had earlier been documented on several Form FDA483 notices, cited 21 CFR §312.60, and complained that (187):

> You failed to personally conduct or supervise the clinical investigation . . .
>
> When you signed . . . **Form FDA 1572**. . . you agreed to take on the responsibilities of a clinical investigator at your site. Your . . . responsibilities . . . include ensuring that the investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; protecting the . . . safety . . . subjects under your care; and ensuring control of drugs under investigation . . . [w]hile **you may delegate certain study tasks** to individuals qualified to perform them . . . **you may not delegate your general responsibilities**. Our investigation indicates that your supervision of personnel to whom you delegated study tasks was not adequate to ensure that clinical trials were conducted according to the signed investigator statement, the investigational plan, and applicable regulations, and in a manner that protected the . . . safety . . . of human subjects.

An unrelated Warning Letter also complained about failures in the chain of responsibilities. The letter referred to Form FDA 1572 and to the agreement to supervise and failure to supervise individuals to whom tasks were delegated, stating that (188), "[y]ou did not adequately supervise individuals to whom you delegated study tasks . . . [y]our lack of oversight resulted in protocol violations, inadequate drug accountability, inadequate informed consent." Failure to supervise was also the issue in yet another Warning Letter, where the problem was failure to supervise "new study coordinators" (189). Yet another Warning Letter provides guidance of the relative responsibilities of the investigator and the monitor. The issue was the responsibility to report amendments of the Clinical Study Protocol to the Institutional Review Board (IRB). The investigator tried to blame the monitor for failing to notify the IRB of the amendment. However, the Warning Letter corrected the investigator's false notion, by writing (190):

> In your December 24, 2012, written response to the violation . . . you said, "The **monitor** failed to inform and educate the site about the amendment to the Protocol . . ." [h]owever, it is **your responsibility as the investigator** (**not the monitor's responsibility**) to ensure that the IRB has approved any changes in the research prior to implementing those changes. In addition, your response is inadequate because you failed to provide evidence of IRB approval.

b. Record Keeping Failure of CRO

This concerns a problem in record keeping. The problem was that the written record stated that one of the study personnel did something that was impossible, namely, giving study drug to two subjects at exactly the same time. The letter complained that it is impossible for one person, the "study coordinator," to administer study drug to two people at exactly the same time.

[187]Warning Letter No. 06-HFD-45-1101 (January 16, 2007) from Gary Zana, Division of Scientific Investigations, Office of Compliance, CDER, U.S. Food and Drug Administration.

[188]Warning Letter No. 08-HFD-45-09-01 (October 1, 2008) from Dr Leslie K. Ball, MD, Office of Compliance, CDER, U.S. Food and Drug Administration.

[189]Warning Letter No. 09-HFD-45-06-01 (June 12, 2009) from Dr Leslie K. Ball, MD, Office of Compliance, CDER, U.S. Food and Drug Administration.

[190]Warning Letter No. 13-HFD-45-08-04 (September 3, 2013) from Thomas N. Moreno, Office of Compliance, CDER, U.S. Food and Drug Administration.