the rationale for administering re-consent forms. The letter complained that (73):

> [y]ou failed to re-consent 11 subjects (#001, 007, 013, 024, 036, 041, 043, 048, 049, 053, and 056) in a timely manner at their next scheduled visit per the IRB's requirement . . . [i]n FDA's review of the documents, we note that several months had elapsed prior to your site re-consenting these subjects with the revised consent form. The revised informed consent document, version 5/23/06, provided information that may have affected the subjects' willingness to stay in the study, because it warned them of additional risks of participating in the study and also provided new information about the study. Thus, your delay in re-consenting these subjects with the revised consent document leads to significant concerns about the adequacy of your oversight over the study to ensure the protection of the rights, safety and welfare of the subjects enrolled in this study.

f. Warning Letter About Using a Consent Form That Had Not Been Approved by the IRB

This concerns a consent form that had been modified by hand-writing, and where the modification was not approved by the IRB. The Warning Letter complained that (74):

> You violated this requirement [21 CFR §312.66] by administering the investigational new drug . . . to Subject 1010 without obtaining IRB approval of the modified informed consent document. Specifically, the IRB-approved version of the informed consent . . . was altered by hand to state that the subject would not receive payment for participation . . . and this altered form was signed by the parent of Subject 1010.

XII. DECISION AIDS

Decision aids can be used in conjunction with a consent form, in the course of a clinical trial, as well as in conventional medical care. Brehaut et al. (75) advocate the use of decision aids for subjects contemplating enrolling in a clinical trial, in view of the fact that consent forms can be confusing. Where confusion occurs with consent forms, it usually takes the form of not understanding "randomization," (76). Confusion also occurs because the subject incorrectly expects the study drug to be effective, even though it might only be an experimental drug.

This example is from an account from a published courtroom opinion. In one particular clinical trial for breast cancer, patients were randomized to receive a biopsy either of the axillary lymph node or of the sentinal lymph node. One patient from this clinical trial was confused about the meaning of randomization. The confusion arose from being "explained that the clinical trial would let the computer decide whether plaintiff [the patient] would have an axillary lymph node or sentinal lymph node biopsy, plaintiff [the patient] thought that the computer would decide the choice that was right for her" (77).

[73]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.

[74]Warning Letter No. 10-HFD-45-01-02 (February 24, 2010) from Dr Leslie K. Ball, MD, Office of Compliance, CDER, U.S. Food and Drug Administration.

[75]Brehaut JC, Lott A, Fergusson DA, Shojania KG, Kimmelman J, Saginur R. Can patient decision aids help people make good decisions about participating in clinical trials? A study protocol. Implement Sci. 2008;3:38.

[76]Stead M, Eadie D, Gordon D, Angus K. "Hello, hello—it's English I speak!": a qualitative exploration of patients' understanding of the science of clinical trials. J. Med. Ethics 2005;31:664–9.

[77]Compton v. Pass. 2010 Mich. App. LEXIS 556.