between the two study arms. In contrast, where PP analysis is used, dropouts among the study population will not dilute the true difference between the two study arms.

VII. MODIFIED ITT ANALYSIS

Modified intent-to-treat (modified ITT) analysis includes fewer subjects than ITT analysis, and greater subjects than PP analysis. In a survey, Abraha and Montedor (35) reported that about half of clinical trials use a modified ITT analysis. Modified ITT excludes specific subjects from the statistical analysis, for example subjects who were enrolled in the trial but later were found not to satisfy the inclusion or exclusion criteria, subjects not taking all scheduled study drugs, subjects with missing data, subjects who did not receive the entire treatment course, subjects who were enrolled and randomized before information on eligibility was obtained, and subjects who died before receiving treatment.

The following clinical study of a bacterial infection provides a concrete example of modified ITT analysis. In a study of *Helicobacter pylori* infections, Vaira et al. (36) compared eradication using standard drug treatment with sequential drug treatment. ITT analysis included all subjects (300 subjects in all). The Clinical Study Protocol required daily doses for ten days.

Subjects excluded from the modified ITT group (but included in the more-encompassing ITT group) were as follows. Five subjects were excluded from the modified ITT analysis for: (1) failure to meet inclusion criteria; (2) failure to receive any study drugs because of severe abdominal pain; (3) discovery that patient was pregnant; (4) subject decided not to take drugs; and (5) subject moved out of the country.

Modified ITT analysis is specifically recommended in FDA's Guidance for Industry on *Helicobacter pylori*-associated duodenal ulcer disease in adults (37) "[s]ponsors should perform efficacy analyses on two specific populations: MITT [modified intent to treat] and per-protocol."

[35] Abraha I, Alessandro Montedori A. Modified intention to treat reporting in randomised controlled trials: systematic review. *Brit Med J.* 2010;340:c2697.

[36] Vaira D, Zullo A, MD, Vakil N. Sequential therapy versus standard triple-drug therapy for *Helicobacter pylori* eradication. *Ann Intern Med*. 2007;146:556–563.

[37] FDA. Guidance for Industry Helicobacter pylori-Associated Duodenal Ulcer Disease in Adults: Developing Drugs for Treatment. October 2009.