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Issues and Interests Identified by Study Sponsors

1. For a reference value related to adequate intakes, particular consideration should be given to the selection of indicators of adequacy for the various age, gender, and life stage groups that will allow for the determination of the type of reference value of highest relevance to the needs of the sponsors. Such needs are most readily met in the case of vitamin D and calcium by the establishment of an Estimated Average Requirement¹ (EAR). The EAR is useful because it is the best type of reference value for assessing the adequacy of estimated nutrient intakes of groups and for planning intakes for groups. It is also the most useful type of reference value when planning and assessing total diets. These are necessary and primary applications by the study sponsors.

2. For reference values related to excessive intakes, Tolerable Upper Intake Levels (UL) for the various age, gender, and life stage groups are needed. Efforts should be made to examine if a critical adverse effect can be selected, which will allow for the determination of a Benchmark Intake² (aka “Benchmark Dose”).

3. In determining the reference values for vitamin D, confounding factors are important considerations, notably those that affect the DRI population groups such as latitude, sun exposure, skin pigmentation, vi-

¹Estimated Average Requirement: The average daily nutrient intake level that is estimated to meet the requirements of half of the healthy individuals in a particular life stage and gender group (*Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*, IOM [2006]).

²Benchmark Intake: The intake of a substance that is expected to result in a prespecified level of effect. (*A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances*, [WHO/FAO]).

tamin D stores, and obesity will be considered. In addition, specification as to whether the EAR and UL are related to lean body mass or to energy intake would be useful, as data allow.

4. The target population of interest for the reference values are the people residing in the United States and Canada, including those whose needs for or sensitivity to vitamin D or calcium may be affected by particular conditions such as obesity or oral contraceptive use; those with highly pigmented skin; those with risk factors for chronic disease; and those with chronic or other diseases that do not alter their requirements for or sensitivity to vitamin D or calcium. For vitamin D, the target population may also include subgroups within the general population whose requirements for vitamin D intakes may need to be considered within the context of limited endogenous synthesis or differences in metabolic handling of vitamin D (e.g., limited sun exposure because of latitude, clothing, institutionalization, dark skin pigmentation; older persons with reduced capacity for dermal synthesis; racial/ethnic differences in metabolic handling of these nutrients). In deriving the reference values, it is useful if the relevance of study populations found in the literature is considered relative to the target population. It is also important to identify as data allow the special populations whose nutrient requirements or sensitivities differ from the general population as described above for whom DRI values are derived (e.g., diseased persons, persons using drugs known to alter the nutrient requirements or safety profiles).