Study Protocol were such that a submitted IND was, in fact, required. This issue narrowly applies only to drugs that are radioactive, and narrowly applies to radioactive drugs that are used for basic research in humans. The Warning Letter stated that (38):

> FDA regulations require that a sponsor submit an IND to FDA if the sponsor intends to conduct a clinical investigation with an investigational new drug . . .and have IND in effect before the investigational drug is used in a clinical investigation . . . [o]ur investigation indicates that you initiated and were responsible for the conduct of a clinical investigation intended to evaluate the use of [redacted] an investigational new drug, as a diagnostic agent, and that you did not have an IND in effect when the study drug was administered to study subjects.

FDA's Warning Letter stated that the Sponsor, "originally believed that the study could be conducted under 21 CFR §361 . . . and, therefore, did not require an IND." This section of the Code of Federal Regulations, which concerns drugs that are recognized as safe, states that:

> Radioactive drugs . . . are generally recognized as safe and effective when administered . . . to human research subjects during the course of a research project intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a radioactively labeled drug or regarding human physiology, pathophysiology, or biochemistry, **but not intended for immediate therapeutic**, diagnostic, or similar purposes **or to determine the safety and effectiveness** of the drug in humans.

Unfortunately for the Sponsor, FDA's Warning Letter pointed out that the Sponsor's *radioactive drug could have a pharmacological influence* on the human subjects. The letter complained that, "[t]here was no documentation to indicate that the proposed dose of . . . 75 μg . . . would not induce an immunological response in humans."

Further referring to Section 361, the Warning Letter referred to additional potential pharmacological effects of the study drug (pyrogenicity), and complained that, "the radioactive drug used in the research must meet . . . standards of identity, strength, quality, and purity as needed for safety and be prepared in sterile and pyrogen-free form . . . [y]ou failed to ensure that the **[study drug]** which was derived from human biological material, was appropriately processed or tested to ensure at it was free of transmissible human pathogens and that it was in a sterile and pyrogen-free form."

IX. INSTITUTIONAL REVIEW BOARD

a. Introduction

FDA's Guidance for Industry provides some of the responsibilities of the Institutional Review Board (IRB). These responsibilities include (39):

- IRB must determine that risks to subjects are minimized;
- IRB must determine that risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects;
- IRB must determine that informed consent will be sought from each prospective subject or the subject's legally authorized representative;
- IRB must determine that safeguards are included to protect vulnerable subjects;

[38]Warning Letter No. 06-HFD-45-06-03 (June 15, 2006) from Joseph Salewski, Division of Scientific Investigation, Office of Compliance, CDER, U.S. Food and Drug Administration.

[39]U.S. Department of Health and Human Services. Food and Drug Administration Guidance for industry. IRB continuing review after clinical investigation approval; February 2012 (25 pp.).