World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Prequalification Unit Inspection services
WHO INSPECTION REPORT
(WHOPIR)
Desk Assessment of Finished Product Manufacturer

Part 1	**General information**	
Company information		
Name of Manufacturer	Merck S. A. de C.V. (Naucalpan de Juárez)	
Corporate address of manufacturer	Merck S. A. de C.V. (Naucalpan de Juárez) Calle 5, No 7 Fracc. Industrial Alce Blanco Naucalpan de Juárez, 53370 Mexique	
Inspected site		
Name & address of manufacturing site	Merck S. A. de C.V. (Naucalpan de Juárez), located at Calle 5, No. 7, Fraccionamiento Industrial Alce Blanco, Naucalpan de Juárez, C.P. 53370, Mexico	
Production Block/Unit	Non sterile dosage forms Biological products	
Desk assessment details		
Date of review	13 July 2022	
Products covered by this desk assessment	NT013 Praziquantel Tablet, Film-coated 600mg (under Assessment)	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments**	
USA FDA	Dates of inspection:	4 to 8 April 2022
	Type of inspection:	GMP
	Block/Unit:	N/A
	Type of products/Dosage forms covered:	Tablets
German Health Authority (RPDA Hessen, De)	Dates of inspection:	1, 8, 17 March 2021 plus documentation review prior to these dates.
	Type of inspection:	Virtual
	Block/Unit:	Non sterile OSD
	Type of products/Dosage forms covered:	Tablets

Part 3	**Summary of the last WHO inspection**
Date and conclusion of most recent WHO inspection	None
Abbreviations	**Meaning** (Delete abbreviations that do not apply to your type of report or add additional ones if needed)
AHU	Air handling unit
API	Active pharmaceutical ingredient
BMR	Batch manufacturing record
BPR	Batch production record
CAPA	Corrective and preventive action
CC	Change control
FPP	Finished pharmaceutical product
GMP	Good manufacturing practices
NC	Non-conformity
NRA	National regulatory agency
PQR	Product quality review
PQS	Pharmaceutical quality system
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
SMF	Site master file
SOP	Standard operating procedure

Part 4	Summary of the assessment of supporting documentation

a) List of all regulatory inspections performed in the last 5 years and their outcomes:

Name of Authority	Jurisdiction	Dates	Scope	Type of inspection	Outcome	Report is available (yes or no)
DIGEMID	Peruvian Health Authority	21May18 to 25May18	GMP certification renewal. Good Manufacturing Practices for non-sterile and non-betalactamic solids (tablets and coated tablets) and sterile and non-betalactamic liquids (parenteral solution) Hormone oral solids, oral solids, liquids, and Sterile liquids. Good Laboratory Practices in Physicochemical and microbiology Laboratories.	Onsite	Approved	Yes
Regierungspräsidium Darmstadt	German Health Authority	04 to 07Sep18 & 10 to 11Sep18	GMP certification renewal. Manufacturing, packaging, labelling, testing and release of Levothyroxine tablets (Hormone oral solids).	Onsite	Approved	Yes
COFEPRIS	Mexican Health Authority	03Dic18 To 07Dic18	GMP certification of expanded areas of syringes (filling line for sterile liquids). Quality Management System, qualification/validation status of areas, equipment, critical systems, computerized systems, analytical methods, personnel, cleaning, and sanitization.	Onsite	Approved	Yes
COFEPRIS	Mexican Health Authority	26Aug19	GMP certification renewal. Manufacturing, packaging, labelling, testing and release of Hormone oral solids, oral solids, liquids, and Sterile liquids.	Onsite	Approved	Yes
COFEPRIS	Mexican Health Authority	02Mar20 to 06Mar20	GMP general conditions and Manufacturing License update to remove from the scope decommissioned areas: cephalosporine oral solids and other oral solids, and powder for reconstitution.	Onsite	Approved	Yes
INVIMA	Colombian Health Authority	03Mar21 to 30Apr21	GMP and GLP certification renewal. Manufacturing, packaging, labelling, testing and release of Sterile liquids (corticoids and common), non-Sterile solids (Thyroid hormones and common) and non-Sterile liquids (common solutions and suspensions).	Desk assessment	Waiting for onsite inspection dates	No
Regierungspräsidium Darmstadt	German Health Authority	01Mar21 to 17Mar21	GMP certification renewal. Manufacturing, packaging, labelling, testing and release of Euthyrox tablets and Euthyrox new formulation tablets as Finished Product and Bulk Product (Hormone oral solids).	Virtual	Approved	Yes
COFEPRIS	Mexican Health Authority	06Apr21 to 08Apr21	GMP general surveillance. Legal and technical documentation, GMP site conditions, computerized systems, Dolo Neurobion (multivitamin) product.	Onsite	Approved	Yes
ANVISA	Brazilian Health Authority	23Aug21	GMP certification renewal. Manufacturing, packaging, labelling, testing and release of Non- Sterile Solids: Tablets, and Non-Sterile Solids (Bulk (Intermediate)): Coated Tablets and Sterile products: low volume parenteral solutions with aseptic preparation.	Desk assessment	Approved	No (Only GMP certificate available)
COFEPRIS	Mexican Health Authority	25Oct21	GMP general surveillance. Legal and technical documentation, GMP site conditions, traceability of Deflox drops product (due to a counterfeit Merck reported to COFEPRIS).	Onsite	Approved	Yes

b) Manufacturing authorization granted by national authorities:

GMP certification and GMP License

c) Site master file:

Generally acceptable

d) Most recent product quality review(s) (PQR)(s) of the concerned WHO product(s):

Not submitted. New product formulation. PQRs will be done annually after validation and commercialization.

e) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s):

Not submitted

f) Master batch manufacturing and packaging record(s) of the product(s) of interest:

Not submitted

g) Recalls in the past three years related to products with quality defects:
None

h) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product(s) has been performed and all matters dealt with:
Not submitted, however regulatory inspections done and completed with favorable outcome including PIC/S members.

i) Copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide the product:
N/A

j) Out-of-stock situations:
None

k) Additional documents submitted:
Analytica data

Part 5	Conclusion – Desk assessment outcome

Based on the GMP evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The site ***Merck S. A. de C.V. (Naucalpan de Juárez),*** located at ***Calle 5, No. 7, Fraccionamiento Industrial Alce Blanco, Naucalpan de Juárez, C.P. 53370***, ***Mexico*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

Part 6	List of guidelines referenced in this 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**
   https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

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**
   untitled (digicollections.net)

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://digicollections.net/medicinedocs/documents/s23457en/s23457en.pdf

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
9789240020900-eng.pdf (who.int)

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
https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

6. 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://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

7. 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
https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

8. 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 TRS No. 961, 957), Annex 1
https://digicollections.net/medicinedocs/documents/s18681en/s18681en.pdf

9. 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.
Short name: WHO TRS No. 957, Annex 3
https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

10. 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
https://digicollections.net/medicinedocs/documents/s19959en/s19959en.pdf

11. 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
https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

12. 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://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

13. 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://digicollections.net/medicinedocs/#d/s21438en

14. 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
https://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

15. 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
https://digicollections.net/medicinedocs/#d/s20177en/

16. 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
https://digicollections.net/medicinedocs/#d/s20175en/

17. 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

18. 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**
https://digicollections.net/medicinedocs/documents/s23697en/s23697en.pdf

19. 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

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**
Essential Medicines and Health Products Information Portal (digicollections.net)

21. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4. **Short name: WHO TRS No. 1033, Annex 4**
9789240020900-eng.pdf (who.int)

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

24. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning 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://digicollections.net/medicinedocs/documents/s23699en/s23699en.pdf

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2. **Short name: WHO TRS No. 1033, Annex 2**
9789240020900-eng.pdf (who.int)

26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6. **Short name: WHO TRS No. 1025, Annex 6**
9789240001824-eng.pdf (who.int)

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. **Short name: WHO TRS No. 1025, Annex 3**
https://www.who.int/publications-detail/978-92-4-000182-4

28. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4. **Short name: WHO TRS No. 1025, Annex 4**
https://www.who.int/publications-detail/978-92-4-000182-4