

Reviewer's report

Title: S-Adenosyl methionine (SAME) versus celecoxib for the treatment of osteoarthritis symptoms: A double-blind cross-over trial.

Version: 1 **Date:** 5 September 2003

Reviewer: Teodoro Bottiglieri

Reviewer's report:

General

This study is a clinical trial designed to compare the efficacy of S-adenosylmethionine (SAME) and celecoxid for the treatment of Osteoarthritis. This paper is well written and the authors have provide a good scientific rational to conduct the study. The findings presented in this paper are important since it is the first study that compares SAME to a COX-2 inhibitor. Furthermore, the last clinical trial of SAME for the treatment of OA was published in 1994.

Discretionary Revisions (which the author can choose to ignore)

Minor Compulsory Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Page 7, line 1: misspelling of the word "transsulfuration" – correct spelling is "transsulfuration"

Page 7, line 7: the term "but it is felt" should be changed to a more scientific term such as "evidence suggests"

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached).

Page 13; line 2: Since the authors have provide data to show that the SAME used in the study contained 55% SR and 45% SS isomer, they should also explain to the reader the significance of the isomers. A brief explanation that the SS isomer is the biological active form that can participate in methyltransferase reactions is required. This can also be emphasized in the discussion. Reader s should be made aware that at the start of the study the effective dose is really 540 mg of SAME (45% of 1200mg), and that other commercial brands of SAME have been tested and found to contain a much higher percentage of "active" SS form of SAME.

Page 23, line 16: The reviewer is concerned that approximately 75% of the way through the study the investigators found that the SAME tablets had lost 51% of it potency. It would be important to know the ratio of active to inactive isomers at this point. The reviewer is assuming that the loss of potency is based on the total (SS + RS) isomer content. Taking into account the percentage of active SAME and the loss of potency that occurred, the actual amount of SAME that was administered is considerably less than the 1200mg per day that the reader is led to believe is given. This should be brought to the readers attention in the discussion. Furthermore, SAME can break-down to S-adenosylhomocysteine (SAH) and methylthioadenosine (MTA). Have the authors checked the SAME tablets for these break down products which can potentially adversely affect the metabolism of the methylation cycle.

Advice on publication: Unable to decide on acceptance or rejection until the authors have

responded to the major compulsory revisions

Level of interest: A paper of considerable merit and interest in its field

Quality of written English: Acceptable

Declaration of competing interests:

I have served as a paid consultant on an advisory board for Pharamvite LLC (Mission Hills, CA).
Pharmavite is a distributor of the dietary supplement, SAME.