National Authority Of Medicines And Health Products

Report No: ***F068/S1/ME/001/2024/NCR***

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 manufacturer[1]

Part 1

Issued following an inspection in accordance with
Art. 63 of Regulation (EU) 536/2014 as amended

The competent authority of Portugal confirms the following:
The manufacturer: ***Technophage Investigacao E Desenvolvimento Em Biotecnologia S.A.***
Site address: ***Rua Henrique Paiva Couceiro 29, Amadora, Lisbon, 2700-451, Portugal***
OMS Organisation Id. / OMS Location Id.: ***ORG-100026448*** / ***LOC-100053344***

Other
(Investigational product) Art. 61 of Regulation (EU) No 536/2014

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2025-10-29***, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

- Commission Delegated Regulation (EU) 2017/1569, as reflected by the product categories stated in Part 2. Commission Delegated Regulation (EU) 2017/1569

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.

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[1] *The 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.*

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

Part 2

Human Investigational 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;

1.1	**Sterile products**
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.4 Small volume liquids Special Requirements 7 Other: Geles for topic use asseptically prepared.(en)
	1.1.3 Batch certification
1.3	**Biological medicinal products (list of product types)**
	1.3.1 Biological medicinal products (list of product types) 1.3.1.5 Biotechnology products Special Requirements 7 Other: Lytic bacteriophages and recombinant proteins (containing AntiBodies).(en)
	1.3.2 Batch Certification (list of product types) 1.3.2.5 Biotechnology products Special Requirements 7 Other: Lytic bacteriophages and recombinant proteins (containing AntiBodies).(en)
1.5	**Packaging**
	1.5.1 Primary Packaging 1.5.1.5 Liquids for external use 1.5.1.9 Pressurised preparations 1.5.1.11 Semi-solids
	1.5.2 Secondary packaging
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility *1.6.2 Microbiological: non-sterility* *1.6.4 Biological*

Clarifying remarks (for public users)

- 1.1.3 - Batch Certification: Only for geles for topic application, including the ones asseptically prepared; includes blinding operations.

Part 3

1.Nature of non-compliance:
During the inspection were identified 3 critical findings, 5 major findings and 2 findings classified as others. As critical deficiencies were identified: • Inoperability of the production area and lack of access control to quality control/production, namely: - Inoperability of the production area, which was under renovation, without any equipment inside, without any communication to the Competent Authority. - Lack of access control to quality control/production, with the possibility of entry of people not belonging to the manufacturing unit being identified from the access hall to the bathroom of the manufacturing and quality control area. • Many of the data/records intended to prove the quality of the products produced proved to be inconsistent, confusing, incomplete, and therefore compromised the correct traceability of the products and materials, namely: - CoA No º 004/2025, BM0738.24001, Working Cell Bank _STA 75/12, dated 10/01/2025, was not signed by the Quality Control Officer and contained inconsistent dates (analysis 01/04/2024, manufacture 27/08/2024) and which also did not correspond to the date of the batch manufacture (25/03/2025 to 27/03/2025). - Logbook records were not always complete, correct and/or made at the time the activities were carried out, and several deficiencies were identified. •In the batch documentation BPR – 081 relating to batch FP 0481- 25001 of TP-122 PSA Cocktail there were pages not numbered and on those that were numbered, the numbering had been handwritten. As major deficiencies, were identified: •The procedures, records and other documents of the quality management system were not always complete, described the activities in full or were correct: - The list of drug substance and drug product produced batches was not up-to-date with regard to the manufacture and approval dates and an incorrect date was identified (date of manufacture of batch No º BM0738.24001 of Working Bank Cell _STA 75/12). - EMM Rooms CL2 (AL0.09, AL0.10, AL0.15, AL0.16, AL0.17, PB0.30, PB0.31) did not cover all the locations to be sampled on the isolator for environmental monitoring. - Deficiencies were identified in manufacturing instructions and batch records, namely incomplete manufacturing instruction (BPR-088, TP-102-DP1 Cocktail FP0607, batch FP0607.25001), as well as failure to record specifications and results (batch documentation IP 0420.25002) and the existence of many erasures in batch documentation FP0481.25001 of TP-122 PSA Cocktail FP0481 (BPR-081). •Logbook entries were not always made completely, correctly and/or at the time the activities were carried out, and it was identified in the Double Agar Overlay Assay Bacteriophage titer logbooks that the meaning of the compliant result for negative control was not identified (logbook nr. 282), as well as results from 08/07/2025 that had not yet been verified (logbook n.º 287). •Use of drug substance batches in the manufacture of finished product without having drug substance CoA nor batch analysis results (e.g. batch IP0420.25002 of Phage 99/10). •Information lacks were identified in the warehouse activities: - In the record of receipt of batch 25267 of RE0788-Bocto Red Time PCR_quarentena of 23/10/2025 was not identified whether the material was in the refrigerator or at room temperature (only QC was mentioned). - There was no easily accessible inventory that would allow verification of the quantities of each drug substance or drug product found in EQ084 (warehouse refrigerator). - In document SOP-001-FR-002, receipt of materials checklist for DP0069, batch 25270, the status was referred to as NA when it should have been Quarantine, and the verification of the manufacturer's name and address was not included (only the supplier's). • No evidence was presented for sterilization cycle 841, relating to the sterilization of the material (lot FP0481. 25001), which would contain information on the preparation of the material to be sterilized.
Action taken/proposed by the NCA **Suspensionof the manufacturing authorisation No. F068/001/2024in Part** **Withdrawal, of current valid GMP certificate No. F068/S1/ME/001/2024** ~~Withdrawal, of current already expired GMP certificate No. F068/S1/ME/001/2024.~~

Recall of batches already released
Each NCA should evaluate and assess the need of recall of the impacted batches.

Prohibition of supply
The manufacturer is prohibited to manufacture and supply Human Investigational Medicinal Products.

Others
Suspension of the manufacturing authorisation No. F068/001/2024 regarding Human Investigational Medicinal Products (ANNEX 2) - ANNEX 2 of the Manufacturing authorization is no longer valid.

Additional comments
Only Human Investigational Medicinal Products are impacted by the issuance of this SNC. The inspection that originated the issuance of GMP Certificate nr F068/S1/ME/001/2024 (the one is being withdrawal, already expired) was performed on 20/01/2022. As per information of the manufacturer there are no alternative manufacturers for the human investigational medicinal products manufactured in this Technophage site (Amadora, Portugal). Upon request, the manufacturer shared information regarding the sponsors and clinical trials in which Technophage participates and/or has participated in the production chain of the investigational medicinal product (information below). For the batches that may be considered affected, please consult the batches below: Id ; Investigational Medicinal Product ; Batch number; Expiry date; Batch certification date (by manufacturer); Clinical trial; Country; Sponsor: 1; Placebo; 20032; 04/2021; 03/12/2020; TP-102_101; Israel; Technophage SA. 2; TP-102; 20059; 04/2021; 03/12/2020; TP-102_101; Israel; Technophage SA. 3; TP-102; 20076; 06/2021; 08/01/2021; TP-102_101; Israel; Technophage SA. 4; TP-102; 21013; 09/2021; 12/04/2021; TP-102_101; Israel; Technophage SA. 5; Placebo; 21046; 12/2021; 25/06/2021; TP-102_101; Israel; Technophage SA. 6; TP-102; 21047; 12/2021; 26/06/2021; TP-102_101; Israel; Technophage SA. 7; TP-102; 21056; 11/2021; 30/08/2021; TP-102_101; Israel; Technophage SA. 8; TP-102; 21067; 01/2022; 23/11/2021; TP-102_101; Israel; Technophage SA. 9; TP-102; 22007; 04/2022; 28/01/2022; TP-102_101; Israel; Technophage SA. 10; Placebo; 22033; 07/2022; 05/05/2022 ; TP-102_101; Israel; Technophage SA. 11; TP-102; 22034; 05/2022; 11/05/2022; TP-102_101; Israel; Technophage SA. 12; TP-102/Placebo; 23058; 10/2023; 23/08/2023; TP-102_102; US / India; Technophage SA. 13; TP-102/Placebo; 23059; 12/2023; 23/08/2023; TP-102_102; US / India; Technophage SA. 14; TP-102/Placebo; 23086; 03/2024; 17/11/2023; TP-102_102; US / India; Technophage SA. 15; TP-102/Placebo; 23105; 04/2024; 19/01/2024; TP-102_102; US / India; Technophage SA. 16; TP-102/Placebo; 23106; 04/2024; 19/01/2024; TP-102_102; US / India; Technophage SA. 17; TP-102/Placebo; 23119; 04/2024; 19/02/2024; TP-102_102; US / India; Technophage SA. 18; TP-102/Placebo; 23120; 04/2024; 19/02/2024; TP-102_102; US / India; Technophage SA. 19; TP-102/Placebo; 23122; 05/2024; 19/02/2024; TP-102_102; US / India; Technophage SA. 20; TP-102/Placebo; 23123; 05/2024; 19/02/2024; TP-102_102; US / India; Technophage SA. 21; TP-102/Placebo; 23124; 04/2024; 19/02/2024; TP-102_102; US / India; Technophage SA. 22; TP-102/Placebo; FP0636A.24001; 04/2025; 08/01/2025; TP-102_102; US / India; Technophage SA. 23; TP-102/Placebo;FP0636B.24001; 05/2025; 08/01/2025; TP-102_102; US / India; Technophage SA. 24; Relert; FP0780.25001; 08/2026; NA; Fase 1/2a TZ-161; Espanha; Technophage SA.

2026-07-13

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

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