



March 20, 2006

Docket No. 2005D-0286
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Sirs:

Takeda Global Research and Development Center, Inc. (TGRD) has the following comments on your Guidance for Industry: INDs – Approaches to Complying with CGMP During Phase 1 Draft Guidance.

We are unclear as to what is included and excluded in this Draft Guidance. We are asking for clarification on specific issues and studies.

Line 224 – This section appears unnecessary if CGMPs are followed, which are required according to this Guidance. This section also appears to cater to a specific sector of the Industry (i.e., small organizations). If this is a general Guidance provided by FDA for Industry to follow, then shouldn't this Guidance apply to all of Industry, irrespective of the size of the organization? Alternatively, provide specific definition of the size of the organization that pertains to the description contained in lines 245-246. More specifically to the content of this section, is it referring to a detailed QC protocol for each and every project, or is this to be captured in a general SOP?

Line 296 – Does this refer to the company, which makes the API or drug product, or the company, which is dosing the study? In cases of absolute bioavailability studies or Absorption, Distribution, Metabolism, Elimination (ADME) studies, TGRD ensures that API is provided to the pharmacy of the clinical investigation site. Does this dosing site then fall under this guidance as well as under the CGCPs?

Line 339 – Does the representative sample need to be stored at the site where it was manufactured or used? Can the sponsor identify a third party to keep the retained samples? In the case of the preceding comment, what sample should be retained? Should samples that we know are not going to be stable for 2 years actually be stored for 2 years? Clinical supplies such as API added to water for a BA study or radiolabeled API are not typically stable for two years.

Line 345 – Can the stability of the product be determined from a previous study? Or is the agency asking for an additional study to be done simultaneously with the IND study to monitor the stability of the specific product used in the clinical investigation?



Line 351 – Does the Agency expect the sponsor to perform shipping studies for clinical supplies being used during this early stage of development (i.e. freeze thaw)?

Line 367 – Please confirm that the sponsor only needs to ensure that all of these items are retained, especially in the event that contract research laboratories or manufacturers are utilized. Does the sponsor really need to retain the maintenance logs for equipment used?

Line 383 –In the Special Production Situations, do these samples need to be retained for two years as well, or is this requirement not applicable to this section? Please clarify.

Sincerely,

A handwritten signature in cursive script that reads "Chris Rojewski".

Chris Rojewski
Manager, CMC, Pharmaceutical Development and Supplies
Takeda Global Research and Development Center, Inc.