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To: Commissioners of Prefectural District Health Department (Bureau)

Director of the Pharmaceutical Safety Division,
Pharmaceutical Safety and Environmental Health Bureau, MHLW
(Official seal omitted)

Self-check etc. of package inserts for in vitro diagnostics using biotin for the measurement system

With respect to in vitro diagnostics using biotin for the measurement system, the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have been warning that incorrect test results may be generated when measured specimens are derived from test subjects who have ingested high doses of biotin.

Along with these alerts, we are requesting commissioners of prefectural district health department (bureau) to ensure that the marketing authorization holders (MAHs) of in vitro diagnostics using biotin for the measurement system under your jurisdiction perform self-check of the package inserts of their products regarding the requirements listed below, revise them if necessary, and notify medical institutions and other relevant parties of the revision together with associated information.

1. MAHs of the in vitro diagnostics using biotin for the measurement system should check their products to determine if the measurement principles and test subjects of the products could lead to test results interfered with biotin contained in specimens if they are derived from test subjects who have ingested high doses of biotin through drugs, supplements, or other similar sources.
2. For the products determined to potentially generate interfered test results as a result of the check described in 1 above, their package inserts should be reviewed to ensure that;

(1) "Biotin (vitamin B_7)" is listed as Interfering Substances/Interfering Drugs in the Operational Precautions section.

(2) The maximum concentration of biotin that has been determined not to interfere with test results is stated in the same section.

3. As a result of the checking in 2 above, if the language of the package inserts is considered insufficient for the required alert, the package inserts should be revised promptly and necessary information should be provided to medical institutions and other relevant parties.

4. Details of the checking of 1 to 3 above and the revision of the package inserts as a result of the check should be reported to the Division of Safety for Medical Devices, Office of Manufacturing Quality and Vigilance for Medical Devices, Pharmaceuticals and Medical Devices Agency by October 15, 2019. Of note, if the revision of a package insert is not completed as of October 15, 2019, the review status as of the date should be reported and the Office should be contacted again later with the revised package insert.