FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) Meeting
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
June 20, 2017

DRAFT QUESTIONS

1. **DISCUSSION:** The Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial was a cardiovascular (CV) outcomes trial conducted as a postmarketing requirement to evaluate CV safety as per the 2008 FDA Guidance titled *Diabetes Mellitus – Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes*. Additional non-CV safety concerns related to liraglutide and other incretin mimetics were also evaluated in LEADER, including potential risk of medullary thyroid carcinoma, pancreatic neoplasm, and pancreatitis. For each of these non-CV safety concerns, please comment on whether the data presented today inform of a causal relationship with liraglutide use. In your discussion, please comment on whether additional studies should be conducted to further evaluate the non-CV safety concern(s).

2. **DISCUSSION:** Please comment on the design and conduct of LEADER as a cardiovascular outcomes trial (CVOT) and whether it adequately addresses the 2008 FDA Guidance.

3. **VOTE:** Do the results of LEADER establish that use of liraglutide in patients with Type 2 diabetes mellitus (T2DM) is not associated with excess cardiovascular risk?

4. **VOTE:** Does the LEADER trial provide the substantial evidence required to establish that liraglutide 1.8 mg reduces cardiovascular risk in patients with T2DM and established CV disease?