National Institute of Pharmacy and Nutrition

Report No: ***OGYEI/37756-2/2021***

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

The competent authority of Hungary confirms the following:
The manufacturer: ***PLAZMACENTRUM Korlátolt Felelősségű Társaság / PLAZMACENTRUM Kft.***
Site address: ***Rákóczi út 42., Budapest, 1072, Hungary***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2021-06-02***, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

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

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;

1.3	Biological medicinal products (list of product types)
	1.3.1 Biological medicinal products (list of product types) 1.3.1.1 Blood products Special Requirements 7 Other: source plasma by plasmapheresis(en)(en)

Part 3

1.Nature of non-compliance:

During the inspection performed on 1-2 June 2021 at Plazmacentrum Budapest 3 critical (n=3) deficiencies were identified in total and several other deficiencies as major. Plazmacentrum showed lack of ability to adhere to the principles of Good Manufacturing Practice. Plazmacentrum did not sufficiently ensured the safety and traceability of the product as summarized by the 3 critical deficiencies: 1. Handling of rejected plasma units assigned for disposal due to biohazard risk was not safe. There was no physical segregation of rejected plasma units (for instance units from infected donors) in the freezer, the labelling was misleading, there was no clearly written instruction for the disposal. 2. The IT software used for plasma management was not validated according to the complexity of the system. The incorrect categorization and validation led to inadequate data governance, eg. the migration of data from previous software did not happen in a controlled way, the audit trail could not be accessed by the company, therefore the data integrity was compromised. 3. The paper based records - that contain raw data - were not archived in a controlled dedicated place. There was no inventory indicating the location of the records, the long term (30 years) traceability of the donor and donation via the blood establishment through to the batch of medicinal product and vice versa was not ensured. Major deficiencies were identified in connection with: - vendor management (eg., vendor selection and approval, very poor technical aspects of contracts) - inappropriate identification and storage of GMP materials - insufficient documentation practice

Action taken/proposed by the NCA

Suspensionof the manufacturing authorisation No. HU-M-PLCTin Full

Withdrawal, of current valid GMP certificate No. 17294-8/2018
GMP certificates invalidated

Prohibition of supply
No recall is necessary. Plasma units currently stored in the manufacturer’s freezer should be placed in quarantine until further notice.

2021-06-10

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

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Confidential
National Institute of Pharmacy and Nutrition
Tel:***Confidential***
Fax:***Confidential***