

Division of Dockets Management  
HFA-305  
Food and Drug Administration  
5600 Fishers Lane, Room 1061  
Rockville, MD 20852

Re: Docket 2005D-0122 : Draft Guidance Exploratory IND Studies

This statement is being submitted by Radioactive Drug Research Committee (RDRC) #0038, located at Lawrence Berkeley National Laboratory. The comments herein pertain to the draft guidance for "Exploratory IND Studies".

**1) Comment relative to Section C.1 Clinical studies of pharmacokinetics or imaging**

The definition of microdose is given as "less than 1% of the dose calculated to yield a pharmacological effect of a test substance and a maximum of  $\leq 100$  micrograms". This definition, which parallels the European Medicines Agency (EMA) position paper, references the maximum mass of the compound to be injected. Mass is not necessarily the best unit to use in this case as it is the number of moles of the compound (i.e. the number of molecules) that will dictate the pharmacological effect. As the molecular weight of test substances increases the number of moles decreases. Thus, we recommend that the maximum number of moles be specified rather than the mass. Given a minimum molecular weight of a typical test substance of 100 g/mol (100  $\mu\text{g}/\mu\text{mol}$ ) then the maximum dose would be 1 micromole.

**Suggested microdose definition:**

A microdose is defined as less than 1% of the dose calculated to yield a pharmacological effect of a test substance and a maximum of  $\leq 1$  micromole.

Respectfully submitted by the members of RDRC 0038 – Lawrence Berkeley National Laboratory

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