Injectable
** Injectable & OSD

10. Training

Procedure is in place to train inspector if he/she wishes to enter aseptic areas including declaration by the inspector. This section other than the review of the activities performed during media simulation and gowning qualifications was not inspected due to time constraints.

11. Personal hygiene

Personnel suffering from illness such as skin rashes, colds, and open lesions to the body were required to report to the department head and were excluded from working in the clean and critical areas. Smoking, eating, drinking, chewing and the storage of food and personal medicines and smoking was prohibited in all storage and manufacturing areas.

12. Premises

Exposed surfaces were smooth, impervious and unbroken. Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Changing rooms were flushed with filtered air. Airlock doors were interlocked.

Rest and refreshment rooms were separate from manufacturing and control areas.

Storage areas were of sufficient capacity. Receiving and dispatch bays protected materials and products from the weather. Segregation was provided for the storage of rejected, recalled, or returned materials or products.

The production of sterile preparations was carried out in clean areas, entries to which were through airlocks for personnel and for equipment and materials. Clean areas were maintained to an appropriate standard of cleanliness and supplied with air that has passed through HEPA.

Access to the manufacturing area was via biometric controls. The bulk lyophilization manufacturing area was located on ground floor and dry powder injectables filling was located on the first floor of the building. The layout facilitates unilateral movement of man and material.

Sufficient space was given to avoid mix ups and cross-contamination. Adequate storage space was provided for samples, reference standards, solvents, reagents and records.

13. Equipment

Equipment was located, designed, constructed, adapted, and maintained to suit the operations to be carried out. The layout and design of equipment minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt.

14. Materials

Incoming starting materials and finished products were quarantined after receipt until they were released for use or distribution. Starting materials were purchased from approved suppliers. Approved suppliers lists for active pharmaceutical ingredients and packaging materials were available and presented to the inspectors. Sterile raw materials were stored in mobile racks.

15. Documentation

In general documents were designed, prepared, reviewed and distributed with care. Documents were approved, signed and dated by the appropriate responsible persons. Documents were regularly reviewed and kept up to date. Records were made or completed when any action was taken.

16. Good practices in production

In general production operations followed defined procedures. Deviations from procedures were recorded and investigated. Checks on yields and reconciliation of quantities were carried out. Access to production premises was restricted to authorized personnel. In-process controls were performed by operators.

Before processing operations were started, steps were taken to ensure that the work area and equipment were clean and free from any starting materials, products, product residues, labels or documents not required for the current operation. Necessary in-process controls and environmental controls were carried out and recorded.

Before packaging operations begun, steps were taken to ensure that the work area, packaging line, printing machine and other equipment were clean and free from any products, materials or documents used previously.

The issues noted from this section have already been addressed and will be verified during future inspections.

17. Good practices in quality control

The QC function was independent of other departments. Adequate resources were available to ensure that all the QC arrangements are carried out. QC personnel had access to production areas for sampling and investigation as appropriate.

Common quality control laboratory was in use for the testing of sterile and non-sterile APIs and finished products.

The laboratory was equipped with the following equipment and instruments:

Equipment	Quantity
HPLC	37
UPLC	01
UV	03
FTIR	01
Gas Chromatograph	03
Dissolution Apparatus	09
Deep Freezer	01
Stability chambers	08

Issues noted from this section have already been addressed and will be verified during future inspections.

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, ***Macleods Pharmaceuticals Ltd***, located at ***Plot No 25-27, Survey No.366, Premiere Industrial Estate, Kachigam, Daman -396210, India (U.T.)*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

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

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/
2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO GMP for APIs*** or ***TRS No. 957, Annex 2***
   http://www.who.int/medicines/publications/44threport/en/

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/
4. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4
   Short name: WHO TRS No. 929, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4
   Short name: WHO TRS No. 937, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

7. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1
   Short name: WHO GPPQCL Guidelines or ***TRS No. 957, Annex 1***
   http://www.who.int/medicines/publications/44threport/en/

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2
   Short name: WHO TRS No. 957, Annex 2
   http://www.who.int/medicines/publications/44threport/en/

9. WHO good manufacturing practices for sterile 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 6
   Short name: WHO TRS No. 961, Annex 6
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7
    Short name: WHO TRS No. 961, Annex 7
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. 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 TRS No. 961, Annex 9***
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3
    Short name: WHO TRS No. 943, Annex 3
    http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2
    Short name: WHO TRS No. 961, Annex 2
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. ***Short name: WHO TRS No. 981, Annex 2***
    http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3. ***Short name: WHO TRS No. 981, Annex 3***
    http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14. ***Short name: WHO TRS No. 961, Annex 14***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3. ***Short name: WHO TRS No. 992, Annex 3***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

20. WHO Recommendations for quality requirements when plant – derived artemisin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6
Short name: WHO TRS No. 992, Annex 6
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5
Short name: WHO GDRMP or ***WHO TRS No. 996, Annex 5***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

22. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10
Short name: WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf