

MEMORANDUM OF CONFERENCE

Date: January 6, 1998
Place: FDA, CFSAN, Washington DC
Purpose: Cancer Assessment Committee Meeting
Subject: Gum Arabic

REF 5

Participants:

CAC Members:

Dr. R. J. Lorentzen, Office of Policy, Planning and Strategic Initiatives (HFS-16);

Chairman *R. J. Lorentzen 1/26/98*

Dr. K. B. Ekelman, Division of Health Effects Evaluation (HFS-225); Executive Secretary

Kenn B. Ekelman 2/13/98

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Rob W. Moch 2/3/98

Dr. D. G. Hattan, Division of Health Effects Evaluation (HFS-225)

David G. Hattan 2/13/98

Dr. C. N. Barton, Experimental Design and Evaluation Branch (HFS-706)

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Dr. S. H. Tao, Contaminants Standards, Monitoring and Programs Branch (HFS-308)

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Dr. T. G. Wilcox, Epidemiology Branch (HFS-728)

Thomas Wilcox 1/29/98

Dr. A. B. Bailey, Division of Product Policy (HFS-207)

Allen B. Bailey 2-4-98

Other Participants:

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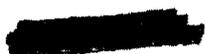
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Dr. G. J. Ikeda, Division of Health Effects Evaluation (HFS-225)

Dr. M. J. Bleiberg, Division of Health Effects Evaluation (HFS-225)

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The purpose of this meeting was to evaluate the results of a National Toxicology Program (NTP) report¹ of carcinogenicity studies of gum arabic in F344 rats and B6C3F₁ mice, published in 1982. Results of these studies were reviewed in a 11/10/97 memorandum to the Cancer Assessment Committee (CAC) from Dr. M. J. Bleiberg (HFS-225), who also presented this information to the Committee at the meeting. CAC review of these studies is needed to complete the administrative record for GRAS Affirmation Petition 3G0287 for use of gum arabic in alcoholic beverages. A 3/7/94 memorandum from M. DiNovi (HFS-247) states that, "assuming that gum arabic is used between 12 and 20% in all beverages, exposure would be approximately 0.75 g/person/day."

In the NTP studies, 50 F344 rats/sex/group and 50 B6C3F₁ mice/sex/group were fed diets containing 0 (controls), 2.5% or 5% gum arabic for up to 103 weeks, then all animals were fed the control diet for the final two weeks of the study. The test materials used in these studies were considered to be representative of commercially available gum arabic during the late 1970s, when the studies were conducted.² Although specifications for commercial gum arabic have changed since then, it is likely that the test materials used in these studies are also representative of commercially available gum arabic today.

In the rat study, there were no statistically significant increased incidences of dosed rats with tumors at any tissue site, compared to controls.

In the mouse study, the NTP report stated that there were no statistically significant increased incidences of dosed mice with tumors at any tissue site, compared to controls. The CAC notes, however, that the reported incidence of female mice with either hepatocellular adenoma, carcinoma or neoplasm N.O.S. (not otherwise specified) was 4/49 or 8% in controls, 2/50 or 4% in the 2.5% dose group and 10/50 or 20% in the 5% dose group ($p = 0.08$ by the Fisher Exact Test). One female control mouse had a liver tumor N.O.S.; if this mouse were excluded from the analysis on the assumption that the hepatocellular origin of this tumor had not been confirmed, the incidence of female mice with either hepatocellular adenoma or carcinoma would be 3/49 or 6% in controls, 2/50 or 4% in the 2.5% dose group and 10/50 or 20% in the 5%

3/49 or 6% in controls, 2/50 or 4% in the 2.5% dose group and 10/50 or 20% in the 5% dose group ($p = 0.04$ by the Fisher Exact Test). The CAC also notes, however, that it is not possible to determine whether or not the neoplasm N.O.S. in question was or was not of hepatocellular origin; that there was no evidence of dose-related hepatocellular adenomas or carcinomas in dosed male mice (controls, 16/49 or 33%; 2.5% dose group, 11/49 or 22%; 5% dose group, 15/50 or 30%); that there was no evidence of dose-related pre-neoplastic lesions that would suggest the presence of an ongoing carcinogenic process in the livers of dosed male or female mice (Tables D1 and D2); and that liver tumors occurred earlier in control female mice than in dosed female mice (weeks to first observed tumor: controls, 44 weeks; 2.5% dose group, 104 weeks; 5% dose group, 98 weeks. In addition, the CAC notes that the background incidence of liver tumors in control B6C3F1 male and female mice is highly variable (the historical control incidence for female mice can range from 3% to 58%)³. For tumors of this type, the CAC ordinarily relies on lower p values, such as $p \leq 0.01$, to help determine the significance of increased tumor incidences in bioassays. Thus, for the reasons detailed above, the CAC concludes that there were no significantly increased incidences of dosed male or female mice with tumors at any tissue site, including the liver, in the NTP.

Based on the results reported by the National Toxicology Program, the Cancer Assessment Committee concludes that consumption of diets containing up to 5% gum arabic by F344 rats and B6C3F1 mice for two years was not associated with increased incidences of tumors at any site.

Karen B. Ekelman
 Karen B. Ekelman, Ph.D.
 Executive Secretary, CAC
 January 20, 1998

References

- 1 National Toxicology Program, Technical Report Series No. 227. May 1982. Carcinogenesis bioassay of gum arabic (CAS No. 9000-01-5) in F344 rats and B6C3F₁ mice (feed study).
- 2 Anderson, D.M. W., Brown Douglas, D.M., Morrison, N.A. and Weiping, W. 1990. Specifications for gum arabic (*Acacia senegal*); analytical data for samples collected between 1904 and 1989. *Food Additives and Contaminants* 7(3):303-321.
- 3 National Toxicology Program report of historical control incidences for tumors in F344 rats and B6C3F1 mice; 11/30/81 and 9/18/97.

cc:
 CAC members
 HFS-225 (Bleiberg, Biddle, Chang, Benz, Flamm)
 HFS-215 (Martin)

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