**NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC**
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This notification is a referral under Article 31 of Directive 2001/83/EC to the CHMP made by European Commission

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| Product Name(s), if appropriate, Strength(s) and Pharmaceutical Form(s)<br><br>Active Substance(s)/Therapeutic class | See Annex |

<Applicant(s)/Marketing Authorisation Holder(s)> <In the referring Member State>

The French Agency on medicinal products, ANSM (Agence Nationale de sécurité du médicament et des produits de santé), conducted an inspection on 19-23 May 2014 (inspection reference GCP-141001-FR) at GVK Biosciences Private Limited (GVK Bio), Swarnajayanthi Commercial Complex, Ammeerpet, Hyderabad 500 038, India.

The findings reported during this inspection raise concerns on the reliability of the clinical part of bioequivalence studies conducted between 2008 and 2014 at the site inspected. Indeed, the following findings were reported:
- falsifications of electrocardiograms were detected in each and every one of the 9 trials inspected by the ANSM;
- these falsifications cast doubts on the authenticity of all other clinical records of these 9 clinical trials. They were therefore considered by the ANSM as not compliant with GCP and their data were considered as not acceptable to support marketing authorisation applications;
- the falsification of these ECGs was performed by at least 10 different individuals. The falsifications took place between at least July 2008 and 2013;
- the systematic nature of the falsifications of electrocardiograms, the extended period of time during which they took place and the number of members of staff involved highlight critical deficiencies in the quality system in place at GVK Bio's clinic in Hyderabad. They also show a lack of GCP training, awareness and understanding of members of GVK Bio staff, a lack of understanding by them of the importance of data integrity and of the possible consequences of their acts, as well as a lack of overview of clinical trial activities by the investigators. The seriousness of the deficiencies identified and the lack of GCP compliance at GVK Bio's clinic in Hyderabad raise questions as to the acceptability of the clinical part of all other bioequivalence trials performed at that site in support of marketing authorisations applications.

These findings are detailed in the ANSM inspection report dated 02 July 2014, to which GVK Bio have responded on 18 July 2014 and in the final inspection report which was issued on 21 July 2014

The CHMP should assess the potential impact of the findings mentioned above on the benefit-risk balance of the medicinal products which have been authorised by the Member States on the basis of relevant trials performed at the inspected site.

Taking into account these critical GCP deficiencies relating to data integrity found on every clinical trial inspected and performed from 2008, the CHMP may consider if the scope of this referral should be extended to studies conducted by GVK Bio in Hyderabad before 2008.

In view of the elements described above and the necessity to take an action at EU level, the European Commission considers that it is in the interest of the Union to refer the matter to the CHMP and requests that it gives its opinion under Article 31 of Directive 2001/83/EC as to whether marketing authorisations of these products should be maintained, varied, suspended, or withdrawn.

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Head of Unit, Medicinal products – authorisations, EMA

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