

X
Karl Mallard
President
Mallard Incorporated
3021 Wabash Avenue
Detroit, MI 48216

JAN 19 1981

Dear Mr. Mallard:

I have received your letter dated December 23, 1980 which requested clarification of certain proposed rules on OTC analgesic combinations.

You first asked at what dosage level would small amounts of caffeine be permitted in combination with acetaminophen and aspirin, if indeed caffeine will be permitted in combination with these ingredients. At this point in time, I cannot specifically answer this question because it raises an issue which will be addressed by FDA in the tentative final monograph on OTC internal analgesic, antipyretic, and antirheumatic drug products, which will probably be published in the FEDERAL REGISTER in late 1981 or early 1982. The agency is currently preparing this monograph after reviewing and evaluating data and information contained in the Internal Analgesic Panel's report, in comments to the proposed monograph, and in the current medical and scientific literature.

Your second question dealt with stability data for two combination products: one containing acetaminophen, aspirin, and caffeine and the other containing only acetaminophen and aspirin. I have referred this portion of your letter to the Division of Drug Product Quality for their direct reply to you under separate cover.

Your third question asked if a currently marketed product containing 250 mg each of acetaminophen and aspirin and 65 mg caffeine meets the criteria for permitted OTC internal analgesic combinations and, if it does not, what would be required to bring such a product into compliance when a final monograph on OTC internal analgesics is published? Such a combination is currently not permitted in the OTC Internal Analgesic Proposed Monograph. However, OTC internal analgesic combinations, including that which you are concerned about, are currently under review by FDA and will be further addressed in the tentative final monograph.

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Your last question referred to section 343.20(d)(7) of the Internal Analgesic Proposed Monograph and asked whether the criteria of 1.9 meq of acid neutralizing capacity and pH of 3.5 apply to the buffering agent(s) or to the finished product. In response, I refer you to that same section, which states: ". . . such that the finished product (emphasis added) contains at least 1.9 meq of acid neutralizing capacity per 325 mg (5 gr) aspirin and results in a pH of 3.5 or greater. . . ." I might add that this section of the proposed monograph will be further addressed in the agency's tentative final monograph.

I regret that I cannot be more specific in answering your questions at this time. Thank you for your interest and concern.

Sincerely yours,

William E. Gilbertson, Pharm. D.
Director
Division of OTC Drug Evaluation
Bureau of Drugs

cc: HFD-510:DDC-600.1/ING-14.5/EXT-6.10/Reading/Rachanow
HFD-512:Reading/Geismar/Konnor
R/D:Konnor:ecw:1/16/81
DOC:06748-0403A
Int:Geismar:Konnor:1/16/81
Int:Rachanow:1/19/81
Final:ecw:1/19/81