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In reply please  
refer to: P5-447-3/OG/PD

Your reference:

Dr Padma GM Rao  
Director - BA/BE  
Manipal AcuNova KMC Hospital Clinical  
Pharmacology Unit  
5<sup>th</sup> Floor, MCODES Building  
KMC Hospital, Attavar  
575001 Mangalore  
Inde

8 May 2008

Dear Dr Rao,

**WHO Prequalification of Medicines Programme  
Inspection of Contract Research Organization (CRO)  
Manipal AcuNova KMC Hospital Clinical Pharmacology Unit, Mangalore, India, 21 January 2008**

Referring to the above-mentioned inspection, please find enclosed the World Health Organization (WHO) Final Conclusion.

We should like to take this opportunity to thank you for your collaboration.

Yours sincerely,

Dr Raul Kiivet  
Manager  
Prequalification Programme  
Quality Assurance and Safety: Medicines

ENCL.

### Inspection Report of a Contract Research Organization Final conclusion

The report is the property of the organization responsible for performing the inspection.

#### Part 1: General information

Name of organization	Manipal AcuNova KMC Hospital Clinical Pharmacology Unit
Physical address	5 <sup>th</sup> floor, MCODES Building, KMC Hospital. Attavar, 575001 Mangalore, India.
Postal address	Same as above
Telephone number	00 91 824 244 5858 / 6141
Fax number	00 91 824 242 5092
Summary of activities	Performance of clinical studies, including bioequivalence trials (clinical and bio-analytical parts)
WHO reference number Study	<b>HA 392</b> # 036-07 Study Title : A randomized, open label, balanced, two treatment, two period, two sequence, single dose, cross-over, bioequivalence study of lamivudine/zidovudine 150mg/300mg tablet (Matrix Laboratories Ltd, India) with Combivir® (Lamivudine/Zidovudine) 150mg/300mg tablet, (GlaxoSmithKline, Inc. USA, in 44 healthy human adult male subjects under fasting conditions.
Start and stop dates for each phase of the clinical study	Period 1 : 6 February 2007 to 8 February 2007 Period 2 : 17 February 2007 to 19 February 2007
Investigational Products	Lamivudine and Zidovudine 150mg/300mg Tablets Manufactured by : Matrix Laboratories Limited, F-4 & F-12, Malegaon, MIDC, Sinnar- 422 113, Nashik District, Maharashtra State, India. Batch number : LZDA116001 Manufacturing date : May 2006
Reference Products	Combivir® (Lamivudine/Zidovudine) 150mg/300mg tablets Manufactured by : GlaxoSmithKline, USA. Batch number : 6ZP1816
Sponsor	Matrix Laboratories Limited, India
Contact person	Dr. Padma GM Rao      padma.rao@acunovalife.com
Personnel met	Dr. Padma GM Rao, Director - BA/BE (KH) Dr R. Rajesh, Sr. QA Associate (KH) Umesh B A, Chief Quality Officer (Bangalore)



	Dr. Vijayan Anand, Clinical Pharmacologist Satish P Prabhu, Quality Assurance Associate <u>From Matrix</u> Ramakrishna Bangaru, Vice President Biopharmaceutics
Names of inspectors:	Dr. Philippe Panouillot for WHO Dr. Olivier Gross ,WHO Dr. Daniela Vieira dos Reis Coordination of Inspection in Pharmaceutical Equivalence and Bioequivalence Centres - CIBIO General Office of Medicines - GGMED Brazilian Health Surveillance Agency - ANVISA Dr. Kelen Soares. Coordination of Inspection in Pharmaceutical Equivalence and Bioequivalence Centres - CIBIO General Office of Medicines - GGMED Brazilian Health Surveillance Agency - ANVISA
Date of inspection:	21 January 2008
Project (if any):	Prequalification Programme : Priority Essential Medicines

**Part 2: Comments on the satisfactoriness of the corrective actions proposed.**

We acknowledge receipt of your responses dated 5<sup>th</sup> April 2008 to the World Health Organization (WHO) report of the above mentioned inspection.

An assessment of the information provided in relation to each observation has revealed that the corrective actions proposed by the sponsor and the CRO were acceptable.

**Part 3: Conclusion**

**Initial Conclusion (January 2008)**

Based on the people met and the documents reviewed, and considering the findings of the inspection, reflected in the observations listed in the inspection report, the studies, clinical part, inspected can be considered to have been conducted at an acceptable level of compliance with WHO Good Clinical Practices (GCP) and Good Laboratory Practices (GLP), by Manipal AcuNova KMC Clinical Pharmacology Unit located in Mangalore, India.

The observations (non-compliances with the WHO guidelines) listed below need to be addressed by the company and verified through evaluation of the documentation of the corrective actions (planned and implemented) submitted by the Research Organization.

**Definitive Conclusion (May 2008)**

Based on the people met and the documents reviewed, considering the findings of the inspection, and the corrective action proposed, the bioequivalence study inspected, con-



ducted by Matrix Laboratories Ltd, Clinical Research Centre located in Hyderabad, India can be considered to be a proof of bioequivalence between test product HA 392 and the relevant comparator.

A handwritten signature in black ink, appearing to be 'Olivier Gross', written over a horizontal line.

WHO  
Dr Olivier Gross  
(On behalf of the inspection team)

08/05/2008  
Date