WHO Response to the USFDA import alert issued for Qinhuangdao Zizhu Pharmaceutical Co Ltd, Active Pharmaceutical Ingredient (API) Manufacturing Site

On 8th March 2017, Qinhuangdao Zizhu Pharmaceutical was placed on the import alert by the USFDA.

The Good Manufacturing Practice (GMP) inspection was carried out by the USFDA at Qinhuangdao Zizhu Pharmaceutical, No. 10, Longhai Avenue, Economic Development Zone, Qinhuangdao, Hebei, China 066004 on 28 November to 1 December 2016. The inspection found failures in the level of adherence to cGMP for APIs. In particular, the USFDA inspection team discovered a breach of data integrity related to testing in the Quality Control laboratory.

WHO Prequalification Team (PQT) had inspected Qinhuangdao Zizhu Pharmaceutical in October 2015 for levonorgestrel, mifepristone and ethinylestradiol APIs. The inspection concluded with 5 major deficiencies including data integrity issues and several minor deficiencies. The manufacturer provided corrective and preventive actions (CAPAs) for all deficiencies; the inspection was closed as compliant based on the CAPAs provided by the manufacturer.

WHO has prequalified two finished pharmaceutical products (FPP) for which the inspected Qinhuangdao Zizhu Pharmaceutical is listed as the levonorgestrel supplier. WHO has also prequalified Mifepristone and ethinylestradiol APIs manufactured by Qinhuangdao Zizhu Pharmaceutical Co Ltd.

To date, WHO-PQT has not received any reports of quality issues on levonorgestrel tablets from the market.

<u>WHO action and advice</u>

WHO has been in touch with Qinhuangdao Zizhu Pharmaceutical Co Ltd. and USFDA to discuss this matter.

At the moment, there is no alternative levonorgestrel API which has been prequalified by WHO-PQT. WHO-PQT is working closely with the FPP manufacturers to identify additional sources for levonorgestrel.

Meanwhile, FPP manufacturers of prequalified products that use levonorgestrel manufactured by Qinhuangdao Zizhu Pharmaceutical are requested to take additional measures such as comprehensive testing upon receipt to help ensure that the quality of all batches of levonorgestrel is assured.

Until further notice, procurement agencies may continue to procure FPPs that contain API produced at Qinhuangdao Zizhu Pharmaceutical. The prequalification status of Qinhuangdao Zizhu Pharmaceutical Co Ltd. prequalified APIs (levonorgestrel, Mifepristone and ethinylestradiol) remains unchanged.

WHO-PQT is planning to conduct an on-site inspection of Qinhuangdao Zizhu Pharmaceutical.

WHO will continue to follow up on this issue and provide updates.