



GE Healthcare

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March 15, 2006

Documents Management Branch (HFA-305)  
Food and Drug Administration  
5600 Fishers Lane  
Room 1061  
Rockville, MD 20852

**Re: Docket No. 2005D-0286  
Comments to Draft Guidance – Approaches to Complying with Current Good Manufacturing Practice During Phase 1**

Dear Documents Management Staff:

Reference is made to the subject docket number published in the Federal Register Volume 71, Number 10, page 2552 which announced the availability of a draft guidance for Industry, entitled "Approaches to Complying with Current Good Manufacturing Practice During Phase 1."

GE Healthcare welcomes this initiative from the FDA. We believe that it is supportive of the concepts put forward in the Critical Path Initiative to eliminate impediments to clinical development of investigational drug products. After reviewing the draft guidance we have comments that we believe will further clarify the guidance. At this time, as requested by the Federal Register notice, GE Healthcare is providing its comments to the draft guidance on the following pages.

Please call me at (609)-514-6573 if you have any questions or comments regarding this submission.

Sincerely,  
GE Healthcare

Fred Longenecker  
Director, Regulatory Development

2005D-0286

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## Draft Guidance for Industry

### Approaches to Complying with Current Good Manufacturing Practice During Phase 1

January 17, 2006 (Docket No. 2005D-0286)

#### GE Healthcare Comments

In the final regulation (Docket No. 2005N-0285) and the draft guidance for industry the Agency has indicated that in exempting "Phase 1" drugs from compliance with Current Good Manufacturing Practices the Agency will rely on its general statutory CGMP authority and investigational new drug (IND) application authority. We interpret this to mean that the Agency is not intending to require that IND submissions for Phase 1 clinical trials include additional CGMP documentation and that documentation which is already required under 21CFR 312.23 – IND Content and Format is sufficient.

GE Healthcare requests that the Agency provide text to this effect in Section III. – "Scope" and/or Section V – "Recommendations for Complying With the Statute" of the guidance for industry when it is finalized.

Section III – "Scope" (the boxed text in line 86) indicates that "in vivo diagnostics" is one class of investigational new human drugs and biological products to which the draft guidance of industry applies. In vivo diagnostics include a number of radiopharmaceutical drugs including Positron Emission Tomography (PET) drugs. The Agency currently has pending a proposed rule (21CFR 212; Docket No. 2004N-0439) and draft guidance for industry (Docket No. 1998D-0266) on "Current Good Manufacturing Practice for Positron Emission Tomography (PET) Drugs." Section 212.5 (b) of the PET CGMP proposed rule states investigational PET drugs are not required to comply with CGMP requirements but instead are expected to comply with Chapter 823 – "Radiopharmaceuticals for Positron Emission Tomography – Compounding" of the US Pharmacopoeia.

GE Healthcare requests that the Agency provide additional text within Section III – "Scope" of the proposed guidance for industry "Approaches to Complying with Current Good Manufacturing Practice During Phase 1" to reflect that the guidance does not apply to investigational PET drugs which instead are addressed in 21CFR212.5.

Section V, Item F (1) – "Laboratory Controls – Testing" states in paragraph 4 (page 9) that representative samples of each product batch should be retained for a period of at least 2 years following study termination or withdrawal of the IND. Such a retention time may not be appropriate for all investigational drugs, specifically for radiopharmaceutical drugs. Referring specifically to radiopharmaceuticals, the 21CFR 211.170(a)(2) states that retention of reserve samples should be three months after the expiration date of the last lot of the drug product

containing the active ingredient if the expiration dating is 30 days or less. For those radiopharmaceuticals with expiration dating greater than 30 days a six month retention time is required. Additionally, as noted in our previous comment, the Agency has a proposed rule (21CFR 212) and draft guidance specifically addressing CGMP for PET drugs, a sub-group of radiopharmaceuticals. The proposed rule and draft guidance do not require a retention period for PET drugs.

GE Healthcare requests that the Agency provide additional clarifying text within Section V, Item F (1) – “Laboratory Controls – Testing” of the proposed guidance for industry “Approaches to Complying with Current Good Manufacturing Practice During Phase 1” in regard to retention time of reserve samples. It should be stated that the requirements of 21CFR 211.170 (a) (2) apply for investigational radiopharmaceutical drug products in general. It should also be re-stated that the subject guidance does not apply to PET drugs which instead are addressed in 21CFR 212 and the Agency guidance on “Current Good Manufacturing Practice for Positron Emission Tomography (PET) Drugs.”