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 Germany (BfArM):

Medicinal products concerned	Medicinal products, which have been authorised or are pending approval based on clinical trials performed at Panexcell Clinical Laboratories Priv. Ltd. See annex I

The Federal Office for Safety in Health Care (BASG), Austria, and the Federal Institute of Drugs and Medical Devices (BfArM), Germany, performed a joint GCP inspection from 14 – 17 October 2019 at the contract research organisation (CRO) Panexcell Clinical Laboratories Priv. Ltd. (EMA Inspection references: GCP/2019/020).

The CRO Panexcell Clinical Laboratories Priv. Ltd. (formerly named the Drug Monitoring Research Institute (DMRI)), is located in Navi Mumbai 400 701, India.

A bioequivalence trial (test substance: doxorubicin) performed by this CRO in 2018/2019 was inspected. The inspection focussed mainly on the bioanalysis and pharmaco-kinetics (PK) of the doxorubicin and doxorubicinol concentrations in plasma. The findings reported during this inspection cast serious doubts on the reliability of the data of this bioequivalence study.

The following critical observations were made during the inspection:

- The reported PK profiles for free doxorubicin and doxorubicinol of several subjects were found to be exceptionally similar. From the verification done during inspection it is apparent that study samples could not have been mixed-up accidentally. The similarities of the profiles are of such extent that they cannot be explained and there are serious doubts whether the reported concentrations of the subjects do actually originate from these. Moreover, the confidence interval, which was >125% after the samples of the first 32 subjects were analysed showed a downwards trend and appeared to be only within the acceptance limit after the affected subject samples were analysed.
- During the inspection in October 2019, study personnel intentionally documented the wrong room temperature in order to pretend that room temperature in the sample processing area was within the acceptance range.

The severity and the extent of the findings of the inspection of BASG and BfArM raise serious concerns relating to the suitability of the quality management system at Panexcell Clinical Laboratories Priv. Ltd. and about the overall reliability of data generated by this CRO and submitted to support the marketing authorisation applications for medicinal products in the EU.

In view of the elements described above and the necessity to take action at EU level, Germany considers that it is in the interest of the Union to refer the matter to the CHMP and requests that it assesses the impact of the findings mentioned above on the benefit-risk

balance of the medicinal products which have been authorized in the EU on the basis of clinical trials performed at Panexcell Clinical Laboratories Priv. Ltd., as well as for pending procedures, based on clinical trials performed by this CRO. The CHMP is requested in particular to provide its opinion under Article 31 of Directive 2001/83/EC as to whether marketing authorizations of these products should be maintained, varied, suspended or revoked.

Signed 

Date 19.02.2020