French National Agency for Medicines and Health Products Safety

Report No: ***15UMB038***

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. 15 of Directive 2001/20/EC

The competent authority of France confirms the following:
The manufacturer: ***TXCELL - BESANCON***
Site address: ***EFS Bourgogne Franche Comté Bâtiment IBFC, 6 rue Docteur Jean François Xavier Girod, BESANCON, 25000, France***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2015-04-23*** , it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC

[1] *The statement of non-compliance referred to in paragraph 111(7) of Directive 2001/83/EC and 80(7) of Directive 2001/82/EC, as amended, shall also be required for imports coming from third countries into a Member State.*

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
	1.1.3 Batch certification
1.3	**Biological medicinal products (list of product types)**
	1.3.1 Biological medicinal products (list of product types) 1.3.1.3 Cell therapy products
	1.3.2 Batch Certification (list of product types) 1.3.2.3 Cell therapy products
1.5	**Packaging**
	1.5.2 Secondary packing

Part 3

1. Nature of non-compliance:

Overall, 22 deficiencies were observed, including 7 major deficiencies on the following topics: 1. The pharmaceutical quality system was deficient as several deviations opened during the period 2014-2015 were overdue and still pending. Namely, 43 non conformities were related to environnemental deviations of which 30 were related to mould contamination during production of investigational batches and Media Process Test. Moreover, some investigational product batches were released whereas deviations cases were still opened. 2. Paper batch record and labels required in aseptic areas were not sterilised or passed into the area by a procedure which achieves the same objective of not introducing contamination. 3. Appropriate alert limits were not set for the results of microbiological monitoring of clean rooms.

Action taken/proposed by the NCA

Suspension of the manufacturing authorisation No. M 14/298 in Part
Suspension of manufacturing operations of new batches including release and distribution, suspension of release and distribution of pending batches, suspension of distribution of released batches. Quality control testing (1.6.2 and 1.6.4) and storage activities are allowed.

Prohibition of supply
However, batches already manufactured and certified, and for which patients have already received the first administration during the clinical trial EUDRACT 2014-001295-65 / TC 355, could be distributed as a validation by the ANSM of the methodology and criteria of the risk analysis related to the product conformity has been performed.

Additional comments
Withdrawal, of current valid GMP certificate n° HPF/FR/76/2014

2015-07-22

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

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French National Agency for Medicines and Health Products Safety
Tel: ***Confidential***
Fax: ***Confidential***