NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC

E-mail: ReferralNotifications@ema.europa.eu

This notification is a referral under Article 31 of Directive 2001/83/EC to the CHMP made by: Denmark

Details on the draft list of products concerned (pending and finalized) are annexed to this notification.

Between 29 September 2015 and 9 October 2015, the US FDA performed a GCP inspection at the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India.

The inspection found significant instances of misconduct, including the substitution and manipulation of study subject samples. The findings reported during this inspection cast serious doubts on the reliability of the data of bioequivalence studies (clinical and bioanalytical part) generated at the site. Therefore the FDA concluded that clinical and bioanalytical studies conducted by Semler Research Private Limited in Bangalore, India are not acceptable as a result of data integrity concerns (http://www.fda.gov/Drugs/DrugSafety/ucm495778.htm).

The WHO also inspected the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India and the clinical facility PA Arcade #21,22,23 Kodigehali Main Road, Sahakaranagar Post, Bangalore 560 092, Karnataka, India between 27 and 31 January 2015, and performed a follow-up inspection between 2 and 5 December 2015 to verify compliance with GLP and GCP. The inspections revealed critical and major deviations which led to the publishing of a WHO notice of concern (http://apps.who.int/prequal/info_applicants/NOC/2016/NOC_Semler12April2016.pdf).

The WHO concluded that the findings indicate the existence of a general or systematic deviation from commonly accepted quality standards, and cannot be ascribed to a single person or two working outside of the quality management system. On these grounds, the WHO pre-qualification team (PQT) recommended an immediate stop to all submissions of dossiers relying in whole or in part on involvement from Semler until the underlying issues have been verified to have been adequately resolved.

The findings of the FDA and WHO inspections raise serious concerns relating to the suitability of the quality management system at these sites and of the reliability of data submitted in applications for marketing authorisations submitted in EU Member States.

In view of the findings described above and the necessity to protect public health in EU, Denmark 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 authorised by the Member States on the basis of relevant trials performed at these sites and also for pending procedures . The CHMP is requested in particular to provide its opinion under Article 31 of Directive 2001/83/EC as to whether marketing authorisations of these products should be maintained, varied, suspended, or revoked.

Signed [redacted]

Date: 28. April 2016

NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC

E-mail: ReferralNotifications@ema.europa.eu

This notification is a referral under Article 31 of Directive 2001/83/EC to the CHMP made by the Germany:

Details on the draft list of products concerned (pending and finalized) are annexed to this notification.

Between 29 September 2015 and 9 October 2015, the US FDA performed a GCP inspection at the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India.

The inspection found significant instances of misconduct, including the substitution and manipulation of study subject samples. The findings reported during this inspection cast serious doubts on the reliability of the data of bioequivalence studies (clinical and bioanalytical part) generated at the site. Therefore the FDA concluded that clinical and bioanalytical studies conducted by Semler Research Private Limited in Bangalore, India are not acceptable as a result of data integrity concerns (http://www.fda.gov/Drugs/DrugSafety/ucm495778.htm).

The WHO also inspected the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India and the clinical facility PA Arcade #21,22,23 Kodigehali Main Road, Sahakaranagar Post, Bangalore 560 092, Karnataka, India between 27 and 31 January 2015, and performed a follow-up inspection between 2 and 5 December 2015 to verify compliance with GLP and GCP. The inspections revealed critical and major deviations which led to the publishing of a WHO notice of concern (http://apps.who.int/prequal/info_applicants/NOC/2016/NOC_Semler12April2016.pdf). The WHO concluded that the findings indicate the existence of a general or systematic deviation from commonly accepted quality standards, and cannot be ascribed to a single person or two working outside of the quality management system. On these grounds, the WHO pre-qualification team (PQT) recommended an immediate stop to all submissions of dossiers relying in whole or in part on involvement from Semler until the underlying issues have been verified to have been adequately resolved.

The findings of the FDA and WHO inspections raise serious concerns relating to the suitability of the quality management system at these sites and of the reliability of data submitted in applications for marketing authorisations submitted in EU Member States.

In view of the findings described above and the necessity to take protect public health in EU, 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 authorised by the Member States on the basis of relevant trials performed at these sites and also for pending procedures . The CHMP is requested in particular to provide its opinion under Article 31 of Directive 2001/83/EC as to whether marketing authorisations of these products should be maintained, varied, suspended, or revoked.

Signed [redacted]

27.04.2016

NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC

E-mail: ReferralNotifications@ema.europa.eu

This notification is a referral under Article 31 of Directive 2001/83/EC to the CHMP made by the SPAIN

Details on the draft list of products concerned (pending and finalized) are annexed to this notification.

Between 29 September 2015 and 9 October 2015, the US FDA performed a GCP inspection at the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India.

The inspection found significant instances of misconduct, including the substitution and manipulation of study subject samples. The findings reported during this inspection cast serious doubts on the reliability of the data of bioequivalence studies (clinical and bioanalytical part) generated at the site. Therefore the FDA concluded that clinical and bioanalytical studies conducted by Semler Research Private Limited in Bangalore, India are not acceptable as a result of data integrity concerns (http://www.fda.gov/Drugs/DrugSafety/ucm495778.htm).

The WHO also inspected the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India and the clinical facility PA Arcade #21,22,23 Kodigehali Main Road, Sahakaranagar Post, Bangalore 560 092, Karnataka, India between 27 and 31 January 2015, and performed a follow-up inspection between 2 and 5 December 2015 to verify compliance with GLP and GCP. The inspections revealed critical and major deviations which led to the publishing of a WHO notice of concern (http://apps.who.int/prequal/info_applicants/NOC/2016/NOC_Semler12April2016.pdf). The WHO concluded that the findings indicate the existence of a general or systematic deviation from commonly accepted quality standards, and cannot be ascribed to a single person or two working outside of the quality management system. On these grounds, the WHO pre-qualification team (PQT) recommended an immediate stop to all submissions of dossiers relying in whole or in part on involvement from Semler until the underlying issues have been verified to have been adequately resolved.

The findings of the FDA and WHO inspections raise serious concerns relating to the suitability of the quality management system at these sites and of the reliability of data submitted in applications for marketing authorisations submitted in EU Member States.

In view of the findings described above and the necessity to take protect public health in EU, SPAIN 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 authorised by the Member States on the basis of relevant trials performed at these sites and also for pending procedures . The CHMP is requested in particular to provide its opinion under Article 31 of Directive 2001/83/EC as to whether marketing authorisations of these products should be maintained, varied, suspended, or revoked.

Signed

[redacted]

Date
27 April 2016

NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC
E-mail: ReferralNotifications@ema.europa.eu

This notification is a referral under Article 31 of Directive 2001/83/EC to the CHMP made by The Netherlands:

Details on the draft list of products concerned (pending and finalized) are annexed to this notification.

Between 29 September 2015 and 9 October 2015, the US FDA performed a GCP inspection at the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India.

The inspection found significant instances of misconduct, including the substitution and manipulation of study subject samples. The findings reported during this inspection cast serious doubts on the reliability of the data of bioequivalence studies (clinical and bioanalytical part) generated at the site. Therefore the FDA concluded that clinical and bioanalytical studies conducted by Semler Research Private Limited in Bangalore, India are not acceptable as a result of data integrity concerns (http://www.fda.gov/Drugs/DrugSafety/ucm495778.htm).

The WHO also inspected the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India and the clinical facility PA Arcade #21,22,23 Kodigehali Main Road, Sahakaranagar Post, Bangalore 560 092, Karnataka, India between 27 and 31 January 2015, and performed a follow-up inspection between 2 and 5 December 2015 to verify compliance with GLP and GCP. The inspections revealed critical and major deviations which led to the publishing of a WHO notice of concern (http://apps.who.int/prequal/info_applicants/NOC/2016/NOC_Semler12April2016.pdf). The WHO concluded that the findings indicate the existence of a general or systematic deviation from commonly accepted quality standards, and cannot be ascribed to a single person or two working outside of the quality management system. On these grounds, the WHO pre-qualification team (PQT) recommended an immediate stop to all submissions of dossiers relying in whole or in part on involvement from Semler until the underlying issues have been verified to have been adequately resolved.

The findings of the FDA and WHO inspections raise serious concerns relating to the suitability of the quality management system at these sites and of the reliability of data submitted in applications for marketing authorisations submitted in EU Member States.

In view of the findings described above and the necessity to take protect public health in EU, The Netherlands 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 authorised by the Member States on the basis of relevant trials performed at these sites and also for pending procedures . The CHMP is requested in particular to provide its opinion under Article 31 of Directive 2001/83/EC as to whether marketing authorisations of these products should be maintained, varied, suspended, or revoked.

Signed

Date 27 April 2016

NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC

E-mail: ReferralNotifications@ema.europa.eu

This notification is a referral under Article 31 of Directive 2001/83/EC to the CHMP made by the UK:

Details on the draft list of products concerned (pending and finalized) are annexed to this notification.

Between 29 September 2015 and 9 October 2015, the US FDA performed a GCP inspection at the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India.

The inspection found significant instances of misconduct, including the substitution and manipulation of study subject samples. The findings reported during this inspection cast serious doubts on the reliability of the data of bioequivalence studies (clinical and bioanalytical part) generated at the site. Therefore the FDA concluded that clinical and bioanalytical studies conducted by Semler Research Private Limited in Bangalore, India are not acceptable as a result of data integrity concerns (http://www.fda.gov/Drugs/DrugSafety/ucm495778.htm).

The WHO also inspected the bioanalytical facility Semler Research Centre Private Ltd, 75A, 15th Cross, 1st Phase, J.P. Nagar, Bangalore – 560 078 India and the clinical facility PA Arcade #21,22,23 Kodigehali Main Road, Sahakaranagar Post, Bangalore 560 092, Karnataka, India between 27 and 31 January 2015, and performed a follow-up inspection between 2 and 5 December 2015 to verify compliance with GLP and GCP. The inspections revealed critical and major deviations which led to the publishing of a WHO notice of concern (http://apps.who.int/prequal/info_applicants/NOC/2016/NOC_Semler12April2016.pdf). The WHO concluded that the findings indicate the existence of a general or systematic deviation from commonly accepted quality standards, and cannot be ascribed to a single person or two working outside of the quality management system. On these grounds, the WHO pre-qualification team (PQT) recommended an immediate stop to all submissions of dossiers relying in whole or in part on involvement from Semler until the underlying issues have been verified to have been adequately resolved.

The findings of the FDA and WHO inspections raise serious concerns relating to the suitability of the quality management system at these sites and of the reliability of data submitted in applications for marketing authorisations submitted in EU Member States.

In view of the findings described above and the necessity to take protect public health in EU, MHRA 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 authorised by the Member States on the basis of relevant trials performed at these sites and also for pending procedures . The CHMP is requested in particular to provide its opinion under Article 31 of Directive 2001/83/EC as to whether marketing authorisations of these products should be maintained, varied, suspended, or revoked.

Signed

Date 27 April 2016