

Spanish Agency Of Medicines And Medical Devices

Report No: *NCF-II/NC2026/01/CAT*

STATEMENT OF NON-COMPLIANCE WITH GMP

Exchange of information between National Competent Authorities (NCAs) of the EEA following the discovery of serious GMP non-compliance at a manufacturer¹

Part 1

Issued following an inspection in accordance with
Art. 111(7) of Directive 2001/83/EC as amended
Art. 94(2) of Regulation (EU) 2019/6 as amended

The competent authority of Spain confirms the following:

The manufacturer: ***Ocb Pharmaceutical S.R.L.***

Site address: ***Calle De Carles Buhigas 5 A, Poligono Industrial Can Castells, Canovelles, 08420, Spain***

OMS Organisation Id. / OMS Location Id.: ***ORG-100025917 / LOC-100054790***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2026-08-27***, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

- The principles of GMP for active substances referred to in Article 51 of Directive 2001/82/EC and Article 47 of Directive 2001/83/EC and an appropriate level of GMP as referred to in Article 46(f) of Directive 2001/83/EC.

Note to receiving authorities: Please contact the issuing authority within 20 working days in case there are critical(2) medicinal products potentially affected by this statement.

Manufacturing Authorisation Holders directly affected by this statement have failed to comply with their obligations under Art. 46 of Directive 2001/83/EC or Art. 93(1)(j) to (l) of Regulation (EU) 2019/6 and as a consequence the Qualified Person referred to in Art. 48 of Directive 2001/83/EC and Art. 97(1) of Regulation (EU) 2019/6 is unable to perform the batch certification referred to in Art. 51 of Directive 2001/83/EC and Art. 97 (6) and (7) of Regulation (EU) 2019/6.

In exceptional circumstances there may be no objection to the Qualified Person certifying affected batches thereby allowing their release provided all of the following conditions are fulfilled:

1. Batch certification is performed in order to maintain supply of critical medicinal products only.
2. A documented risk assessment has been performed by, or on behalf of, the Qualified Person and additional actions have been implemented by the manufacturing and/or batch release site to mitigate the risks posed by the non-compliance. Note: Repeated testing alone is not normally sufficient risk mitigation but, together with other actions, can form part of a strategy commensurate with the nature and the level of risk.
3. A thorough risk-benefit evaluation has been performed for the acceptance of risk and a report prepared that takes full account of the nature of the non-compliance with the involvement of:
 - The Manufacturing Authorisation Holder and the Qualified Person of the site responsible for

batch certification.

- The manufacturing site subject to this Statement of Non-Compliance, if different from the above.
- The relevant Marketing Authorisation Holder(s).

The report has been shared with the National Competent Authorities of the countries in which distribution of the affected batches is anticipated and that any comments from those authorities have been taken into account.

4. Written confirmation has been obtained from the National Competent Authorities in whose territories the affected batches are intended to be distributed that the product is considered critical on its territory, and that there is no objection to distribution.
5. The Supervisory Authority has been informed, if different from the above, and it has not suspended or revoked the relevant Manufacturing Authorisation.
6. The affected Marketing Authorisations have not been revoked or suspended.
7. Any further conditions imposed by the Supervisory Authority and other involved National Competent Authorities are met.

¹The statement of non-compliance referred to in paragraph 111(7) of Directive 2001/83/EC and Art. 94(2) of Regulation (EU) 2019/6, as amended, is also applicable to importers.

²See Appendix 3 of the relevant procedure in the Compilation of Union Procedures.

Part 2

Human Medicinal Products
Veterinary Medicinal Products

1 NON-COMPLIANT MANUFACTURING OPERATIONS

Include total and partial manufacturing (including various processes of dividing up, packaging or presentation), batch release and certification, storage and distribution of specified dosage forms unless informed to the contrary;

1.4	Other products or manufacturing activity
	1.4.1 Manufacture of 1.4.1.3 Other: Manufacturing of active substances(en)

Manufacture of active substance. Names of substances subject to non-compliant:

BISMUTH CITRATE(en)

BISMUTH SUBCITRATE COLLOIDAL(en)

BISMUTH SUBGALLATE(en)

BISMUTH SUBNITRATE(en)

BISMUTH SUBSALICYLATE(en)

SODIUM AND BISMUTH TARTRATE(en)

BISMUTH TRIBROMOPHENATE(en)

BISMUTH OXIDE(en)

BISMUTH SUBCARBONATE(en)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance:BISMUTH CITRATE

3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps: Separation of the active substance of mother waters by centrifugation. Washing with deionized water
3.5	General Finishing Steps
	3.5.1 Physical processing steps: drying, milling 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance:BISMUTH SUBCITRATE COLLOIDAL

3.1	Manufacture of Active Substance by Chemical Synthesis
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	3.1.2 Manufacture of crude active substance
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing
Active Substance:BISMUTH SUBGALLATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps: Separation of the active substance of mother waters by centrifugation. Washing with deionized water
3.5	General Finishing Steps
	3.5.1 Physical processing steps: drying, milling or micronisation 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing
Active Substance:BISMUTH SUBNITRATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps: Separation of the active substance of mother waters by centrifugation. Washing with deionized water
3.5	General Finishing Steps
	3.5.1 Physical processing steps: drying, milling 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing

	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing
Active Substance:BISMUTH SUBSALICYLATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps: Separation of the active substance of mother waters by centrifugation. Washing with deionized water
3.5	General Finishing Steps
	3.5.1 Physical processing steps: drying, milling or micronisation 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing
Active Substance:SODIUM AND BISMUTH TARTRATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing
Active Substance:BISMUTH TRIBROMOPHENATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps: Separation of the active substance of mother waters by centrifugation. Washing with deionized water
3.5	General Finishing Steps
	3.5.1 Physical processing steps: drying, milling

	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing
Active Substance:BISMUTH OXIDE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps: Separation of the active substance of mother waters by centrifugation. Washing with deionized water
3.5	General Finishing Steps
	3.5.1 Physical processing steps: drying, milling 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing
Active Substance:BISMUTH SUBCARBONATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps: Separation of the active substance of mother waters by centrifugation. Washing with deionized water
3.5	General Finishing Steps
	3.5.1 Physical processing steps: drying, milling 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Part 3

1. Nature of non-compliance:

During the inspection, a total of nine (9) deficiencies were identified, one (1) of them were classified as critical and eight (8) as major. The deficiencies identified demonstrate significant weakness in the pharmaceutical quality system implemented at the site and raise serious concerns regarding the reliability of manufacturing, storage, documentation, cross contamination control, traceability and quality assurance oversight activities. The critical deficiency related to the repackaging, relabelling and distribution of bismuth subsalicylate originating from a Chinese manufacturing operating outside the EU GMP framework. The inspection demonstrated that OCB PHARMACEUTICAL, S.R.L. assigned new batch numbers, issued certificates of analysis containing analytical results copied from supplier documentation, removed or replaced original labels and distributed the material to pharmaceutical costumers without adequately preserving the identity of the original manufacturer and the traceability of the supply chain. These practices gave the material the appearance of being associated with OCB PHARMACEUTICAL, S.R.L. manufacturing activities, not complying with GMP Part II requirements concerning the integrity and traceability of the supply chain. Major deficiencies were identified in the effectiveness of the deviation, investigation, CAPA and risk management system; data integrity controls, personnel qualification and training; material management and traceability; contamination and cross-contamination control measures; maintenance and cleaning of facilities and equipment; documentation practices; and quality system governance. The combination of these deficiencies indicates that the quality management system is not capable of consistently ensuring the manufacture, storage and distribution of active substances in compliance with GMP Part II requirements. Particular concerns were identified regarding the design, maintenance, qualification and operation of HVAC systems and differential pressure controls, recurring environmental monitoring excursions, deficiencies in cleaning practices, uncontrolled access between classified and technical areas, inadequate investigation of contamination events and the lack of effective reassessment of cross-contamination risks following multiple significant quality incidents. These deficiencies may have compromised the effectiveness of controls intended to prevent contamination and cross-contamination of active substances manufactured at the site. In addition, deficiencies in governance and management oversight were observed. The inspection findings demonstrate that quality-related decisions were not always supported by adequate quality risk management principles and the quality unit did not exercise sufficient authority to ensure that manufacturing activities were restricted, suspended or adequately controlled when significant quality concerns were identified.

Action taken/proposed by the NCA

Recall of batches already released

No specific quality defects on concrete batches present in the market were detected, and thus no action/recall is deemed necessary against concrete batches released and placed on the market.

Prohibition of supply

Suspension of the distribution and sale of any active pharmaceutical ingredient or intermediate that has been manufactured, repackaged or relabelled in the facilities of OCB PHARMACEUTICAL, S.R.L. manufacturing site at the Canovelles. In the event that the competent authorities of the countries deem it necessary, they may use the available stock of these products for their markets upon express request.

Suspension or voiding of CEP (action to be taken by EDQM)

Suspension of CEP for active substances manufactured in OCB PHARMACEUTICAL, S.R.L. in Canovelles should be considered. The CEP that it has are: - Bismuth subnitrate (R0-CEP 2021-190 Rev.00)

Others

Action on the Manufacturing Authorisation: Temporary suspension of all manufacturing activities of active pharmaceutical ingredients and / or intermediates performed at the OCB PHARMACEUTICAL, S.R.L. manufacturing site at Canovelles. These measures will be maintained until all the deficiencies observed in the inspection have been corrected and it has been verified through a new inspection. Recommendations/proposed actions: Manufacturers of finished medicinal products using active pharmaceutical ingredients manufactured at the OCB PHARMACEUTICAL, S.R.L. site of Canovelles should not use, release for manufacture, or further process such active substances unless they

perform scientifically justified testing, using suitably validated analytical methods and representative sampling plans, to demonstrate that the affected active pharmaceutical ingredients batches do not contain traces of other bismuth salts at levels that may impact product quality, safety or compliance with the approved specifications. In case of out of specification results are detected, national competent authority (NCA) should be informed by the marketing authorization holder (MAH). This manufacturer should not be authorised in any new/ongoing marketing authorisation or variation applications for these active pharmaceutical ingredients as long as the non-compliance statement is in force. Marketing Authorisation Holders are recommended to evaluate the introduction of alternative qualified sources for active substances currently supplied by OCB PHARMACEUTICAL, S.R.L. in order to mitigate any potential supply impact resulting from the regulatory measures adopted.

Additional comments

Current EU-GMP part II certificate NCF-II/2421/001/CAT has been withdrawn from EudraGMDP. This Statement of non-compliance is signed by Clara Pareja Rossel, Generalitat de Catalunya, and sent to Eudra by AEMPS.

2026-09-28

Name and signature of the authorised person of the
Competent Authority of Spain

Confidential
Spanish Agency Of Medicines And Medical Devices
Tel: **Confidential**
Fax: **Confidential**