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Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Desk Assessment of Active Pharmaceutical Ingredient (API) Manufacturer

Part 1	**General information**
Company information	
Name of Manufacturer	Farmabios S.p.A.
Corporate address of manufacturer	Via Pavia 1, 27027 Gropello Cairoli, Pavia, Italy Tax Code (C.F.): 00180280182 Tel: +39 382 8191 Fax: +39 382 815886
Inspected site	
Name & address of manufacturing site	Via Pavia 1, 27027 Gropello Cairoli, Pavia, Italy GPS Coordinates: N45° 10.161'; E09° 00.198' DUNS: 428680078
Synthetic Unit/Block/Workshop	Oral steroids department RS10 Micronisation department RM01
Desk assessment details	
Date of review	16/06/2026
APIs covered by this desk assessment	Medroxyprogesterone Acetate, Grade: Sterile-micronized Note: this is supplied as a sterile API (however, micronization and gamma irradiation sterilization are performed by contract manufacturers, as approved in the dossier).
List of documents submitted	a. list of all regulatory inspections performed in the last 3 years and their outcomes. b. The full inspection reports, including deficiency letters, for inspections performed by a competent stringent regulatory authority in the past three years with a certified translated copy where this is not in English. c. Proof of CAPA implementation and final decision by the competent stringent regulatory authority (AIFA only). d. A copy of the manufacturing authorization and GMP certificate granted by the local national authority. e. Updated master site file whose approval date was not more than one year ago. f. The list of all the products including API manufactured onsite. g. The most recent product quality review (PQR) of the concerned products,

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	h. The completed Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s). i. The list of any recalls in the past three years related to any product manufactured on site with quality defects. j. A confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product has been performed and all matters dealt with. k. Master batch manufacturing and packaging records of the WHO product of interest. l. 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. m. Description of any recent or foreseen out-of-stock situations. n. A list of notifications of upcoming inspections by competent national regulatory authorities in the next 6 months. o. Table to specify which parts of the manufacturing process for the concerned product were covered by the inspection of the competent SRA authorities performed in the last 3 years.	
Any documents missing?	No documents were deemed to be missing.	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments**	
Agencia Italiana del Farmaco (AIFA)	Dates of inspection:	10th 14 March 2025
	Type of inspection:	General GMP inspection and for-cause inspection
	Block/Unit/Workshop:	Not specified.
	Type of APIs covered:	Manufacture of active substances (highly toxic products, hormones or substances with hormonal activity), by chemical synthesis (both sterile aseptically prepared and non-sterile), including micronisation activities. A large number of APIs were covered, including the API that was submitted for WHO prequalification.
Agencia Italiana del Farmaco	Dates of inspection:	20-24 November and 28-29 November 2023
	Type of inspection:	- General Review.

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(AIFA)		-Review of major changes
	Block/Unit/Workshop:	Not specified
	Type of APIs covered:	Manufacture of active substances (highly toxic products, hormones or substances with hormonal activity), by chemical synthesis (both sterile aseptically prepared and non-sterile), including micronisation activities. A large number of APIs were covered.
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The site was not previously inspected onsite by WHO. A desk assessment was performed in 2020 on the basis of SRA reports.	
Summary of manufacturing activities	- Manufacturing of API by chemical synthesis - Manufacturing of Sterile API aseptically prepared and gamma irradiated - Extraction of Active Substances from sources: purification, modification and extraction of substance from plant or animal - General finishing steps: drying, micronisation, primary and secondary packaging - - Quality control testing - Importation of API	
General information about the company and manufacturing site	Farmabios manufactures API of different markets, both human and veterinary use. It is authorized by AIFA to produce and import APIs for human use.	
Focus of the last WHO inspection	Not applicable.	
Areas inspected	Not applicable.	
Out of scope and restrictions (last WHO inspection)	Not applicable.	
WHO products covered by the last WHO inspection	The last desk assessment also focused on the medroxyprogesterone acetate API.	
Additional products to be covered by this	There are no additional products covered compared to the last desk assessment.	

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desk assessment:	
Abbreviations	**Meaning**
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 regulatory authority	Scope	Outcome
1	Italian Health Authority (AIFA) 28th February – 3rd March 2023	Authorization of new manufacturing building and new product	Satisfactory, CAPA closed and accepted.
2	Italian Health Authority (AIFA) 20th-24th November And –28th-29th November 2023	General GMP inspection, verification of compliance to Annex 1 (sterile manufacturing area), authorization of equipment and manufacturing areas.	Satisfactory, CAPA plan closed and accepted.
3	Italian Health Authority (AIFA) 10th-14th	General GMP inspection, authorization of	Satisfactory, CAPA closed and accepted.

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	March 2025	equipment, manufacturing areas and new products.	

b) Manufacturing authorization and GMP certificate granted by national authorities:
Certificate of GMP Compliance issued by the Italian Medicines Agency (AIFA) on 05th December 2025. The certificate remains valid for a maximum period of 36 months from the date of inspection (14 March 2025).

The following note of relevance to the WHO API, was included at the bottom of the GMP certificate registered in the EudraGMDP database:
"Terminal sterilization by gamma irradiation is outsourced for Medroxyprogesterone acetate sterile, Triamcilonone esacetonide sterile and, as alternative to the sterile filtration, even for Beclometasone dipropionate sterile. According to Italian legislation, all the sterile active substances and/or biological active substances and/or active substances deriving from human and animal tissues, organs, fluids are authorized according to art. 40 of Dir. 2001/83/EC and the production process is performed in accordance with the EU-GMP, including its Annex 1, as laid down in Dir. 2003/94/EC. On a risk-based approach, the validity of the GMP certificate for this manufacturing site is not more than 36 months from the latest general GMP inspection conducted on 2025/03/14, except for AIFA's re-evaluation of the risk profile."

c) Site master file:
A detailed Farmabios Site Master File was submitted and subsequently reviewed.
The Site Master File is comprehensive and well-structured, covering all essential aspects of Farmabios S.p.A.'s operations, including company profile, authorized manufacturing activities, quality management system, personnel, premises, equipment, production, and quality control. It demonstrates a robust and independent quality framework, supported by clear SOPs, validated processes, and consistent GMP inspection outcomes. Overall, the document is complete, detailed, and provides a reliable reference for regulatory and inspection purposes."

d) List of all the products and dosage forms manufactured on-site:
The Site Master File notes that Medroxyprogesterone Acetate is produced in shared manufacturing lines (Oral Steroids Department RS10 and Micronisation Department RM01).
Regarding the list of different products manufactured onsite: AIFA inspection reports demonstrate that effective measures against cross-contamination are in place and have been verified during inspection. In particular, the RS40 department employs glove-box loading for raw materials and closed-loop solvent transfer systems, both specifically designed to mitigate contamination risks. Furthermore, both the Site Master File and the AIFA report highlight GMP safeguards such as validated cleaning procedures, independent air-handling systems, negative-pressure rooms, and controlled material flows, all of which ensure robust protection against cross-contamination.

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO product(s):
Product Quality Review (PQR) for Medroxyprogesterone Acetate Micronised Sterile was submitted. A significant number of batches were manufactured during the period. No batches were reprocessed or reworked, and no recalls were reported.

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Two Out-of-Specification (OOS) results, which were not confirmed, were reported in this PQR. One OOS case was attributed to Impurity B, which exceeded the specified limit of 0.5% in six batches. These batches were subsequently reviewed and re-analyzed, and the results were confirmed to be within specification. The OOS was determined to have resulted from improper sample handling, leading to potential degradation.

Another OOS case was reported concerning chromatographic peaks that could not be evaluated during batch analysis. The investigation identified instrumental defects in the HPLC system, which were subsequently corrected. Additionally, one batch was found to have an unevaluable peak due to contamination of the vial used during analysis; this issue was addressed and resolved.

Two justified complaints were reported in the product quality review. One claim concerned a brown spot observed on a thermosealed coupled bag. The investigation traced the issue to human error during final visual checks at the PE bag manufacturer. Corrective actions were implemented, including operator training and the placement of QA-issued signage in the packaging room to highlight cosmetic defects. As the affected batch had been packed earlier in June 2022, prior to these measures, no further CAPA was required. The defect was classified as cosmetic, with no impact on the quality of the API.

There were 5 returns batches due to commercial reasons. These batches were scheduled to be reprocessed following commercial return, in order to meet different micronization specifications requested by the customer. The reprocessing activity has not yet been scheduled when this desk assessment was assessed.

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

Batch manufacturing and packaging record(s), including the analytical part of the last commercial batches of the PQ products were submitted.

The batch manufacturing, micronisation, packaging, and analytical records for Medroxyprogesterone Acetate Micronized Sterile (WHO PQ product) are complete, detailed, and fully aligned with GMP expectations. The documents cover the entire production cycle — from synthesis and unmicronized batch processing, through micronisation in controlled areas, to final analytical release testing. They include critical process parameters, in-process controls (IPC), environmental checks, validated cleaning and equipment readiness steps, and comprehensive QC data (identity, purity, assay, particle size distribution, sterility, endotoxins, residual solvents).

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

well, -structured, and fully aligned with GMP documentation standards. It details each stage of synthesis and processing, including raw material charging, reactor preparation, inertization, controlled agitation, temperature monitoring, filtration, and in-process controls (UV checks, IPC conformity assessments). The record also specifies allowable variations in reagent quantities, operator sign-offs, and equipment readiness checks, ensuring traceability and reproducibility

h) If any of the products are sterile, the completed batch records for the most recent media fill validation that is relevant to the product(s) of interest and report on its outcome:

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The company confirmed that the sterilization step for Medroxyprogesterone Acetate, Sterile-micronized use Gamma radiation is performed at a contracted facility therefore media fill validation is not relevant.

i) Recalls in the past three years related to products with quality defects:
The company provided a statement confirming that no recalls have taken place on site for the last three years.

j) 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:
A letter was submitted confirming that self-inspections had been conducted, along with external inspections performed by customers.

k) 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:
The company confirmed that no warning letters have been issued by any regulatory authorities against the site until the application for desk assessment was submitted.

L) Out-of-stock situations:
The company declared that no out-of-stock situation is foreseen for WHO PQ products.

m) A list of notifications of upcoming inspections by competent national regulatory authorities in the next 6 months;
The company confirmed that no notifications have been received regarding any upcoming inspections in the next six months.

n) Additional documents submitted:
The company submitted a list of blocks/workshops used to manufacture the WHO API and a list of areas and products covered by the AIFA inspection. The company also stated that Medroxyprogesterone acetate is manufactured on shared production lines, specifically within the Oral Steroids Department (RS10) and the Micronisation Department (RM01).

Additional information was submitted in support of the resolution of issues from the last AIFA inspection.

Part 5	**Conclusion – Desk assessment outcome**

Based on the previous WHO desk assessment 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 ***Farmabios S.p.A.*** located at ***Via Pavia, 1, 27027 Gropello Cairoli, Pavia, Italy*** 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 guidelines referenced in this inspection report**

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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***
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 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://www.who.int/publications/m/item/trs-1025-annex-4

5. 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 1019, Annex 3
https://www.who.int/publications/m/item/trs1019-annex3

6. 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

7. 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.
Short name: WHO TRS No. 1052, Annex 4

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3
   https://www.who.int/publications/m/item/trs957-annex3

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 2.
   Short name: WHO TRS No. 1044, Annex 2
   TRS 1044 - 56th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
    Short name: WHO TRS No. 1044, Annex 4
    TRS 1044 - 56th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9.
    Short name: WHO TRS No. 961, Annex 9
    https://cdn.who.int/media/docs/default-source/medicines/norms-and standards/guidelines/distribution/trs961-annex9-modelguidanceforstoragetransport.pdf?sfvrsn=b80e925f_5

12. 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

13. 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

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
    Short name: WHO TRS No. 981, Annex 2

https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs981-annex2-who-quality-risk-management.pdf

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3.
Short name: WHO TRS No. 981, Annex 3
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/prequalification/trs981-annex3-who-variations-prequalified-product.pdf?sfvrsn=809e81b_2

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
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/distribution/trs992-annex4.pdf?sfvrsn=2a1980f0_2

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
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/distribution/trs992-annex5.pdf?sfvrsn=99aedfbe_2

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**
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/regulatory-standards/trs966-annex10.pdf?sfvrsn=5d94f486_2

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
https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1010-annex8-who-gmp-heating-ventilation-airconditioning.pdf?sfvrsn=c77698e2_0

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

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https://extranet.who.int/pqweb/sites/default/files/documents/TRS1010_Annex10.pdf

21. 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

22. 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

23. 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

24. 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/m/item/annex-2-trs-1033

25. 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

26. 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