(5.3.5.1.1) are as follow [sic]…patient did not provide 2 consents" (174,175). Thus, a fair amount of missing data during an early part of the approval process delayed the approval process for the drug. But when the drug was finally approved, the fact that two consent forms were missing did not prevent the FDA from approving the drug.

d. Writing style in case report forms

The Case Report Form (CRF) is the instrument used for reporting adverse events in clinical trials. Moon (176) details the content and appearance of a typical case report form used for clinical trials. Some case report forms may capture only AEs occurring at a given point in time, while other case report forms may be designed to capture cumulative information on AEs. An example of a poor case report form may contain fields for inputting white blood cell counts, where the field looks like this:

Neutrophils _____; Lymphocytes _____.

In contrast, a high-quality case report form will include the unit, and the field will look like this:

Neutrophils (cells/mL blood) _____; Lymphocytes (cells/mL blood) _____.

Case report forms should avoid double negatives, specify time points where appropriate, and should avoid lumping more than one question in a single sentence. This advice of a bad case report form and a good case report form is shown in Table 24.2 (177).

Ene-Iordache et al. (178) describe issues relating to electronic case report forms, such as the requirement for the data-entry person to add an electronic signature, and the issue of the audit trail. Moreover, Headlee (179) teaches that case report forms may be designed in parallel with the writing of the Clinical Study Protocol, and that the form should include checkboxes to capture AEs expected from the drug of interest, such as neurological AEs. Also, this author recommends using checkboxes instead of spaces for writing, where appropriate, to increase the efficiency of filling, and the legibility, of the forms.

[174] Clinical Review Section of Application No. STN/BLA 125084 (page 51 of 149 pages total, no date provided).

[175] United States Food and Drug Administration. Center for Drug Evaluation and Research (CDER). Application No. STN/BLA 125084; ERBITUX (Cetuximab). All of the correspondence documents are incorporated by reference in an approval letter dated February 12, 2004.

[176] Moon KK. Techniques for designing case report forms in clinical trials. *ScianNews*. 2006;9:1 [7 pages].

[177] NHMRC Clinical Trials Centre, University of Sydney. Outreach. An Australian initiative to support clinical trials (September 2009) 2 pages.

[178] Ene-Iordache B, Carminati S, Antiga L, et al. Developing regulatory-compliant electronic case report forms for clinical trials: experience with the demand trial. *J Am Med Inform Assoc*. 2009;16:404–408.

[179] Headlee D. The paper trail: CRFs, source documents and data collection tools. SoCRA SOURCE. May 2004; 30 (4 pages).