This lists the variety of purposes that can be served by a run-in period:

1. To allow a washout period.
2. Permitting time to detect baseline adverse events.
3. To screen for and exclude potential study subjects who are likely to experience excessive safety issues during the study.
4. To screen for and include only study subjects with controllable pain.
5. To determine a maximally tolerable dose.
6. To achieve and ensure steady-state in vivo concentrations of study drug, where the study drug is administered during the run-in period.
7. To allow a period of adjustment of lifestyle of the study subjects, for example, changes in dietary patterns.
8. To ensure that metabolic characteristics of all study subjects are similar, prior to administering drugs.
9. To ensure that potential study subjects can adhere to, or comply with, the study protocol.
10. To allow time to confirm that all study subjects meet the inclusion and exclusion criteria.
11. Detecting potential study subjects who show a desired, or homogeneous, response to the study drug, with the goal of including only these subjects.
12. Decision tree to determine whether a subject should receive treatment A or treatment B.
13. To create a self-control group.

Details of these categories of run-in periods are provided below.

a. Washout Period

Washout periods can minimize the lingering effects of a previously administered drug. These lingering effects may influence data that are later collected regarding safety and efficacy of the study drug in question. Schwartz et al. (8) used a 2-week washout period in a study of asthma. Prior to enrollment in the study, study subjects had received chronic treatment with an anti-asthma drug. After the 2-week washout period, during which subjects did not take any drug for asthma, subjects were randomized and allocated to study drug or placebo.

b. Detecting Baseline Adverse Events

Kramer (9) illustrates the rationale of detecting lingering adverse events resulting from a previously administered drug. This rationale is to detect adverse events arising from previous drug therapy, but also to detect possible adverse events related to withdrawal of the previous drug therapy.

c. Excluding Potential Study Subjects Who Have Safety Issues Correlating With the Study Drug

Greenspan et al. (10) used a run-in period (3 months) as a miniature clinical trial, in order to exclude subjects who had adverse events (at least, during the run-in period) to the study drug. This refers to the drug used in the clinical trial of interest, and not to any drugs administered prior to the clinical trial. The study drug was hormone replacement therapy for preventing bone loss. After the run-in period, subjects

[8]Schwartz HJ, Blumenthal M, Brady R, et al. A comparative study of the clinical efficacy of nedocromil sodium and placebo. How does cromolyn sodium compare as an active control treatment? Chest 1996;109:945–52.

[9]Kramer M. Placebo run-in for antidepressant trials. Neuropsychopharmacology 1996;15:105.

[10]Greenspan SL, Resnick NM, Parker RA. Combination therapy with hormone replacement and alendronate for prevention of bone loss in elderly women: a randomized controlled trial. J. Am. Med. Assoc. 2003;289:2525–33.