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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT

Desk Assessment of Finished Product Manufacturer

Part 1	**General information**
Company information	
Name of Manufacturer	ACME Formulation Pvt. Ltd
Corporate address of manufacturer	N/A
Inspected site	
Name & address of manufacturing site	**Acme Formulation Pvt. Limited** Ropar Road, Nalagarh, Distt. Solan Himachal Pradesh - I74101, India D-U-N-S:67-739-1975 GPS coordinates: Latitude: "N 31° 2' 40.411" Longitude: E 76° 42' 17.245"
Synthetic Unit/Block/Workshop	Hormone Block
Manufacturing license number	Forms 25 & 28 MNB705/101 & MB/05/102, valid till 13.02.2025
Desk assessment details	
Start and end dates of review	31 May – 4 June 2021
Products covered by this desk assessment	**Finished Pharmaceutical Product** / **Prequalification status** Misoprostol Tablet 200mcg / Prequalified
List of documents submitted	1. SMF and Annexures 2. National Institute of Pharmacy and Nutrition, Hungary Inspection report and related CAPAs 3. EU GMP certificate 4. List of Regulatory Authority inspections 5. List of products manufactured at site 6. GMP certificate 7. List of Product permission 8. Manufacturing License 9. PQR January 2020 – December 2020 10. Environmental monitoring trend data January 2020 – December 2020 11. Purified water trend data January 2020 – December 2020 12. BMR Misoprostol Tablet 200mcg 13. BPR Misoclear (Zambia) 14. Analytical raw data Misoclear (Zambia) 15. Declaration: self-inspection 16. Declaration: product recall, warning letters, out of stock, upcoming inspections 17. Master BMR Misoprostol Tablet 200mcg 18. Master BPR Misoclear (Zambia)

	19. SOP "Product Quality Review"	
Part 2	**Summary of SRA/NRA inspection evidence and comments**	
OGYEI National Institute of Pharmacy and Nutrition, Hungary	Dates of inspection:	15-19 July 2019
	Type of inspection:	Product specific, general GMP inspection
	Block/Unit/Workshop:	Hormone Block
	Type of products/Dosage forms covered:	Misoprostol Tablet 200mcg
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	Last WHO on-site routine inspection was performed 17-19 January 2018 Initial conclusion 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, a decision on the compliance of Acme Formulation Pvt. Ltd. (Hormone Block), Ropar Road Nalagarh Dist. Solan Himachal Pradesh, 174101 India with WHO GMP guidelines will be made after the manufacturer's response to the observations hasbeen assessed. *Final conclusion* CAPAs were submitted and assessed by the PQT: Inspection Team and the inspection, following the review of the CAPA, was closed 15 June 2018 as compliant with the standards of GMP published by WHO.	
Brief summary of manufacturing activities as per SMF	Manufacturer of tablets and capsules, including sex hormones	
General information about the company and manufacturing site as per SMF	The Acme Group comprised of four sites, namely: Acme Formulation, Acme Generics, Immacule Lifesciences and Veritas Research. The latter was incorporated in 2017. Acme mostly provided contract manufacturing services to more than eighty clients. The company was founded in 2003 and the site in Nalagarh became operational in 2004. The Hormone Block was established in 2007 and in 2009 a new section was introduced for the manufacture of sex hormone products. At the time of inspection, the company was phasing out production of levothyroxine and had planned the facilities to be converted and dedicated to manufacture of sex hormones. The Nalagarh facilities were located approximately 65Km from Chandigarh International Airport. ACME Formulation Pvt. Ltd, was established in 2004 in Nalagarh, Distt. Solan (Himachal Pradesh). Company had been licensed in February 2005 to manufacture formulations. Commercial production started in April 2005 with the production of tablets & capsules. The site is situated in Nalagarh, District, Solan, Himachal Pradesh at 0.2 Km from Ropar bypass road, connecting Nalagarh and is 65 km from Chandigarh International Airport. The site is situated in an open space with adequate field surrounding the factory.	

	The site has two separate manufacturing building as follows: • General Block For manufacturing General group Tablets & capsules. The company is primarily involved in manufacturing of tablets and capsules (General group) only on job work basis i.e. contract manufacturing. The drugs being manufactured are Anti-inflammatory, Analgesic, Anti-Histamine, Anti-pyretic, Anti-Bacterial, Hypoglycemic, Antihypertensive and other forms. • Hormone Block Company has introduced a Separate and dedicated Hormone products manufacturing block in year 2007 in the same premises. In 2009 a section was created for the manufacturing and packing of female Sex Hormone Products.
Focus of the last WHO inspection	Production and quality control of Misoprostol tablet 200mcg
Areas inspected	Pharmaceutical quality system • Product quality review • Quality Risk Management • Change and deviation management • CAPA management • OOS Good manufacturing practices for pharmaceutical products Sanitation and hygiene Qualification and validation Complaints Product recalls Contract production, analysis and other activities Self-inspection, quality audits and suppliers' audits and approval Personnel Training Personal hygiene Premises Equipment Materials Documentation Good practices in production Good practices in quality control Document reviewed including but not limited • Quality Manual - Management Review • Organization Chart • Job descriptions for key personnel • Responsibilities of the quality units and production • Complaints and Recalls • Deviation control and change control • Material release • Validation and qualification • Equipment calibration • Data integrity • Sampling and testing of materials

	• Batch processing records • Materials management system • Purified water system • Heating, Ventilation and Air conditioning system Site visited: • Hormone Block • QC laboratories including chemical and microbiological • Starting material and finished goods warehouse
Out of scope and restrictions (last WHO inspection)	Products not submitted to WHO for Prequalification
WHO products covered by the last WHO inspection	Misoprostol tablet 200mcg
Abbreviations	**Meaning**
BMR	Batch manufacturing record
BPR	Batch production record
CAPA	Corrective and preventive action
CC	Change control
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
SOP	Standard operating procedure

Part 4	**Summary of the assessment of supporting documentation**

a) Manufacturing authorization and GMP certificate granted by the local authority:
Forms 25 & 28 MNB705/101 & MB/05/102, issued by Health and Family Welfare Department Himachal Pradesh, valid till 13.02.2025

GMP certificate HFW-H (Drugs) 10/2005 (Vol-VII), issued by Health and Family Welfare Department Himachal Pradesh, valid till 13.02.2023

b) Site master file (SMF):
SMF submitted and reviewed. SMF written according to the WHO TRS No. 961, Annex 14

c) List of all the FPPs manufactured on-site:

Sr. No.	Total Number of Products: 405 General block	
	Therapeutic groups	**Number of products**
01	Analgesic	150
02	Cardiovascular	50
03	Enzyme	20
04	Urinary Tract	20
05	Antacid/Gastrology	24
06	Anticold/Ant allergic	20
07	Antidiabetic	30
08	Antibiotics	25
09	Antifungals	05
10	Central Nervous	05
11	Vitamins and Iron Supplements	10
12	Erectile	08
13	Anti-Malaria	18
14	Peripheral Neuropathy	05
15	Anti-Asthmatics	02
16	Vasodilator	10
17	Anti Firinotytic	01
18	Anti-Platelet	02
19	Hormones	13

d) List of all regulatory inspections performed in the last 3 years:

Name of Regulatory Authority	Dates of inspection
Directions de la Pharmacie de Medicament & des Laboratoires, Ivory Coat	25/11/2016
Food, Medicine and Health care Administration and control authority, Ethiopia	28/04/2016 to 29/04/2016
National Agency for Food and Drug Administration and Control, Nigeria	11/01/2017 to 12/01/2017
Tanzania Food and Drugs Authority, Tanzania	16/11/2017 to 17/11/2017
Medicines Control Authority of Zimbabwe, Zimbabwe	07/07/2017 to 10/07/2017
National Institute for the Surveillance of Drugs and Food INVIMA, Columbia	06/11/2017 to 10/11/2017
The Republic of Sudan Federal Ministry of Health National Medicines and Poisons Board, Sudan	09/12/2017 to10/12/2017
Republic of the Philippines Department of Health, Philippines	14/02/2018 to 16/02/2018
Ministry of Health Guinea, Guinea	27/05/2019 to 28/05/2019
Ministry of Health Pharmacy and Poison Board, Kenya	13/12/2018 to 15/12/2018
Pharmacy, Medicines & Poisons Board Malawi, Malawi	04/03/2019
National Drug Authority, Uganda	14/11/2019 to 15/11/2019
Medicines Control Authority of Zimbabwe, Zimbabwe	08/03/2021 to 12/03/2021
National Institute of Pharmacy and Nutrition, Hungary	15/07/2019 to 19/07/2019
Health and Family Welfare Department, Himachal Pradesh, India	23/01/2020 to 24/01/2020

e) Most recent product quality review (PQR) of the concerned WHO FPP:
PQR Misoprostol Tablets 200 mcg January 2020 – December 2020 submitted and reviewed.

f) Batch manufacturing and packaging records, including the analytical part, for the most recently released batch of relevant FPPs:
Submitted and reviewed:
- BMR Misoprostol Tablet 200mcg
- BPR Misoclear (Zambia)
- Analytical raw data Misoclear (Zambia)

g) Master batch manufacturing and packaging records of the FPPs of interest:
Submitted and reviewed
- BMR Misoprostol Tablet 200mcg
- BPR Misoclear (Zambia)

h) Recalls in the past three years related to FPPs with quality defects:
Declaration submitted: no product recalls reported in the last 3 years

i) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the FPP has been performed and all matters dealt with:
Confirmation submitted: that a full self-inspection dedicated to the FPP has been performed and all matters dealt with

j) Copy of any warning letter, or equivalent regulatory action, issued by any authority for their market, to which the site provides or has applied to provide the API:
Declaration submitted: no warning letter, or equivalent regulatory action, issued

k) Out-of-stock situations:
Declaration submitted: no out-of-stock situation

l) Additional documents submitted:
SOP "Product Quality Review"

Part 5	**Conclusion – Desk assessment outcome**

Based on the previous WHO inspection and 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 **Acme Formulation Pvt. Limited Hormone Block**, located at ***Ropar Road, Nalagarh, Distt. Solan Himachal Pradesh - I74101, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

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

Part 6		**List of guideline**

1. 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**
http://www.who.int/medicines/publications/44threport/en/

2. 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**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

3. 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

4. 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

5. 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

6. 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. 957, Annex 1
http://www.who.int/medicines/publications/44threport/en/
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.
Short name: WHO TRS No. 957, Annex 3
http://www.who.int/medicines/publications/44threport/en/

8. 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

9. 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

10. 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

11. 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

12. 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

13. 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/

14. 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/

15. 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

16. 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

17. 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

18. 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.
Short name: WHO Multisource guidance or **WHO TRS No. 996, Annex 10**
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

19. 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/

20. 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

21. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
Short name: WHO TRS 1010, Annex 9
https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1

22. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Forth 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

23. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Forth 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

24. 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-Forth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6.
Short name: WHO TRS No. 1025, Annex 6
https://www.who.int/publications-detail/978-92-4-000182-4

25. Points to consider when including Health-Based Exposure Limits (HBELs) 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 1033, Annex 2**
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations¨

26. 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 1033, Annex 3**
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

27. 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 1033, Annex 4**
https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations