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In reply please  
refer to: P5-447-3/AvZ/SC

Your reference:

Mr M. Kuriakose  
Senior General Manager - Europe & Africa  
Ajanta Pharma Ltd  
b-4/5/6, MIDC Industrial Area  
Paithan District  
Aurangabad 431 128  
Maharashtra State  
Inde

24 March 2009

Dear Mr Kuriakose,

### Prequalification of Medicines Programme Notice of Concern

In June 2008 the World Health Organization's (WHO) Prequalification of Medicines Programme implemented a Notice of Concern procedure that is applied when an inspection is performed and serious observations are made that result in concern about the site's compliance with specified standards such as those relating to Good Manufacturing Practices (GMP). This notice is issued in accordance with this procedure.

An inspection of your pharmaceutical product manufacturing facility at Ajanta Pharma Ltd, b-4/5/6, MIDC Industrial Area, Paithan District, 431 128, Aurangabad, Maharashtra, was conducted by inspectors from the WHO Prequalification of Medicines Programme from 19 to 22 January 2009. This inspection revealed several major deviations from the WHO GMP standards as published in WHO publications. These deviations were presented to you during the inspection and listed in the Inspection Report prepared after the inspection.

Following the inspection, you were sent a copy of the Inspection Report by email. In addition, it was posted to you with a covering letter dated 3 February 2009. You were requested to respond to the observations listed in the Inspection Report within 30 days from the date of the letter. Your response has been received and evaluated, and there are some major observations that are of concern, as these have not been adequately addressed. They are detailed below with the evaluation of your response.

These non-compliances included (but are not limited to):

1. **The company was not able to provide sufficient assurance that validation and qualification was fully implemented to an acceptable level of compliance with current WHO norms and standards.** (*Ref: Supplementary guidelines on good manufacturing practices : validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4; [http://whqlibdoc.who.int/trs/WHO\\_TRS\\_937\\_eng.pdf](http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf)*)

.../...

2. **The HVAC system of the company did not meet current requirements including supporting documentation, test results and reports, control, monitoring and qualification.** (Ref: Supplementary guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems for non-sterile pharmaceutical dosage forms. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 2; [http://whqlibdoc.who.int/trs/WHO\\_TRS\\_937\\_eng.pdf](http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf))
3. **The company did not follow its quality systems to prevent possible cross-contamination in a consistent manner. (See also other points in this NOC).** (Ref: Quality Assurance of pharmaceuticals. A compendium of guidelines and related materials. Volume 2, Second updated edition. Good manufacturing practices and inspection. World Health Organization, Geneva, 2007; [http://www.who.int/medicines/areas/quality\\_safety/quality\\_assurance/production/en/index.html](http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/index.html))
4. **The company failed to exercise sufficient control over some materials.** (Ref: Quality Assurance of pharmaceuticals. A compendium of guidelines and related materials. Volume 2, Second updated edition. Good manufacturing practices and inspection. World Health Organization, Geneva, 2007; [http://www.who.int/medicines/areas/quality\\_safety/quality\\_assurance/production/en/index.html](http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/index.html))
5. **The company was unable to provide sufficient reliable documented evidence of process validation including but not limited to source data for quality control and analytical test results.** (Ref: Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4; [http://whqlibdoc.who.int/trs/WHO\\_TRS\\_937\\_eng.pdf](http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf))

WHO will withhold prequalification of all new products manufactured at this site until these major observations have been satisfactorily addressed and WHO has verified and confirmed the acceptability of the corrective actions. In addition, if these major observations are not corrected within a reasonable timeframe, WHO may consider suspension of the product(s) listed as prequalified from this manufacturing site, and/or may recommend suspension of procurement of all prequalified products manufactured at this site.

#### **Publication of the Notice of Concern**

Your attention is drawn to the World Health Assembly Resolution WHA57.14 "Scaling up treatment and care within a coordinated and comprehensive response to HIV/AIDS" of 22 May 2004, which among other actions, requests WHO:

"3.(4) to ensure that the prequalification review process and the results of inspection and assessment reports of the listed products, aside from proprietary and confidential information, are made publicly available;"

.../...

In accordance with the above resolution and the Notice of Concern procedure, WHO will publish this Notice of Concern on its web site. Please note that a Notice of Concern will remain active on the WHO Prequalification of Medicines Programme web site until satisfactory corrective actions have been submitted and accepted by WHO.

Yours sincerely,

A handwritten signature in black ink, appearing to be 'Lembit Rago', with a long horizontal stroke extending to the right.

Dr Lembit Rago  
Coordinator  
Quality Assurance and Safety: Medicines