

II. CONCLUDING REMARKS

The simplest type of run-in period is one where a placebo is taken during this period, and only persons found to comply are actually enrolled in the trial. In a review, Senn (51) provided additional remarks on placebo run-in periods:

*Many trials...are preceded by a **placebo run in**, in which all patients are given placebo. The practice is common within the pharmaceutical industry and recommended by standard texts as a means of weeding out noncompliers before randomisation, eliminating placebo responders, ensuring that patients are stable, washing out previous treatment, or simply to provide a period for baseline measurement.*

The list of Senn (52) discloses an unusual reason for a placebo run-in period, namely, eliminating *placebo responders*. This particular rationale might be desired in clinical trials on anti-depressants, but it would be irrelevant to clinical trials in oncology or infections.

Run-in periods that are a step greater in complexity are those that screen potential subjects who are relatively free from safety issues, and run-in periods that conduct a screen that confirms a diagnosis of the disease in question. Run-in periods can be used to exclude potential subjects who are found not to comply with the inclusion/exclusion criteria set forth by the Clinical Study Protocol. For example, the run-in period used by Boushey et al. (53) excluded potential subjects showing excessive symptoms, too few symptoms, withdrawal of consent, loss to follow-up, failure to meet adherence criteria, use of excluded medications, and presence of an excluded medical condition. This type of run-in period might be viewed as inconsistent with the tenets of intent to treat (ITT) analysis. Hence, investigators planning to use a run-in period to detect subjects who do not meet the requirements of the Clinical Study Protocol should first consult with their statistician.

⁵¹ Senn S. Are placebo run ins justified? *Brit Med J.* 1997;314:1191–1193.

⁵² Senn S. Are placebo run ins justified? *Brit Med J.* 1997;314:1191–1193.

⁵³ Boushey HA, Sorkness CA, King TS, et al. Daily versus as-needed corticosteroids for mild persistent asthma. *New Engl J Med.* 2005;352:1519–1528.