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United States General Accounting Office  
Washington, DC 20548

Resources, Community, and  
Economic Development Division

B-285796

July 28, 2000

The Honorable George P. Radanovich  
House of Representatives

The Honorable Mike Thompson  
House of Representatives

Subject: National Toxicology Program: Procedures Were Followed in Listing Alcoholic Beverage Consumption as a Known Carcinogen

Each year, Americans consume significant quantities of alcoholic beverages, including beer, spirits, and wine. In 1997, sales of these beverages amounted to about \$70 billion. While light to moderate use of alcoholic beverages could offer potential health benefits, such as possible cardiovascular benefits, high levels of consumption could create a number of health problems, such as liver damage and a variety of cancers.

In 1978, the Secretary of Health and Human Services established the National Toxicology Program (NTP) to provide information to health regulatory and research agencies, scientific and medical communities, and the public about potentially toxic substances. NTP is required to issue a biennial report listing all substances that are either known to be carcinogens in humans or may reasonably be anticipated to be human carcinogens and to which a significant number of people residing in the United States are exposed. In this regard, NTP recently concluded that alcoholic beverage consumption is a known human carcinogen, particularly at the highest levels of consumption<sup>1</sup> and when used in conjunction with smoking.<sup>2</sup>

Concerned about whether NTP, in deciding to list alcoholic beverage consumption as a known carcinogen, adequately considered all available scientific studies, provided opportunities for public comment, and followed its standard voting procedures of straight majority rule, you asked us to examine NTP's listing procedures, including whether they were consistently applied to the review of alcoholic beverages. Specifically, you asked us to

- identify the procedures NTP uses to list a substance as either a known or a reasonably anticipated human carcinogen and
- determine whether NTP followed its procedures in determining to list alcoholic beverage consumption as a known human carcinogen.

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<sup>1</sup>The report did not define the highest levels of consumption.

<sup>2</sup>9<sup>th</sup> Report on Carcinogens, May 2000.

As agreed with your offices, we reviewed NTP's listing procedures, as well as specific documentation applicable to the listing of alcoholic beverages. We also discussed the listing procedures with program officials responsible for making listing decisions. In addition, we interviewed officials representing the alcoholic beverage industry regarding their concerns about the listing procedures, as well as any specific concerns they had about the application of these procedures to the review of alcoholic beverage consumption. Furthermore, we reviewed documentation related to their concerns provided by these officials. This report summarizes our answers to your questions. Enclosure I documents the information we provided to your staff on June 19, 2000.

In brief, we found the following:

- The procedures used by NTP to make listing decisions constitute a comprehensive, multistep process. Among other things, these procedures provide for the careful consideration of relevant scientific literature, input from leading scientists representing a variety of disciplines, and repeated opportunities for industry and public comment.
- NTP consistently applied its listing procedures in deciding to list alcoholic beverage consumption as a known human carcinogen.

#### National Toxicology Program's Listing Procedures

NTP's review process starts when a substance, mixture, or exposure circumstance is nominated for review.<sup>3</sup> Such groups as federal or state agencies, international scientific organizations, industry, labor, academia, and the public can make a nomination. The nomination, generally supported by numerous scientific studies, is then sequentially reviewed by a series of four committees consisting of scientists from government, academia, and industry who represent a wide variety of disciplines. Each committee conducts its own independent analysis of the carcinogenicity of each nomination and votes whether to list it as either a known human carcinogen or reasonably anticipated to be a human carcinogen. During this phase of the review process, there are three opportunities for public comment on the nomination, including an open public forum for discussing why a substance should or should not be listed. Once the committees complete their review, the nomination is compiled, along with other nominations, into the *Report on Carcinogens* and forwarded to the Director, National Toxicology Program, for a final independent review. The Director then forwards the report to the Secretary of Health and Human Services and provides a briefing and recommendation on how each substance or mixture should be listed in the final *Report on Carcinogens*. The process, generally about 2 years in length, is completed when the Secretary approves the report for publication and submits it to the Congress.

#### Procedures Consistently Applied

We found that NTP consistently applied its prescribed procedures in deciding to list alcoholic beverage consumption as a known human carcinogen. Nominated for review in February 1997, and supported by a large number of scientific studies cited as references for review, it was listed in the *9<sup>th</sup> Edition of the Report on Carcinogens*. As the nomination went through the review process, each committee conducted its own independent analysis of the available scientific data and voted in the majority to list alcoholic beverage consumption as a known human carcinogen. A minority of the committee members voted against the listing because

<sup>3</sup>A mixture relates to such consumer products as smokeless tobacco and alcoholic beverages, while an exposure circumstance relates to the use of such products as sunlamps.

of the high level of consumption needed to cause cancer, the potential cardiovascular benefits of low to moderate consumption, and the impact of confounding factors, such as smoking and alcoholic lifestyle. During the review process, public comments—both for and against the listing—were also received. According to NTP officials and relevant documentation, both the dissenting opinions from committee members and related public comments were addressed to the satisfaction of the various committee members and incorporated into the report as appropriate. As a result of this process, the Director, National Toxicology Program, recommended that alcoholic beverage consumption be listed as a known human carcinogen. The Secretary of Health and Human Services approved this recommendation in May 2000 for listing in the *9<sup>th</sup> Edition of the Report on Carcinogens*.

We provided a draft of this report to NTP officials for their review and comment. We discussed their comments during a teleconference with the Acting Director, Environmental Toxicology Program, and other NTP officials. They generally agreed with the report's contents and provided us with some technical comments, which have been incorporated where appropriate.

We conducted our review from May 2000 through July 2000 in accordance with generally accepted government auditing standards.

As agreed with your office, we will make copies of this report available to others upon request. If you have any questions or need additional information, please contact me or Jim Jones at (202) 512-5138. Key contributors to this report include Paul Bollea and Sheldon Wood.



Robert E. Robertson  
Associate Director  
Food and Agriculture Issues

Enclosure



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National Toxicology Program  
Listing of Alcoholic Beverage Consumption as a  
Known Human Carcinogen

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## **Objectives of Review**

- Identify the procedures used by the National Toxicology Program (NTP) to identify substances that are either known or reasonably anticipated to be human carcinogens.
  - Determine whether NTP followed these procedures in deciding to list alcoholic beverage consumption as a known human carcinogen.
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## Results in Brief

- NTP's procedures include a comprehensive seven-step process that incorporates independent reviews of scientific literature by various committees and provides opportunities for public comment. Committees consist of scientists from government, academia, and industry who represent a variety of disciplines.
  - NTP followed its established procedures in determining to list alcoholic beverage consumption as a known human carcinogen.
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## **Seven Steps in NTP's Review Process**

- Nomination
  - National Institute of Environmental Health Sciences Review Group (RG1)
  - Interagency Working Group (RG2)
  - NTP Board of Scientific Counselors, Report on Carcinogens Subcommittee
  - NTP Executive Committee
  - NTP Director
  - Secretary, Health and Human Services
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Objective 1: Procedures NTP uses to identify known or suspected carcinogens.

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## **Nomination of Substance for Review**

- Nominations, supported by scientific studies, can be submitted by federal or state agencies, industry, labor, academia, and the public.
  - NTP officials estimate that 85 to 90 percent of the nominations are based on (1) reviews prepared by the International Agency for Research on Cancer (part of the United Nations World Health Organization) and (2) the results of NTP's Bioassay Program.
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Objective 1: Procedures NTP uses to identify known or suspected carcinogens.

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## **National Institute for Environmental Health Sciences Review Group (RG1)**

- Prioritize nominations and decide what substances can be reviewed for the next *Report on Carcinogens*.
  - Solicit public comment via the *Federal Register* on the carcinogenicity of the substance.
  - Have a contractor perform a literature search and prepare the first draft of a background document summarizing the search results.
  - Identify primary reviewers to prepare the first draft of a summary statement on the carcinogenicity of the substance.
  - Vote to list or delist the substance, as appropriate.
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## Interagency Working Group (RG2)

- Identify new primary reviewers to review the background document and summary statement provided by RG1 and make changes as necessary.
  - Vote to list or delist the substance after independent review of all relevant documentation.
  - Finalize the background document, which becomes the document of record.
  - Issue a notice in the *Federal Register* announcing the next review meeting and solicit comments on the listing decision.
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Objective 1: Procedures NTP uses to identify known or suspected carcinogens.

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### **NTP Board of Scientific Counselors' Report on Carcinogens Subcommittee**

- Hold a 2-day meeting, open to the public (first used for the *8th Edition of the Report on Carcinogens*).
  - Identify new primary reviewers to lead the discussion as the group performs an independent review of all relevant documentation.
  - Vote to list or delist the substance.
  - Issue a notice in the *Federal Register* to solicit final public comments on the listing decision (period of 60 days allowed). The notice includes the results of the RG1, RG2, and Board of Scientific Counselors' Report on Carcinogens Subcommittee meetings.
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Objective 1: Procedures NTP uses to identify known or suspected carcinogens.

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## **NTP Executive Committee**

- Perform an independent review of the background document, summary statement, results of prior three votes, and all public comments.
  - Vote to list or delist the substance (vote not publicized).
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Objective 1: Procedures NTP uses to identify known or suspected carcinogens.

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### **NTP Director**

- Is briefed by the Head, Report on Carcinogens, and other NTP staff; receives all documentation for review.
  - Makes final recommendation on listing or delisting the substance.
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Objective 1: Procedures NTP uses to identify known or suspected carcinogens.

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## **Secretary, Health and Human Services**

- Is briefed by NTP staff; all documentation is made available for review.
  - Gives final approval to list or delist the substance.
  - Sends the *Report on Carcinogens* to the Congress and publishes a notice in the *Federal Register*.
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## **Alcoholic Beverage Consumption Nominated in February 1997**

- NTP accepts nomination from recommendation made by the International Agency for Research on Cancer.
  - Nomination is supported by a large number of scientific studies that NTP needed to assess.
  - For the first time, NTP reviews “mixtures” and “exposure circumstances” (i.e., consumer products, such as alcoholic beverage consumption, smokeless tobacco, sunlamps) in addition to individual substances.
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Objective 2: Did NTP follow its procedures  
in listing alcoholic beverage consumption?

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**National Institute for Environmental Health Sciences  
Review Group (RG1)**

- Identified over 800 references in the literature search.
  - Voted 6-1 to list alcoholic beverage consumption as a known human carcinogen.
  - Dissenting vote related to a member's desire to have "heavy consumption" in the first paragraph of the summary statement.
  - Added paragraph on potential benefits of alcoholic beverage consumption to the summary statement.
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Objective 2: Did NTP follow its procedures in listing alcoholic beverage consumption?

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### **Interagency Working Group (RG2)**

- Voted 7-0 to list alcoholic beverage consumption as a known human carcinogen.
  - Voted 4-3 to remove the paragraph on potential benefits, stating that the *Report on Carcinogens* is a cancer document and not a cardiovascular document.
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**NTP Board of Scientific Counselors'  
Report on Carcinogens Subcommittee**

- Voted 9-3-1 to list alcoholic beverage consumption as a known human carcinogen.
  - Three dissenting voters noted the possible impact of confounding factors (i.e., smoking and lifestyle).
  - One abstaining voter was not comfortable with the discussion on synergy between alcohol and smoking.
  - Added confounding effect of smoking to the summary statement.
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## Final deliberations

- NTP Executive Committee voted 7-0 to list alcoholic beverage consumption as a known human carcinogen.
  - NTP Director recommended the listing.
  - Secretary of Health and Human Services approved the listing.
  - Alcoholic beverage consumption was listed in the *9th Edition of the Report on Carcinogens*, May 2000, as a known human carcinogen based on sufficient evidence of carcinogenicity from human studies.
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Objective 2: Did NTP follow its procedures in listing alcoholic beverage consumption?

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## Conclusion

- NTP followed its established procedures in determining to list alcoholic beverage consumption as a known human carcinogen.
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