Spanish Agency of Medicines and Medical Devices

Report No: ***INS16-001c***

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. 111(7) of Directive 2001/83/EC as amended
Art. 80(7) of Directive 2001/82/EC as amended
Art. 15 of Directive 2001/20/EC

The competent authority of Spain confirms the following:
The manufacturer: ***FARMA MEDITERRANIA, S.L.***
Site address: ***C/ Sant Sebastià, s/n, Sant Just Desvern, Barcelona, 08960, Spain***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2016-01-13*** , 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
- The principles and guidelines of Good Manufacturing Practice laid down in Directive 91/412/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 Medicinal Products
Veterinary Medicinal Products
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
1.5	**Packaging**
	1.5.2 Secondary packing
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility *1.6.3 Chemical/Physical*

Part 3

1. Nature of non-compliance:

Critical deficiencies a) Lack of an effective pharmaceutical quality assurance system b) Release of batches of medicinal products produced without completing all of the manufacturing protocols, without being checked quality assurance unit and without the approval of the technical director. c) Use in quality control a non-qualified chromatographic equipment, with operating faults and an with an unvalidated computerized management system. As a result, the integrity, reliability, up-to-dateness, originality and authenticity of the data that are obtained cannot be guaranteed. d) Transfer of some of the final analytical quality controls of medicinal products to a third party, without appropriately transferring the control methods and without the authorization of the relevant health authority e) Manufacture of medicinal products using procedures that have not been appropriately validated or have not been periodically revalidated. f) Acceptance of results of repeated analytical controls and sterility tests of finished medicinal products without having undertaken an in-depth investigation to determine the root cause of a previously result obtained which was out of specifications. g) Although a visual inspection of injectable medicinal products reveals a high number of critical quality defects (the presence of visible particles) non deviations are opened and is not investigated. c) Do not do any quality control on a statistical sample of units of injectable medicinal products that have passed the visual inspection. Major deficiencies a) Do not do the annual quality product review of medicinal products manufactured. b) Deviations in the manufacturing processes are not investigated suitably and in-depth. c) The simulation of the aseptic manufacturing process is not performed every six months and samples used in the simulation are not incubated at the right temperature. c) The air treatment system in manufacturing areas is not properly qualified, as it is only checked when it is “at rest” but not “in operation”. e) Medicinal products are manufactured without full compliance with conditions established in the marketing authorisation dossier and/or without carrying out all the established process controls. f) Manufacturing and quality control documents of each batch of medicinal products manufactured are not filed correctly. g) The facilities have been modified considerably without the authorization of the relevant health authority h) Test of growth promotion of culture media, which are used in the sterility testing, in the simulation of the aseptic manufacturing process or in the environmental control of critical manufacturing areas, is not carried out. h) Do not analyse all of the specification parameters for raw materials used in the manufacturing.

Action taken/proposed by the NCA

Suspension of the manufacturing authorisation No. 0164 in Full
Suspension of the manufacturing and quality control of medicinal products activities

Recall of batches already released
Withdrawal from the market of all batches of all medicinal products that have been manufactured by this pharmaceutical company during 2014, 2015 and 2016

Prohibition of supply
To prohibit to place on the market any batch manufactured by the pharmaceutical company. To stop supply customers with medicinal products that are manufactured and to informed them about the measures taken

Additional comments
The statement of non-compliance with GMP has been signed and issued by Cristina Iniesta Blasco as General Director of Dirección General de Ordenación y Regulación Sanitarias, Departamento de Salud, Goverment of Catalonia, Travessera de les Corts, 131-159, 08028 Barcelona (España)

2016-02-02

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

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