FAX/SPEED POST

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P.K. Guha
Director

No: 32-10/2009-SS/3176 Dated : 21/12/2009.

To
Shri Sudhir Kumar
Under Secretary to the Govt. of India
Ministry of Health & Family Welfare
Nirman Bhavan, New Delhi 110 108.

Subject : Testing of Albupax (Paclitaxel Injection), Batch No.202013 & 202119 Manufactured by M/s. Natco Pharma Ltd., Hyderabad, AP.

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Sir,

This is with reference to your letter No.F.QA/GNL/BCN/INV-ABR/09-DCG(I) dated 21st December, 2009 (received through fax) on the above mentioned subject.

The points raised in your above mentioned letter are clarified below:

1. That the said drug was tested twice in CDL, Kolkata in the Toxicology Section under the supervision of experienced senior Scientific Officers and in both the occasions, the samples were found to contain Endotoxin and therefore, the sample did not pass the Bacterial Endotoxin test.

It is not correct that the "Lonza Kit" supplied by the firm was not used by the CDL, Kolkata for test of Endotoxin for the said sample.

As such on 7.5.2009, the sample was tested with "Lonza Kit" (supplied by M/s. Natco Pharma Limited) as well as with "Charles River Endosafe Kit", both at a time on the same day in the Toxicology department.

2. When Endotoxin tests were carried out simultaneously with the both test kits, it was found that the Lonza Kit (supplied by the firm) did not respond to the Lysate even with positive control and no gel formation was observed which indicates the doubt about the quality and purity of the Lonza Kit (supplied by the firm). At the same time test was also carried out with Lal Kit using Charles River Endosafe (regularly used for many years in CDL, Kolkata for all bacterial Endotoxin Tests). While carrying out the positive

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control with Endotoxin, negative tests for reagent blank and diluent blank used were also carried out. The response of the sample with Endotoxin Lal reagent Kit was found positive and accordingly report was released declaring the sample as 'Substandard' with regards to 'Bacterial Endotoxin Test'. The full procedure required to carry out Bacterial Endotoxin Test as per I.P. was followed by CDL, Kolkata.

On receipt of representations from M/s. Natco Pharma Limited, a committee consisting of expert Scientific Officers was constituted. The same Bacterial Endotoxin Tests were repeated once again on 9.6.2009 as per I.P. with the remaining sealed sample using freshly procured LAL Kit including LAL reagent water of M/s. Charles River Endosafe, in the presence of committee consisting of the following officers:

1. Dr. M.F.A. Beg, S.S.O. (Ph.Research) and Govt. Analyst
2. Dr. A.K. Khasnobis, S.S.O. (Toxicology)
3. Mr. R.K. Rishi, Pharmacologist (S.S.O.)
4. Dr. Ardhendu B. Sarma, S.S.A. (Toxicology)
5. Mrs. Maya Basu, Asstt. Chemist (Toxicology)

The same standard method was followed in the second repeat tests also and was observed by all the Senior Officers of the committee. It was concluded that the sample contained Endotoxin and, therefore, it did not pass the Bacterial Endotoxin Test. The copy of the committee report duly signed by all the committee members is enclosed herewith for ready reference in Annexure – I.

As such the same was explained vide this office earlier letter dated 13.07.2009 to the DCG(I).

Therefore, the claim made by the firm with regards to the use of Test Kit and the procedure followed by the CDL, Kolkata is not agreeable by the CDL, and we stand by its test report which had already been released, declaring the sample 'as not of standard quality'.

Yours faithfully,

Encio.: Annexure - I.

P.K. Guha

(P. K. Guha)
Director
Central Drugs Laboratory
Kolkata

Copy to the Drugs Controller General (India), Dte. General of Health Services, FDA Bhavan, Kotla Road, Near Mata Sundari College, ITO, New Delhi 110 002.

(P. K. Guha)
Director
Central Drugs Laboratory
Kolkata

Annexure – I

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Endotoxin test for the subject samples, SZW-1, DCA(S)-5(A), DCA(S)-5(B) AND SZN-1, has been carried out following standard method prescribed in the Indian Pharmacopoea. CDL, Kolkata has been doing Bacterial Endotoxin test of hundreds of samples since last many many years .

LAL Kit used, of Charrles River Endosafe, USA, is one of the most sensitive, reliable and authentic one. Moreover, while carrying over the testing the positive control with endotoxin and blank for reagents and diluent used, has also been carried out.

In order to check the sensitivity of Lonza kit, the test was also carried out for positive control.There the kit did not response to endotoxin and no gel formation was observed which indicated a doubt about the quality/ purity of the Lonza kit supplied by the firm.

The said samples were initially tested on 07/05/2009 both with Lonza kit as well as with Charles River Endosafe kit. The observation of Lonza kit had been indicated above. Therefore, the results obtained with Lonza were not considered.Whereas, the response with Endosafe kit was positive, and accordingly the report was released declaring the samples are of sub-standard with respect to Bacterial Endotoxin test.

After receiving the representation of the firm, the endotoxin test was repeated on 09/06/2009 with a freshly procured LAL kit including LRW of Charles River Endosafe in presence of a committee consisting of the following officers –

1. Dr. M. F. A. Beg, S.S.O.(Ph. Research) and the Govt. Analyst
2. Dr. A.K. Khasnobis, S.S.O.(Toxicology)
3. Mr. R.K Rishi, Pharmacologist (S.S.O)
4. Dr.Ardhendu B Sarma, S.S.A (Toxicology)
5. Mrs.Maya Basu, Asstt. Chemist (Toxicology)

Same standard pharmacopoeal method was followed in the next testing and testing was observed by all the senior officers.

It is concluded that samples were containing endotoxin and therefore, do not pass the Bacterial Endotoxin test. Report released accordingly.

9.6.09 (Dr.M.F.A.Beg) | 9/6/09 (Dr.A.K.Khasnobis) | 9/6/09 (Mr.R.K.Rishi) | 09/06/09 (Dr.A.B.Sarma) | 09/06/09 (Mrs.M.Basu)