Italian Medicines Agency

Report No: ***IT/UAO/NCR/MED/1/2015***

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

The competent authority of Italy confirms the following:
The manufacturer: ***IASON ITALIA SRL***
Site address: ***Via GASTONE MARESCA, 38/38A, ROMA, 00138, Italy***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2015-10-08*** , 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 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 5 Radiopharmaceuticals
	1.1.3 Batch certification
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:

During the inspection 19 deficiencies were identified, 3 of them were rated as critical deficiencies and 11 as major deficiencies. The main deficiencies were related to the Quality Management and the Quality Assurance Systems also in terms of sterility assurance and risk of contamination/defects of the final product. One critical deficiency was related to failure to fully investigate and document out-of-specification results for microbiological environmental monitoring in class A isolator and class B/C surrounding areas, in manufacture of radiopharmaceuticals aseptically prepared. The company didn't carry out an appropriate and full-scale investigation to determine what caused the OOSs. An appropriate level of corrective action analysis was not applied during the investigation and the true root cause(s) were not determined. Failure to address the root cause due to ineffective CAPA revealed a lack of the quality assurance framework system. Another critical deficiency was reported with regards to production processes which were considered not satisfactory controlled: it was found that for the manufacture of some batches of the radiopharmaceutical Pcolina (Iasocholine) a non suitable reagent was used (expired dibromomethane). Moreover, for some batches of released RPs master batch documents were incomplete. No adequate review by QA or QP. Furthermore, preparation of the starting material set for radiopharmaceuticals was performed in condition not appropriate to guarantee an adequate level of chemical and microbiological containment. The inspection's team has rated also as critical the observation related to the number of personnel in force to the manufacturing site, which were considered not appropriate to conduct all the activities in accordance with the GMP and to maintain the quality management system and its effectiveness. The remaining major deficiencies were related to specific aspects of the Quality Assurance System with regards to PQR assessment, revalidation and recalibration of critical equipment, data integrity in the context of HPLC management, storage of materials and documentation system.

Action taken/proposed by the NCA

Suspension of the manufacturing authorisation No. aM29/2014 in Full
On 7th October 2015 the company has informed AIFA about the decision to suspend the manufacturing activities and

the production of the following radiopharmaceuticals: 18F-Fludeoxyglucose, 18F-Sodium fluoride and 18F-Fluoromethylcholine as reported in the decree n. aM71/2015. The manufacturing authorization of IASON ITALIA S.r.l., Via Gastone Maresca 38/38A - 00138 – Roma (RM) - Italy has been suspended by AIFA on 8th October 2015 with decree n. aM – 153 and the relevant MIA was withdrawn from EUDRAGMDP. The decree reported in NCR (aM29/2014), is the previous since the manufacturing site is suspendend.

2015-12-01

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

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