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Global Research & Development

Manager, Worldwide Regulatory Strategy - EU
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Head, Clinical Trials Unit
Medicines and Healthcare Products Regulatory Agency
1, Nine Elms Lane
London SW8 5NQ

Dear [REDACTED]

Response to Notice of Non-Acceptance for a Clinical Trial Application

PF-00446687 200 mg Powder for Oral Solution

EudraCT Number: 2007-001036-31

Protocol Number: A8361011

Internal SAN number: 4748

Protocol Title: A 2-Cohort, Multi-Centre, Randomised, Double Blind (3rd Party Open), Placebo Controlled 4-Way Crossover Study to Assess the Efficacy of Single Oral Doses of PF-00446687 on Erectile Function in Men Suffering from Erectile Dysfunction, using 100 mg Sildenafil as the Positive Control.

Following receipt of the Notice of Non-Acceptance for the Clinical Trial Application supporting protocol A8361011, please find below the sponsor's responses to the grounds for non-acceptance raised by the MHRA.

The protocol should stipulate that, for three months after the last dose, a barrier method of contraception should be used, if engaging in sexual activity with women of child-bearing potential.

The protocol and informed consent document have been amended as requested to stipulate that for the duration of the study and till three months after the last dose, a barrier method of contraception should be used, if engaging in sexual activity with women of child bearing potential. A copy of the amended protocol has been appended to this response.

It is assumed that, in the absence of stability data, the drug substance is tested to and complies with its specification prior to use in manufacture of the drug product.

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01000006580791151 Approved 12-May-2007 09:44

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It is confirmed that PF-00446687-01 drug substance, [REDACTED] was tested to and complies with its specification as detailed in *Table 1: Batch Analysis for PF-00446687-01*, [REDACTED] and therefore has been assessed as suitable to use in the manufacture of the drug product.

01603006592781.151 Approved 12 May 2007 09:44

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Table 1. Batch Analysis for PF-00446687-01, [REDACTED]

Batch Number:		[REDACTED]
Usage:		Clinical
Site of Manufacture		Sandwich
Batch Size (Active):		5.5 Kg
Date of Manufacture		February 2007
Test Name	Acceptance Criteria	
Description		
Appearance		
Solution Clarity		
Identification		
Identity (FT-IR)		
Identity (Chiral HPLC)		
Assay		
PF-00446687 (HPLC)		
HCl counter-ion		
Impurities		
Residue on Ignition		
Heavy Metals		
Water		
PF-00847127		
Individual Unspecified Impurities		
Total Related Impurities		
Isopropylchloride		
Residual Solvents		
2-Methyltetrahydrofuran		
Propan-2-ol		

NMT = Not more than

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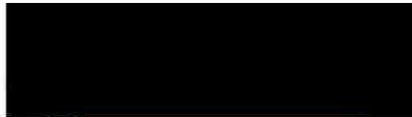


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Since the method of production is considered to be manufacture, a copy of the MA(IMP) for the sites of manufacture of the oral active and placebo solutions should be provided.

The MA(IMP) licence for each of the clinical sites is attached. Please note that, at present, the licence for MDS Pharma Services GB Limited contains a number of discrepancies and has been returned to the MHRA for amendment. MDS Pharma have been in contact with the MHRA and the licence is currently being amended. The amended version authorising non-sterile production is expected to be available by May 25th and before the start of study A8361011. Attached is a declaration from the MDA Pharma Services Qualified Person confirming that MDS Pharma Services is legally authorized by the MHRA to dose prepare for the A8361011 study.

I hope the responses provided satisfactorily address the grounds for non-acceptance. However, if you require any further information, or clarification on any matter, please do not hesitate to contact me.



Manager
Worldwide Regulatory Strategy - EU

Encl.:

- 1) Amended Protocol
- 2) Copies of the manufacturing authorisations for the sites of manufacture of the oral active and placebo solutions & QP declaration for MDS Pharma Services

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