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

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Mylan Laboratories Limited
Corporate address of manufacturer	Mylan Laboratories Limited, Plot No. 564/A/22, Road No. 92, Jubilee Hills, Hyderabad – 500096, Telangana, INDIA. Phone: +91-40-3086-6666 / 3086-6444
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Mylan Laboratories Limited Plot No H12 & 13 MIDC, Waluj Industrial area Chhatrapati Sambhajinagar (Formerly known as Aurangabad) Maharashtra 431 136 India Latitude: 19.8762º N Longitude: 75.3433º E DUNS: 863996098
Unit / block / workshop number	Manufacturing building (including warehousing premises) QC/QA building Utilities building
Manufacturing license number	Form 25 No. AD/089 and Form 28 No. AD/064 granted on 28.12.2010 and valid up to 27.12.2025, to manufacture the tablet and hard gelatine capsules dosage forms.
Inspection details	
Dates of inspection	28 April – 2 May 2025
Type of inspection	Routine inspection
Inspection record number	INSP-FPP-2022-0047
Introduction	
Brief description of the manufacturing activities	The site manufactures, packages, tests, and releases oral solid dosage forms (tablets and hard gelatine capsules) for human use. No other activity, except for the manufacturing and packaging of solid oral dosage forms, is carried out at the site.

General information about the company and site	Mylan Laboratories Limited is the Indian subsidiary of Viatris, a generics and specialty pharma company. In India, Mylan operate at four manufacturing sites as below listed: • FDF1 in Nashik, Maharashtra • FDF2 in Chhatrapati Sambhajinagar, Maharashtra [formerly known as Aurangabad • FDF3 in Indore, Madhya Pradesh • FDF4 in Jadcherla (Hyderabad), Telangana Mylan FDF-2 Plant (subject of this inspection) was acquired in 2010 and is located in the Waluj Industrial Area, about 23 km from the airport. The formulation plant covers 36,000 sq. meters and build up area is 34,432 sq. meters with an annual production capacity of 5 billion dosage units. The facility was constructed in year 2008-10. No mutagenic, immune suppressant, teratogenic products, toxic or hazardous substances, β-lactam antibiotics, or cephalosporins are produced on site.
History	The site has been subject to regular WHO inspections since 2013, including onsite inspections in 2012, 2013 and 2016 as well as desk assessments in 2019 and 2022. In addition, the site has been subject to several inspections by several regulatory authorities as below listed:

Inspection Authority	Inspection Dates
DPML, Cameroon	27 – 28 Jan. 2025
CDSCO, India	2 – 4 Dec. 2024
PPB, Kenya	12 – 16 Dec. 2024
NDA, Uganda	3 – 4 Oct 2024
FDA Maharashtra, India	22 – 23 Jul. 2024
FDA Maharashtra, India	21 – 22 Mar. 2024
FDA, Ghana	8 – 9 Jun. 2023
NAFDAC, Nigeria	6 –7 Mar. 2023
FDA, Taiwan	14 – 17 Feb. 2023
HPRA, Ireland	30 Jan. – 3 Feb. 2023
FDA Maharashtra, India	12 – 13 Dec. 2022
Ministry of Health, Belarus	23 – 25 May 2022
CDSCO, India	10 – 11 Nov. 2021
Zazibona (Zambia, Zimbabwe, Botswana and Namibia)	26 – 30 Jul. 2021
USFDA	20 – 28 Feb. 2020

Major changes since last WHO inspection	**Main Changes in Premises/Facility included the following:** • Expansion of Warehouse facility • Creation of additional Change Parts Room • Creation of additional In process Store Area • Creation of additional Coating Area • Expansion of existing Change Rooms and creation of additional Change Rooms • Creation of additional Encapsulation Area • Expansion of Compression Area

	• Creation of additional Accessories Store • Creation of additional Blending Area • Creation of additional Document Storage space • Expansion of existing Encapsulation Suite • Bifurcation of Compression Area into two process Areas • Creation of additional Primary Packaging Areas **Main Changes in Equipment/Instruments/Utilities/Systems included the following:** • The major equipment's installed includes additional Fluid Bed Processors, Compression Machine, Coating Machine, Encapsulation Machine, Blister Packaging Machine etc • The major instruments installed includes additional HPLC, LC MS/MS, GC MS/MS, Stability Chamber, etc • The major utilities installed includes new AHU systems, heat exchanger in water distribution system, etc • The major software system installed includes Data Historian, MYMES, SAP Fiori System, • Serialization and Aggregation System, etc
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	**The following GMP subjects were covered during the inspection:** 1. Pharmaceutical quality system 2. Good manufacturing practices for pharmaceutical products 3. Sanitation and hygiene 4. Qualification and validation 5. Complaints 6. Product recalls 7. Contract production, analysis and other activities 8. Self-inspection, quality audits and suppliers' audits and approval 9. Personnel 10. Training 11. Personal hygiene 12. Premises 13. Equipment 14. Materials 15. Documentation 16. Good practices in production 17. Good practices in quality control **The following areas were visited during the inspection:** • Raw material, packaging material, finished goods warehouse (housed within the manufacturing building) • Production of solid dosage forms building • Quality Control and Quality Assurance building • Engineering and utility building
Restrictions	Products, facilities, blocks and/or areas that are not under the scope of WHO prequalification program.

Out of scope	Products, facilities and/or areas not related to WHO prequalification
WHO products numbers covered by the inspection	

#	Product Name	ePQS #	Status
1.	Cycloserine Capsules 250mg	TB304	Prequalified
2.	Darunavir (Ethanolate) Film Coated Tablet 800mg	HA683	Prequalified
3.	Isoniazid Tablet 100mg	TB308	Prequalified
4.	Isoniazid Tablet 300mg	TB285	Prequalified
5.	Lamivudine / Zidovudine Dispersible Tablet 30mg/60mg	HA572	Prequalified
6.	Oseltamivir (Phosphate) Capsules 75mg	IN011	Prequalified
7.	Pretomanid Tablet 200 mg	TB386(a)	Prequalified
8.	Efavirenz Film Coated Tablet 600mg	HA403	Prequalified
9.	Emtricitabine / Tenofovir Disoproxil Fumarate Film Coated Tablet 200mg/300mg	HA417	Prequalified
10.	Lamivudine / Zidovudine Film Coated Tablet USP 150mg/300mg	HA392	Prequalified
11.	Lamivudine / Nevirapine / Zidovudine Dispersible Tablet 30mg/50mg/60mg	HA433	Prequalified
12.	Efavirenz / Emtricitabine / Tenofovir Disoproxil Fumarate Film Coated Tablet 600mg/200mg/300mg	HA444	Prequalified
13.	Tenofovir Disoproxil Fumarate Film Coated Tablet 300mg	HA410	Prequalified
14.	Lamivudine / Tenofovir Disoproxil Fumarate Film Coated Tablet 300mg/300 mg	HA414	Prequalified
15.	Efavirenz / Lamivudine / Tenofovir Disoproxil Fumarate Film Coated Tablet 400mg/300mg/300 mg	HA721 (a)	Prequalified
16.	Efavirenz / Lamivudine / Tenofovir Disoproxil Fumarate Film Coated Tablet 600mg/300mg/300mg	HA466	Prequalified
17.	Darunavir (Ethanolate) Film Coated Tablet 600mg	HA685	Prequalified
18.	Bedaquiline Fumarate Tablet 100mg	TB408	Pending
19.	Moxifloxacin (Hydrochloride) Dispersible Tablet 100mg	TB399	Pending
20.	Linezolid Dispersible Tablet 150mg	TB417	Pending

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
CPV	Continued process verification

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
NCA	National control authority
NCL	National control laboratory
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

At Mylan Waluj FDF2, in general, there was a comprehensively designed and correctly implemented pharmaceutical quality system (PQS) incorporating GMP and QRM.

Mylan Waluj FDF2 assumed responsibility for the quality of the pharmaceutical products and ensured that they are fit for their intended use, comply with the requirements of the marketing authorization and did not place patients at risk due to inadequate safety, quality or efficacy. The attainment of this quality objective was the responsibility of senior management.

Senior management at Mylan Waluj FDF2 had the ultimate responsibility to ensure an effective PQS was in place, was adequately resourced, and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organization.

In general, all parts of the PQS were adequately resourced and maintained, including being provided with sufficient competent personnel, suitable premises, equipment and facilities.

The PQS implemented by Mylan Waluj FDF2 ensured the following, among others:

- production and control operations were clearly specified in a written form and GMP requirements were adopted;
- managerial responsibilities were clearly specified in job descriptions;
- arrangements were made for the manufacture, supply and use of the correct starting and packaging materials, the selection and monitoring of suppliers and for verifying that each delivery was the correct material from the approved supply chain;
- all necessary controls on starting materials, intermediate products, and bulk products and other in-process controls, calibrations and validations were carried out;
- the finished product was correctly processed and checked, according to the defined procedures;
- processes are in place to assure the management of outsourced activities;
- satisfactory arrangements exist to ensure, as far as possible, that the pharmaceutical products were stored, distributed and subsequently handled so that quality was maintained throughout their shelf-life;
- there was a procedure for self-inspection and/or quality audit that regularly appraised the effectiveness and applicability of the PQS;
- pharmaceutical products were not sold or supplied before the authorized persons had certified that each production batch had been produced and controlled in accordance with the requirements of the marketing authorization and any other regulations relevant to the production, control and release of pharmaceutical products;
- product and processes were monitored and the results taken into account in batch release, in the investigation of deviations and, with a view to taking preventive action to avoid potential deviations occurring in the future;
- arrangements were in place for the prospective evaluation and approval of planned changes and their approval prior to implementation taking into account regulatory notification and

approval where required. After implementation of any change, an evaluation was undertaken to confirm that the quality objectives were achieved and that there was no unintended adverse impact on product quality;
- regular reviews of the quality of pharmaceutical products were conducted with the objective of verifying the consistency of the process and identifying where there is a need for improvement;
- a state of control was established and maintained by developing and using effective monitoring and control systems for process performance and product quality;
- continual improvement was facilitated through the implementation of quality improvements appropriate to the current level of process and product knowledge;
- there was a system for QRM; and
- deviations, suspected product defects and other problems were reported, investigated and recorded. Appropriate level of root cause analyses was applied during such investigations. The most likely root cause(s) was/were identified, whenever possible, and appropriate corrective actions and/or preventive actions (CAPAs) were identified and taken when applicable. The effectiveness of CAPAs were monitored.

The PQS was defined and documented. A quality manual was established and contained a description of the quality management system including management responsibilities.

The quality manual outlined the current PQS implemented at Mylan Waluj FDF2, ensuring compliance with ICH Q10 and other applicable Good Practices (GxP). The quality manual included the quality mission statement, responsibilities, organization of quality system (based on 6 components namely materials, laboratory, facilities and equipment, validation, production, and packaging and labelling), document hierarchy based on pyramidal structure with global quality manual at the top, followed by global quality policies; global quality good practices; SOP (regional and/or site) along with work instructions; and records and reports at the bottom of the pyramidal structure.

Management reviews

Periodic management reviews were conducted on regular basis. The senior management was well involved in the management reviews. The reviews covered the operation of the PQS, identified opportunities for continual improvement of products, processes and the system itself.

A procedure was well-established and implemented for management reviews. The procedure provided guidance on the conduct of management reviews on monthly basis for suitability and effectiveness. However, the timeline may change based upon unforeseen circumstances in concurrence with the Site Quality Head. MRs were carried out by the Site Head and Site Quality Head along with Head of QA, Head of QC, Head of Production, Head of Engineering, Head of Warehouse, Head of Technical Services, and Head of Regulatory Affairs. Representation from other departments (e.g., supply chain) may also join the MRs.

The records of the last two management reviews were reviewed and did not give rise to any non-conformities.

Quality risk management (QRM)

The concepts and principles of QRM were followed by Mylan Waluj FDF2, both proactively and retrospectively. The QRM, applied by quality assurance team, ensured that the evaluation of the risk

to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient; and that the level of effort, formality and documentation of the QRM process was commensurate with the level of risk.

A procedure for QRM was in place. The procedure covered different stages and phases of QRM, including hazard identification, risk analysis and risk evaluation along with risk control and risk communication. The procedure included a generic risk matrix (using FMEA methodology) with varying ranges of severity, occurrence and detectability (varying from 1 to 5 for each risk parameter) along with a risk level (based on RPN calculation). The SOP also listed several risk analysis tools including FMEA, RRF, FTA, HACCP, HAZOP, PHA and fishbone diagram. One of the annexes related to the SOP was the list of risk assessments (planned ones irrespective of unplanned ones which may be needed e.g., in case of change control). The latter list included risk assessments which needed to be conducted on regular basis (if not earlier due to change) and the frequency of such periodic risk assessment was set at 2 years (+/- 1 month).

A risk register was established, where QRM exercises were logged. The risk register was reviewed and few QRM exercises were reviewed.

Product quality review (PQR)

Mylan Waluj FDF2 established a system for periodic quality reviews of all pharmaceutical products, including export-only products. The objectives of the PQR included verifying the consistency of the existing process and the appropriateness of specifications for both starting materials and finished products, to highlight any trends and to identify product and process improvements. The PQRs were conducted and documented annually, and took into account previous reviews. The PQR included aspects related to the following:

- review of starting materials and packaging materials used for the product, especially those from new sources and in particular the review of supply chain traceability of active substances;
- review of critical in-process controls, and finished product results;
- review of all batches that failed to meet established specification(s) and their investigation;
- review of all significant deviations or non-conformances, the related investigations and the effectiveness of resultant CAPAs taken;
- review of all changes made to the processes or analytical methods;
- review of dossier variations submitted, granted or refused;
- review of the results of the stability monitoring programme and any adverse trends;
- review of all quality-related returns, complaints and recalls and the investigations performed at the time;
- review of adequacy of any other previous corrective actions on product processes or equipment;
- post-marketing commitments for new dossiers and variations to the dossiers;
- the qualification status of relevant equipment and utilities, (e.g., HVAC, water and compressed gases) and a review of the results of monitoring the output of such equipment and utilities; and
- review of technical agreements to ensure that they are up to date.

Mylan Waluj FDF2 evaluated the results of the PQR and an assessment was made as to whether CAPA or any revalidation had been undertaken, under the PQS. Quality reviews were grouped by market. The authorized person responsible for final batch certification ensured that the quality reviews were performed in a timely manner and was accurate.

The SOP for annual product review was well-established and implemented. The procedure provided for annual review of WHO prequalified products (from date of prequalification attainment) and the APR should be completed within 2 calendar months from the end date of the review period. The SOP mandated that APR be prepared even if no batches were manufactured during the review period. The SOP also provided for grouping of products for APR preparation if the manufacturing formula and process were common for multiple markets and for products with a common blend/dose proportionate formulation. Process capability and efficiency were among the subjects considered within the APR with defined ranges, along with actions for PPK (based on a minimum of 25 batches), control chart (based on a minimum of 12 batches) or trend chart (based on a minimum of 6 batches).

The following PQRs of the products related to WHO prequalification programme were reviewed:

- APR/PQR for Tenofovir Disoproxil Fumarate & Lamivudine Tablets 300 mg /300 mg in bottles – review period from Feb 2024 to Jan 2025
- APR/PQR For Lamivudine & Zidovudine Tablets USP 150mg/ 300mg (HA392) in bottles – review period from Jun 2023 to May 2024
- APQ/PQR For Darunavir (as ethanolate) Tablets 600 mg (HA685) in bottles – review period from Oct 2023 to Sep 2024

No PQRs were prepared for the three products under assessment by WHO prequalification, as only exhibit batches were manufactured and no commercial batches (or batches intended for commercialization) were produced as of the date of the inspection.

Handling of deviations

The SOP for handling of incident investigation was in place. The procedure defined incident as a deviation from process, procedure or specification that is detected after the deviation's occurrence. In addition, the procedure applied to manufacturing incidents which included any OOS/OOT, yield variance, AQL failure and product not complying with requirements during annual retention sample inspection. Incidents could be generated by any staff at Mylan Waluj FDF2 who had access to the computerized system used to track incidents (Trackwise®). If the person did not have access to the computerized system, the supervisor to whom the incident was reported could initiate the incident in the computerized system on behalf of the founder. Three categories of incident were defined in the SOP, namely minor, major and critical ones. The major and critical incidents, as well as manufacturing incidents, had to be thoroughly investigated, including provisions for impact assessment. Minor incidents could be closed without investigation if no associated impact was estimated. All incidents and manufacturing incidents had to be trended. For any new incident or manufacturing incident, a software query was necessary to be performed to find any associated trends. The SOP also provided for investigation procedure which was complemented with a site-specific procedure for root cause analysis.

In addition, the SOP on Handling of Operational Interruptions and Incidences was reviewed and related records of few such incidents were spot-checked.

The quarterly trend review of incident investigations for Q4 2024 was reviewed.

One more incident was spot-checked based on the review of PQR of T/L tablets 300mg/300mg

CAPA management

SOP for CAPA with effectiveness check was reviewed. The procedure provided for CAPA initiation, approval, implementation, closure and effectiveness check. Timeline for CAPA implementation was set, as per the SOP, for 45 calendar days from the date of initiation of CAPAs related to documentation and training or 90 calendar days for CAPAs involving short term physical or mechanical interventions. Two extensions can be made, only upon justification, after managerial approval and a third extension can be also made with Site Quality Head or Head QA.

The summary of CAPA with effectiveness checks, Quarter-IV, Year 2024 was reviewed and few CAPAs were spot-checked.

Change Control

SOP for change management process was well-established and implemented. The SOP gave detailed procedural instructions on managing changes including initiation/creation, review, implementation, completion, closure and notification to health authorities (if applicable). Changes were classified into minor, major and critical based on in-depth risk and impact assessments (and considering related regulatory guidance).

In addition, the change control summary of Quarter-IV, Year 2024 was reviewed and few changes were spot-checked.

2. Good manufacturing practices for pharmaceutical products

In general, Mylan Waluj FDF2 applied the main concepts and principles of GMP aiming primarily at managing and minimizing the risks inherent in pharmaceutical manufacture to ensure the quality, safety and efficacy of products. Under GMP, the following activities were implemented:

- all manufacturing processes were clearly defined, systematically reviewed for associated risks in the light of scientific knowledge and experience, and shown to be capable of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications;
- qualification and validation were performed;
- all necessary resources were provided, including sufficient and appropriately qualified and trained personnel, adequate premises and space, suitable equipment and services, appropriate materials, containers and labels, approved procedures and instructions, suitable storage and transport, adequate personnel, laboratories and equipment for in-process controls;
- instructions and procedures were written in clear and unambiguous language;
- procedures were carried out correctly and personnel are trained to do so;
- records were made during manufacture to show that all the steps required by the defined procedures and instructions had in fact been taken and that the quantity and quality of the product were as expected. Any significant deviations were fully recorded and investigated with the objective of determining the root cause and appropriate corrective and preventive action was implemented;
- records covering manufacture and distribution, which enable the complete history of a batch to be traced, were retained in a comprehensible and accessible form;
- the proper storage and distribution of the products minimized any risk to their quality and took account of good distribution practices (GDP);

- a system was available to recall any batch of product from sale or supply;
- complaints about marketed products were examined, the causes of quality defects investigated and appropriate measures taken in respect of the defective products to prevent recurrence.

For further details, please refer to the respective sections detailing each of the aforementioned GMP activities.

3. Sanitation and hygiene

In general, a high level of sanitation and hygiene was practised in different aspects of the manufacture of pharmaceutical products at Mylan Waluj FDF2. The scope of sanitation and hygiene covered personnel, premises, equipment and apparatus, production materials and containers, products for cleaning and disinfection, and anything that could become a source of contamination to the product. Potential sources of contamination were eliminated through an integrated comprehensive programme of sanitation and hygiene.

For further details on hygiene and sanitation, please refer to sections 11 and 12 respectively.

4. Qualification and validation

Mylan Waluj FDF2 identified what qualification and validation work was required to prove that the critical aspects of their particular operation were controlled.

A validation master plan (VMP) documented and clearly defined the key elements of a qualification and validation programme at Mylan Waluj FDF2. The VMP included a commitment to maintain continued validation status as well as clear roles and responsibilities to undertake the qualification and validation activities.

Qualification and validation established and provided documentary evidence that:

- the premises, supporting utilities, equipment and processes had been designed in accordance with the requirements for GMP (DQ);
- the premises, supporting utilities, equipment and processes had been built and installed in accordance with the requirements for GMP (IQ);
- the premises, supporting utilities, equipment and processes operated in accordance with the requirements for GMP (OQ);
- specific processed consistently produced a product meeting its predetermined specifications and quality attributes (PQ and PV).

The aspects of operation, including significant changes to the premises, facilities, equipment or processes, which may affect the quality of the product, directly or indirectly, were qualified and validated as appropriate.

Qualification and validation were not treated as one-time activities; instead, an ongoing programme was maintained following initial implementation, with periodic reviews conducted annually.

Qualification and validation activities were carried out in accordance with predefined and approved protocols. The results and conclusions were documented in comprehensive qualification and validation

reports. Processes and procedures were established on the basis of the results of the validation performed.

The VMP was reviewed and found to provide comprehensive guidance for qualification and validation activities including validation approaches, documentation, area qualification, equipment qualification, process validation, packaging validation, cleaning validation, method validation and computerized system validation.

Cleaning validation

Cleaning validation was performed according to well established policies and procedures as indicated in the validation master plan and respective procedures and protocols. Cleaning validation studies were required to be refreshed with introduction of any new molecule/product to the production facility. Cleaning validation activities included assessment of the impact of the new molecule/product along with update of the product information sheet followed by product specific cleaning validation protocol and report, as applicable. Sampling for cleaning validation was solely performed using swab method with justification that swabbing was deeded sensitive and accurate in comparison to rinse samples and also considering that equipment could be disassembled (including detailed swab sampling plans/locations) and as such no difficult-to-reach areas were estimated.

The following cleaning validation related documents were reviewed:

- Cleaning validation procedure.
- Protocol for Cleaning Validation of compression machine.
- Report for Cleaning Validation of compression machine.
- Impact assessment on equipment groups, Bedaquiline Tablets 100 mg.
- Impact assessment on equipment groups, Linezolid dispersible tablets 150 mg.
- Product information sheet, new product introduction, Bedaquiline tablets.
- Impact assessment on equipment groups, Moxifloxacin dispersible tablets 100 mg.
- Product information sheet, new product introduction, Olmesartan Medoxomil, Amlodipine Besylate and Hydrochlorothiazide Tablets.
- Product information sheet, new product introduction, Bedaquiline tablets.
- Product information sheet, new product introduction, Linezolid dispersible tablets 150 mg.
- Risk based evaluation for identification of swab sampling locations Fluid Bed Dryer (FBD).
- Risk based evaluation of process of equipment and accessories for Identification of Swab sampling locations.
- Risk based evaluation for identification of swab sampling locations Rapid Mixer Granulator.
- Protocol for estimation of Residue by Rinse Sampling Method.
- Risk based evaluation for identification of swab sampling locations, compression machine.

Analytical procedure validation (AMV)

The analytical method validation Report for determination of Bedaquiline Fumarate Residue By HPLC was spot-checked. This AMV was executed in connection with the cleaning validation study prior to introduction of that FPP to the production block.

Validation of computerized systems

Computerized systems were validated prior to their use, in proportionality to their criticality and risk to manufacturing activities. In addition, as part of the lifecycle management, the computerized systems

were subject to periodic review in accordance with SOP on periodic review of GxP computerized systems (SOP-001352495, effective date: 14/02/2022). The list of computerized systems used at the site was reviewed and the following documents were spot-checked:

- Schedule for periodic review of GxP computerized systems used at the QC laboratory for 2024.
- Schedule for periodic review of GxP Computerized System used at the QC laboratory for 2025.
- Annual computerized systems validation master plan (CSVMP).
- Periodic review of MYMES (the computerized system used during dispensing operations with related electronic records attached to the BMRs) December 2023.

Process validation

Manufacturing operations were subject to extensive process validation prior to commercialization and prior to implementation of significant changes as guided by the validation master plan as well as the respective procedures. Example process validation documentations were reviewed as follows:

- Process performance qualification (PPQ) report of Bedaquiline Tablets 100 mg.
- Process performance qualification (PPQ) report of Linezolid Dispersible Tablets 150 mg.
- Process performance qualification (PPQ) report of Moxifloxacin Dispersible Tablets 100 mg.
- Packaging Validation Report of Clopidogrel/Acide Acetylsalicylique Mylan 75/75 mg.

5. Complaints

All complaints and other information concerning potentially defective products were carefully reviewed in accordance with written procedures. Corrective actions were taken where applicable.

Written procedures describing the action to be taken, including the need to consider a recall, in the case of a complaint concerning a possible product defect were in place.

The responsibility for complaints management including root cause investigations and CAPA as applicable was undertaken a number of staff at the QA department. The authorized person was made aware of any complaint, investigation or recall. In addition, the person responsible for QC was involved in the review of such investigations.

An impact assessment was performed for each complaint, evaluating both the affected and any potentially related batches. All decisions and actions taken in response to a complaint were documented and cross-referenced with the associated batch records.

Trending of complaints was conducted regularly by reviewing complaint records for any indications of specific or recurring issues requiring further attention.

The complaints management procedure included provisions for informing the competent authorities if Mylan Waluj FDF2 was considering action following possibly faulty manufacture, product deterioration, a suspect product or any other serious quality problems with a product.

The SOP for complaints was well-established and implemented. The procedure provided for complaints receipt, registration, acknowledgement, classification (triage), investigation, response and closure. The SOP also mandated the trending of received complaints on a regular basis with recording in a well-established trending report.

A register was available for complaints received by Mylan Waluj FDF2. The register was reviewed and few complaints were spot-checked.

In addition, the quarterly trend review (market complaints) quarter-IV (October to December- 2024) along with year-2024 (previous three quarters - January to September 2024) was reviewed.

6. Product recalls

A system was in place at Mylan Waluj FDF2 to promptly and effectively recall from the market any products known or suspected to be defective, when necessary.

A written procedure was established for the organization of any recall activity. Recall operations could be initiated promptly and were capable of reaching the required level within the distribution chain. The procedure included instructions for storing recalled products in a secure, and segregated area while awaiting a decision on their disposition. It also provided for the prompt notification of all competent authorities in the countries where the affected product batch had been distributed, informing them of the intention to recall the batch due to confirmed or suspected defects.

The authorized person was designated as the responsible person for the execution and coordination of recalls. The authorized person could readily access the distribution records which contained sufficient information on wholesalers and directly supplied customers to permit an effective recall.

The progress of the recall process, when applicable, was monitored and recorded. Records included the disposition of the product. A final report was needed to be issued, including a reconciliation between the delivered and recovered quantities of the products. The effectiveness of the recall arrangements was tested and evaluated through regular mock exercises, particularly in the absence of actual recall events.

The SOP for product recall and withdrawal was well-established and implemented. The procedure provided for actions for initiation, execution, effectiveness and closing or recall events as well as procedural guidance on mock recall.

The records of the last actual and mock recall were reviewed.

7. Contract production, analysis and other activities

This subject was not covered during the inspection due to time constraint. It is worth noting, though, that no production activities were contracted out by Mylan Waluj FDF2.

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

A system of self-inspection was established at Mylan Waluj FDF2 to evaluate the manufacturer's compliance with GMP in all aspects of production and QC. Self-inspections were performed routinely, and might be, in addition, performed on special occasions as the needed.

A procedure for self-inspection was in place, including provisions for an effective self-inspection follow-up programme. The team responsible for self-inspection consisted of personnel trained in and experienced with GMP. Arrangements were in place to prevent staff from self-inspecting their respective areas of work. All recommendations for corrective action were implemented.

Suppliers' audits and approval

The person responsible for QC had the responsibility, together with the quality unit, for approving suppliers who could reliably supply starting and packaging materials that meet established specifications. Before suppliers were approved and included in the approved suppliers' list or specifications, they were evaluated. The evaluation took into account the supplier's history and the nature of the supplied materials as well as an audit if required.

The SOP for vendor management was well-established and implemented. The list of approved suppliers at Mylan Waluj FDF2 was reviewed and the documentation related to the following suppliers was spot-checked.

- Audit report of packaging vendor.
- Audit report of API vendor.
- Audit tracker of printed packaging material suppliers.

9. Personnel

Mylan Waluj FDF2 had a well-established organization chart along with adequate number of personnel.

Key posts, including heads of production, the heads of quality, comprising the quality assurance and quality control functions, as well as the authorized person, were occupied by full-time personnel. The heads of production and quality were independent of each other.

Personnel at Mylan Waluj FDF2 had the necessary qualifications and practical experience to carry out all the manufacturing, including production and control, tasks. Individual responsibilities were clearly defined and understood by the persons concerned and recorded as written job descriptions. In general, the responsibilities placed on any one individual were reasonable and not so extensive as to present any risk to quality. Duties and functions could be delegated to designated deputies with a satisfactory level of qualifications; however, the responsibilities were not delegated. There were no gaps or unexplained overlaps in the responsibilities of personnel concerned with the application of GMP.

The heads of the production and the quality had their responsibilities dedicated from each other and also shared some responsibilities including authorization of written procedures and retention of records; monitoring and control of the manufacturing environment and plant hygiene; training, including the application and principles of QA; approval and monitoring of suppliers of materials; performance and evaluation of in-process controls; and monitoring of compliance with GMP requirements.

The organization chart of Mylan Waluj FDF2 was in-place. The organogram clearly indicated separation of production and quality functions. The job descriptions of the key personnel were reviewed including job descriptions of Head of OSD Quality, Head of OSD Site Operation, General Manager - Quality Assurance, Sr. General Manager - Quality Control, and General Manager - Quality Assurance.

All personnel were aware of the principles of GMP that affect them. This was ensured through initial onboarding training which included basic principles of GMP, including hygiene instruction.

Measures were in place to prevent unauthorized people from entering production, storage and QC areas.

Batch Release

A procedure was in place for the approval of the release of a finished batch for supply. According to the batch release procedure, the authorized person was responsible for compliance with technical and regulatory requirements related to the quality of finished products and the approval of the release of the finished product for supply. No batch of product was be released for supply prior to certification by the authorized person. The function of the approval of the release of a finished batch could be delegated to few designated persons who had appropriate qualifications and experience.

Approval of batches for release by the authorized person comprised checks and verification of the following:

- the marketing authorization (including provisions of the WHO prequalification) and the manufacturing authorization requirements for the product had been met for the batch concerned;
- the principles and guidelines of GMP had been followed;
- the principal manufacturing and testing processes have been validated;
- all the necessary checks and tests had been performed and account taken of the production conditions and manufacturing records;
- any planned changes or deviations in manufacturing or QC had been notified, including obtaining regulatory approval if needed, in accordance with a well-defined reporting system before any product was released.
- any additional sampling, inspection, tests and checks had been carried out or initiated, as appropriate, to cover planned changes and deviations;
- all necessary production and QC documentation had been completed and endorsed by supervisors trained in appropriate disciplines; and
- appropriate audits, self-inspections and spot-checks were carried out by experienced and trained staff.

The list of product batches released over the last 2 years was reviewed, and a few batch release records were spot-checked. In addition, the list and the criteria of a couple of release responsible persons dated was reviewed.

10. Training

Mylan Waluj FDF2 established a written training programme, based on a well-established procedure, for all personnel whose duties required them to enter manufacturing areas or control laboratories.

The training programme comprised initial training of newly recruited personnel as well as continuing training, including provisions for assessment of the training effectiveness periodically. The initial training of newly recruited personnel included basic training on the theory and practice of GMP and training relevant to the duties assigned to them. Specific training was given to personnel working in areas where contamination was a hazard (e.g., clean areas and areas where infectious materials were handled).

Training activities, including assessment of the effectiveness, were well documented and records of the same were available.

Visitors and untrained personnel were restricted from production and QC areas. If entry was necessary, they received prior instructions on personal hygiene and the prescribed protective measures (including clothing) and were closely supervised.

Consultant and contract staff were qualified for the services they provided and evidence of the same was included in the training records.

The SOP for training was well-established and implemented. The procedure provided for training planning and implementation including induction training, on-the-job training, refresher training on SOPs and external training.

11. Personal hygiene

Personnel underwent health examinations prior to and during employment, including periodic eye checks of personnel conducting visual inspections.

Training in personal hygiene was provided to all personnel, and a high level of personal hygiene was observed by all those concerned with manufacturing processes.

Personnel were instructed to wash their hands before entering production areas. Instructions and pictograms to this effect were posted and complied with.

Persons with apparent illness or open lesions that might adversely affect the quality of products were not allowed to handle starting materials, packaging materials, in-process materials or finished products.

Direct hand contact with materials and products was avoided (please refer to the observation made during the tour of the production areas and the corrective action made by the manufacturer during the course of the inspection, as detailed below in section 16).

Personnel wore clean body coverings appropriate to the duties they perform, including appropriate hair coverings. Used reusable clothes were stored in separate closed containers until properly laundered and disinfected. Personal hygiene procedures, including the wearing of protective clothing, applied to all persons entering production areas including supervisors, visitors and inspectors.

Smoking, eating, drinking, chewing, and keeping plants, food, drink, smoking material and personal medicines were not permitted in production, laboratory and storage areas.

The SOP for personal hygiene, and the SOP for medical checkup were implemented.

12. Premises and utilities

In general, the premises were appropriately located, designed, constructed, adapted, and maintained to suit the operations being carried out.

The layout, design, and construction of the premises minimized the risk of errors, enabled effective cleaning, sanitation, and maintenance, and thereby helped prevent cross-contamination and reduced the accumulation of dust or dirt. Where dust was generated (e.g. during sampling, weighing, mixing and powder processing operations), measures were taken to avoid cross-contamination and facilitate

cleaning in the form of design and equipment controls (e.g., negative pressure of process rooms in relation to the common corridor, dust collectors, use of personal protective equipment [PPE]) and procedural controls (e.g., campaign production, SOPs along with personnel training). In general, the design of the premises ensured the logical flow of materials and personnel which some exceptions which were controlled through procedural controls. Electrical supply, lighting, temperature, humidity and ventilation were appropriate and did not adversely affect, directly or indirectly, either the pharmaceutical products during their manufacture and storage, or the accurate functioning of equipment.

Premises were carefully maintained, in such a way that repair and maintenance operations did not present any hazard to the quality of products.

Premises were cleaned and disinfected according to detailed written procedures. Cleaning records were maintained. Premises were designed and equipped so as to afford maximum protection against the entry of insects, birds or other animals. There was a programme for pest control including relevant procedure and records.

In general, the premises were well designed and maintained, providing measures to reduce the risks of contamination and cross-contamination. Operators at the production areas, particularly those where dust is generated (e.g., compaction, sieving and compression rooms), were supported with filtered breathing air respirator for safety reasons.

All production, quality control, storage/warehousing, and utilities areas were visited during the inspection, on several occasions over all days of the inspection. As part of these visits, the following layouts were reviewed:

- Drawing of Plot Plan,
- General Schematic Drawing of Room Name & Room Number for QA/QC Block First Floor,
- General Schematic Drawing of Room Name & Room Number for Solid Dosage Ground Floor Area,
- General Schematic Drawing of Room Name and Room Number for Warehouse Ground Floor, and
- General Schematic Drawing of Room Name and Room Number for QA/QC Block Ground Area.

Ongoing production and quality control operations were witnessed including spot-checks of the following documents:

- Batch Record for dabigatran etexilate capsules 150mg.
- Batch Packaging Record for clopidogrel and acetylsalicylic acid tablets 75/75mg.
- Column usage record of HPLC equipment.
- Daily balance verification record of balance at the QC laboratory.
- Media preparation and quality control log.
- Incubator usage log.

The WHO prequalified products were manufactured at defined production areas. These areas were visited where actual production operations of few products were observed namely Darunavir Tablets 600mg (granulation process), lamivudine and Zidovudine Tablets USP 150/300mg (compression

process). The layouts showing personnel and materials flows as well as zoning and pressure differentials of these areas were reviewed.

Indeed, the production block comprised of several process rooms including:

- Wet granulation (7 process rooms)
- Compaction (4 process rooms)
- Wurster coating (Pellets) (7 process rooms)
- Blender (10 process rooms)
- Tablet compression (12 process rooms)
- Encapsulation (3 process rooms)
- Coating (11 process rooms)
- Packaging Line for bottles (3 process rooms)
- Packaging Line for blisters (7 process rooms)
- Packaging of bulk shipment packs (1 process room)

The SOP for cleaning and sanitization of process room/other manufacturing area was in place.

Ancillary areas

Rest and refreshment rooms were separate from manufacturing and control areas. Facilities for changing and storing clothes and for washing and toilet purposes were easily accessible and appropriate for the number of users. Toilets were not directly connected to production or storage areas.

Maintenance workshops were separated from production areas. Parts and tools were stored in designated and dedicated rooms or lockers in the production areas.

Storage areas

Storage areas were of sufficient capacity and allowed orderly storage of the various categories of materials and products with proper separation and segregation: starting and packaging materials, intermediates, bulk and finished products, products in quarantine, and released, rejected, returned or recalled materials and products. Highly active materials, narcotics, other dangerous substances presenting special risks of abuse, fire or explosion were stored in safe and secure areas.

Storage areas were clean, dry, sufficiently lit and maintained within acceptable temperature limits. Storage conditions (e.g. temperature, humidity) were provided, controlled, monitored and regularly recorded.

Receiving and dispatch bays were separated from each other and protected the materials and products from the weather. Receiving areas were designed and equipped to allow containers of incoming materials to be cleaned before storage.

Quarantine areas were clearly marked and their access restricted to authorized personnel. Special attention was paid to sampling and the safe and secure storage of printed packaging materials.

There were separate sampling areas, equipped with sampling booths, for starting materials which enabled sampling to be conducted in such a way as to prevent contamination or cross-contamination.

Weighing and dispensing areas

Separate weighing areas were available at the production suite and were used for the weighing of starting materials including APIs and excipients. The weighing areas were properly designed, operated and maintained for the intended use, including for example, provisions for dust control (e.g., dispensing booths) and were supported with a computerized system to manage dispensing operation. Printouts of the electronic records of the latter system were attached to BMRs.

Production areas

At Mylan Waluj FDF2, Premises were laid out in such a way as to allow the production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels. The interior surfaces of the production areas (walls, floors and ceilings) were smooth and free from cracks or open joints, should not shed particulate matter, allowing easy and effective cleaning and, if necessary, disinfection.

No manufacturing operations of highly active products, such as some antibiotics, hormones, cytotoxic substances and certain non-pharmaceutical products, were conducted in the facilities of Mylan Waluj FDF2.

Supporting utilities

Heating, ventilation and air-conditioning (HVAC)

HVAC systems were inspected where few AHUs were visited and spot-checked for cleanliness and calibration status of monitoring devices. In addition, the following procedures related to HVAC systems operations along with environmental monitoring of the production areas were reviewed:

- SOP on Monitoring and Cleaning of HVAC Filters, Dust Collector Filters & Equipment Filters.
- Summary for trend analysis report of environmental monitoring program (January – December 2024).
- Summary for trend analysis report of air sampling monitoring method (April – June 2024).
- SOP on microbial monitoring of OSD areas.
- Microbial monitoring location list.
- Microbial monitoring location for settle plate and air sampling method.

Water for pharmaceutical use

The SOP on monitoring of water quality along with Water Trends 2024 were reviewed and provided evidence of the proper operation and quality of the water for pharmaceutical use utilities.

13. Equipment

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

Non-dedicated equipment was cleaned according to validated cleaning procedures between being used for production of different pharmaceutical products to prevent cross-contamination.

An example of equipment qualifications was spot-checked (performance qualification report of blister packing machine).

14. Materials

Materials were properly managed at Mylan Waluj FDF2 in terms of receipt, quarantine, testing, storage, release and dispensing. An enterprise resource management programme was used for materials management, including provisions for quarantine and release.

Dedicated materials sampling areas were available at the raw materials warehouse while dispensing was performed at dedicated dispensing areas at the production suite.

15. Documentation

Documentation was covered as part of the inspection of other GMP elements/subjects. In general, good documentation practices were implemented at Mylan Waluj FDF2. Documents in the form of specifications and testing procedures of starting materials, intermediates and finished products; master formulae; packaging instructions; batch manufacturing records; batch packaging records and SOPs were approved, signed and dated by the appropriate responsible persons with unambiguous contents. Documents were regularly reviewed and kept up to date.

16. Good practices in production

Production operations, including receipt and cleaning, quarantine, sampling, storage, dispensing and labelling, processing and packaging followed clearly defined procedures in accordance with the applicable manufacturing and marketing authorizations as well as WHO prequalification provisions and commitments. Deviations from instructions or procedures were documented, investigated and decided upon, including provisions to extend the investigation to other batches of the same product and other products that might have been associated with the specific deviation.

Access to production premises was restricted to authorized personnel. No non-medicinal products were produced onsite.

Production records were reviewed as part of the approval process of batch release before transfer to the authorized person.

Prevention of cross-contamination and bacterial contamination during production

Cross-contamination should be avoided by taking appropriate technical or organizational measures including conducting campaign production followed by appropriate cleaning and line clearance following validated procedures; providing appropriately designed airlocks, pressure differentials, and air supply and extraction systems; wearing protective clothing and personal protective equipment (PPE); using validated cleaning and decontamination procedures; and using cleanliness status labels on equipment.

Production areas where susceptible products were processed underwent periodic environmental monitoring (e.g. for microbiological and particulate matter).

Processing operations

Before the start of any processing operation, area clearance was made to ensure the work area and equipment were clean and free from any starting materials, products, product residues, labels or documents not required for the operation.

After use, production equipment was cleaned without delay (within a limit established through dirty equipment holding time [DEHT]) according to validated cleaning procedures and kept under clean and dry conditions. Time limits for storage of equipment after cleaning and before use was established according to validated clean equipment holding time (CEHT).

Packaging operations

Different products were packaged in areas of close proximity with physical segregation. Area/line clearance was always performed before the beginning of packaging operations. The area/line clearance was performed according to a well-established procedure and checklist, and the clearance operations was documented in the respective records. The name and batch number of the product being handled was displayed at each packaging line.

Online verification of all labels by automated electronic means were in place and checks were made to ensure that any electronic code readers, label counters were operating accurately. In addition, regular online in-process control of the product during packaging was implemented.

Checks on yields and reconciliation of packaged quantities were carried out to ensure that there were no discrepancies outside acceptable limits. Any significant deviation from the expected yield was recorded and investigated. Upon completion of a packaging operation, any unused batch-coded packaging materials were destroyed and the destruction recorded.

The batch manufacturing records, batch packaging record and analytical records of the following batches were spot-checked:

- Darunavir tablets 600mg
- Darunavir tablets 600mg
- Tenofovir and Lamivudine tablets 300mg/300mg
- Tenofovir and Lamivudine tablets 300mg/300mg
- Clopidogrel/salicylic acid tablets 75mg/75mg
- Clopidogrel/salicylic acid tablets 75mg/75mg

A number of procedure and records related to production operations were reviewed, including:

- SOP on In-Process Control
- SOP on In-Process Parameters Monitoring
- SOP on Safety mechanism challenges during packaging

17. Good practices in quality control

The quality control was independent from production at Mylan Waluj FDF2. The QC operations were under the authority of a person (Head QC) with appropriate qualifications and experience.

QC was in charge of sampling, inspecting, and testing starting materials, packaging materials, and intermediate, bulk, and finished products, and for monitoring environmental conditions for GMP purposes. Other QC responsibilities included establishing, validating and implementing all QC procedures; evaluating, maintaining and storing reference standards for substances; monitoring of the stability of the active pharmaceutical ingredients and finished products; and participation in other quality related activities as needed (e.g., QRM, investigation of complaints).

Adequate resources were available to ensure that all the QC arrangements were effectively and reliably carried out, including adequate facilities, trained personnel and approved procedures.

Samples of starting materials, packaging materials, intermediate products, bulk products and finished products were taken by methods and personnel approved by the QC department.

Sufficient samples of starting materials and finished products were retained to permit future examination of the product if necessary. The retained samples of finished products were kept for the appropriate time in their final pack.

In-process control
In-process control records were maintained and formed a part of the batch records.

Finished products
There was an appropriate laboratory determination of satisfactory conformity to predetermined specification prior to release of the finished product. Products failing to meet the established specifications or any other relevant quality criteria were rejected.

Retention/control samples
Retention (also called controlled) samples from each batch of finished product were kept, in their final containers, for at least one year after the expiry date.

Samples of active starting materials were retained for at least one year beyond the expiry date of the corresponding finished product.

Retention samples of materials and finished products were of a size sufficient to permit at least two full re-examinations.

Stability studies
The QC laboratory evaluated the quality and stability of finished pharmaceutical products. A written programme for ongoing stability determination was developed and implemented. Stability was determined prior to finished product marketing and following any significant changes, for example, in materials, processes, equipment or primary packaging materials.

The following documents and procedures, along with associated records, were reviewed:

- The SOP on in-process and finished product sampling.
- In process specification of Tenofovir Disoproxil Fumarate & Lamivudine Tablets 300/300 mg.
- The SOP on microbial enumeration test.
- Analytical data of darunavir Tablets 600 mg.
- Analytical data of tenofovir disoproxil fumarate & lamivudine tablets 300/300 mg.
- The SOP on procedure for receipt, issuance, use and rejection of HPLC Columns.

Several reference and working standards were used in varying quality control testing activities. In order to manage such standards, the SOP for management of analytical standards was in place. The procedure provided, among others, the general considerations and requirements for pharmacopoeial reference standards, in-house reference standards, working standards, as well as storage and issuance of these standards. The SOP also guided the use of impurity standards, solvent standards, and

calibration standards. Disqualification of standards was also addressed in the SOP. The following related records were spot-checked:

- Protocol and report for Darunavir working standard qualification.
- Protocol and report for Zidovudine working standard qualification.

The SOP for laboratory investigation report (LIR) was reviewed and few laboratory incidents were spot-checked.

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, ***Mylan Laboratories Limited*** located at ***Plot No H12 & 13 MIDC, Waluj Industrial area Chhatrapati Sambhajinagar (Formerly known as Aurangabad) Maharashtra 431 136 India*** was considered to be operating at an acceptable level of compliance with WHO good manufacturing practices for pharmaceutical products 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 GMP 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-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
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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 TRS No. 957, Annex 2
   https://www.who.int/publications/m/item/annex-2-trs-957

3. 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/publications/m/item/trs1010-annex9

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
Short name: WHO TRS No. 1033, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-1033

5. 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
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6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052), Annex 4.
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7. 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 3.
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https://www.who.int/publications/m/item/trs957-annex3

8. 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
https://www.who.int/publications/m/item/Annex-8-trs-1010

9. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2.
Short name: WHO TRS No. 1019, Annex 2
https://www.who.int/publications/m/item/trs1019-annex2

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 4
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf

11. WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
Short name: WHO TRS No. 1044, Annex 2
https://www.who.int/publications/m/item/trs1044-annex2

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***
https://www.who.int/publications/m/item/trs943-annex3

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
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Short name: WHO TRS No. 981, Annex 2
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Short name: WHO TRS No. 981, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-981

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
https://www.who.int/publications/m/item/tr961-annex14

17. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3.
Short name: WHO TRS No. 1019, Annex 3
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https://www.who.int/publications/m/item/trs992-annex4

19. 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**
https://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport

20. 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
https://www.who.int/publications/m/item/trs992-annex5

21. WHO Recommendations for quality requirements when plant – derived artemisinin 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
https://www.who.int/publications/m/item/trs-992-annex-6

22. 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.
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23. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
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27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3.
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