

Yes—the use of placebo is essential in headache trials.

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In 1962, the Congress of the United States passed the Kefauver-Harris Amendment that mandated that manufacturers provide evidence of drug effectiveness in addition to safety in order for the Food and Drug Administration (FDA) to approve the agent for a specific clinical indication. The FDA in 1970 published guidelines describing what acceptable controls in a clinical trial were. The double-blind randomized clinical trial was established as the “gold standard” for the emerging pharmaceutical industry. In 2012, the International Headache Society (IHS) Clinical Trials Committee published guidelines for controlled trials of drugs in migraine: Third Edition. In 2002, the World Medical Association Declaration of Helsinki stated that when an effective treatment for a disease existed, it was unethical to assign patients in a research study to a treatment known to be less effective. Standards for the acceptable use of a placebo in clinical trials have changed over time, and (with informed consent), it is now considered acceptable to use placebos in clinical trials where withholding the best current treatment will result in only temporary discomfort and no serious adverse effects. The IHS guidelines state that research protocols should allow the use of rescue medication any time after the first primary efficacy time point. This is necessary for the evaluation of “new treatments”. In sum, demonstration of treatment efficacy demands that the target (active) agent must be shown to be statistically significantly superior to an inert substance (placebo) not believed to be a specific therapy for the target condition.