French National Agency for Medicines and Health Products Safety

Report No: ***15UMB113***

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: ***THERAVECTYS - VILLEJUIF***
Site address: ***1 Mail du Professeur Georges Mathé, Bâtiment Villejuif Biopark, VILLEJUIF, 94800, France***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2015-11-20*** , 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) 1.1.1.2 Lyophilisates 1.1.1.4 Small volume liquids
	1.1.2 Terminally Sterilised (processing operations for the following dosage forms) 1.1.2.3 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) 1.3.1.2 Immunological products 1.3.1.4 Gene therapy products
	1.3.2 Batch Certification (list of product types) 1.3.2.2 Immunological products 1.3.2.4 Gene therapy products
1.5	**Packaging**
	1.5.2 Secondary packing
1.6	**Quality control testing**
	1.6.3 Chemical/Physical *1.6.4 Biological*

Part 3

1. Nature of non-compliance:
An inspection performed by ANSM from 17 to 20 November 2015 raised 45 deficiencies, including 5 critical deficiencies and 17 major deficiencies on the following topics: 1) The implementation of exemption SOP for manufacturing operations which is not compliant to GMP principles, for example, Media Fill Test were performed with unqualified equipment. 2) The lack of sample area for incoming materials and their systematic use in quarantine status for manufacturing operations. 3) Appropriate measures in terms of monitoring locations, alert and action limits rationale, were not set for particle and microbiological monitoring in clean rooms grade A and B. 4) No protocol for clean rooms' qualification was established and clean rooms classification didn't fulfill ISO14644 requirements. 5) Some analytical methods and process were not validated for the clinical trial EudraCT : 2015-000845-21. Following the inspection, Theravectys decided to stop the production on going, to reject the 2 manufactured investigational batches and to withdraw the authorisation's request for which the ANSM assessment was on going, for the clinical trial EudraCT : 2015-000845-21. No investigational batch was distributed.

Action taken/proposed by the NCA
Suspension of the manufacturing authorisation No. F 15/154 in Part Suspension of manufacturing operations of investigational medicinal products including quality control testing and batch certification. Storage activities are allowed.
Additional comments Decision n° S 16/050 dated February 22nd 2016 suspends F15/154 dated September 07th 2015 for 1 year.

2016-03-03

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***