

GREENBERG  
ATTORNEYS AT LAW  
TRAURIG

Nancy E. Taylor  
(202)331-3133

May 15, 1998

Dr. C.W. Jameson  
National Toxicology Program  
Report on Carcinogens  
MD EC-14  
P.O. Box 12233  
Research Triangle Park, NC 27709

Dear Dr. Jameson:

As individuals with many years of active involvement and interest in public health policy, we write to commend the NTP on its review of saccharin for possible delisting, and to strongly urge that the progress made with respect to saccharin not be derailed by the ill-considered and anomalous vote of four members of the Subcommittee of the Board of Scientific Counselors ("the Subcommittee").

A review of the record of the Subcommittee's October 30, 1997 meeting and a comparison of its vote with the conclusion of numerous other bodies, including the overwhelming votes of two other NTP review groups, RG1 and RG2, demonstrates that as a matter of public policy the Subcommittee's position should be rejected in the NTP's final analysis.

When the Subcommittee's meeting was publicly announced in the Federal Register, the public was reminded that a "major change" had been made in the Report on Carcinogens. As the announcement described, that important and positive change was "a result of the criteria revision" which brought into consideration "all relevant data, including mechanistic data." This revision held the promise that the review of saccharin, and other substances, would be done with the benefit of the most thorough and advanced scientific analysis available. In short, the NTP review of saccharin appeared to be a clear opportunity to bring public policy in line with the best science.

The NTP's communications to the public and the press heralding the review left the strong impression that an objective review of the scientific data would lead to delisting of saccharin. That expectation was neither surprising nor inappropriate. After all, the question for listing is whether saccharin is "known to be a human carcinogen" or is "reasonably anticipated to be a human carcinogen," not whether it is remotely possible that it may be a carcinogen. As we understand the public record, the scientific evidence does not support a "reasonable anticipation" of carcinogenicity. Indeed, as you know, that was the conclusion of two other NTP panels.

GREENBERG TRAURIG HOFFMAN LIPOFF ROSEN & QUENTEL  
A PARTNERSHIP OF PROFESSIONAL CORPORATIONS  
1300 CONNECTICUT AVENUE, N.W.  
WASHINGTON, D.C. 20036  
202-331-3100 FAX 202-331-3101  
MIAMI NEW YORK WASHINGTON, D.C.  
FORT LAUDERDALE WEST PALM BEACH TALLAHASSEE ORLANDO

In any event, what we and the public expected from the Subcommittee was a careful and thoughtful review that gave appropriate weight to the scientific evidence. Unfortunately, what the record reveals is an exercise that did not fulfill those worthy expectations in a number of respects.

### **1. The Subcommittee Was Improperly Constituted**

The Subcommittee's first failing was in its composition. Specifically, the Subcommittee was not properly constituted as required by the Charter of the Board of Scientific Counselors, dated November 14, 1996 ("the Charter," copy appended). The Charter, which allows for "standing and ad hoc subcommittees," provides that such bodies shall be "composed of members of the parent committee." Charter at 2. The Charter directs that the parent committee, here the Board of Scientific Advisers, "shall consist of 25 members, including the Chair" and that "members shall be selected by the Secretary, or designee, from recognized authorities knowledgeable in designated scientific fields." *Id.* While the parent committee may fulfill the Charter's provisions, the Subcommittee did not.

Contrary to the Charter's mandate, the Subcommittee included four members who were not "members of the parent committee." According to the listing provided by the NTP, the Subcommittee had four vacancies which were filled by "Expert Consultants." Although they may not have voted, participation by those consultants was no substitute for a properly constituted deliberative body.

### **2. Members Not Participating Distorted the Subcommittee's Vote**

The Subcommittee's conduct of its official business was also marred by the fact that not all of the properly designated members were present and participated as required. Although officially designated to participate in the body's deliberations and ultimately to vote, Carol J. Henry, Ph.D., was absent from the entire meeting when the matter of delisting for saccharin was considered by the Subcommittee. As a result, Dr. Henry did not cast a vote on the question of delisting. The absence of Dr. Henry as a participant is particularly significant since her vote may well have affected the final outcome of the Subcommittee's vote on the question of delisting of saccharin. The Subcommittee ultimately voted against delisting, with 4 votes against, and 3 in favor of delisting. Dr. Henry's vote could well have resulted in a tie, requiring the Chairman of the Subcommittee to cast the tie-breaking vote. With Dr. Henry absent, neither her vote nor the Chairman's was counted on this important issue.

### **3. The Subcommittee Failed to Conduct a Balanced Review**

Although required to by statute, the Subcommittee did not conduct a review that was "fairly balanced in terms of the points of view represented." 5 U.S.C.A. App. 2 § 5(b)(2). Only one member of the Subcommittee, Clay Frederick, Ph.D., has specific knowledge of, or experience in, the food and beverage industry. The Subcommittee had nine members

designated and is inadequate to comply with the statutory requirement that the Subcommittee be "fairly balanced." The lack of "fairly balanced" representation prevented the Subcommittee from exercising independent judgment, as required by statute. See 5 U.S.C.A. App. 2 § 5(b)(3). Industry views should have been more fully represented on the Subcommittee to ensure a truly balanced review of the scientific merits for delisting.

#### **4. The Subcommittee Did Not Provide Expert Advice**

The Subcommittee also failed to fulfill its mandate to furnish "expert advice." That is the role of the Subcommittee, as envisioned under section 2 of the Federal Advisory Committee Act ("FACA"). 5 U.S.C.A. App. 2. Dr. Nicholas Hooper, a designated member of the Subcommittee, readily confessed that he lacked substantive knowledge on the scientific merits of delisting saccharin. See Transcript, at 46.<sup>1</sup> Dr. Nicholas did not meet the requirements of offering "expert advice" to the NTP. Moreover, comments made by Dr. George Friedman-Jimenez, another Subcommittee member, highlight the incongruity of the deliberations. At the public meeting, Dr. Jimenez focused, inappropriately, on epidemiologic studies, and concluded they "are not completely reassuring." Transcript at 72, line 4 - 6. Dr. Jimenez then opined that "I don't think I would vote to list saccharin at this point given the epidemiology that exists, but ... I don't feel comfortable to delist it based on the epidemiology." Id., line 6 - 9. It is difficult to understand this view, since it is logical to conclude that if epidemiologic studies would not support the listing of saccharin as "reasonably anticipated" to be a human carcinogen, then there is no justification to vote against delisting that chemical. Under NTP rules, the criteria applied for listing a substance in the first instance, are the same for delisting. It seems apparent that at least one of the four members voting against delisting did not properly understand NTP guidelines or the role of the Subcommittee. Accordingly, his vote should be disregarded.

The same is true of the other Subcommittee members voting against delisting, all of whom failed to articulate sound reasons for their votes. There was no apparent adherence to the "reasonably anticipated" standard rather than a consideration of a possibility that was limited or remote. Similarly, there was no explanation of why the Subcommittee's conclusion was at odds with others conclusions, including the votes of RG1 and RG2. The Subcommittee's failure to provide such explanations forcefully demonstrates a failure to provide "expert advice."

#### **5. The Subcommittee Failed to Adequately Consider Mechanistic Data**

The public meeting of the Subcommittee also failed to address specific criteria which were identified by the NTP as appropriate for governing the delisting inquiry. Among these criteria, the need to consider data relating to mechanism of action or factors that

---

<sup>1</sup> References to Transcript denote the minutes of the public meeting held by the Subcommittee on October 30, 1997.

may be unique to a given substance was explicitly noted. The NTP explained that in the delisting inquiry, consideration should be given to the fact that there may be substances for which there is evidence of carcinogenicity in laboratory animals based on mechanisms which do not operate in humans and, therefore, would pose no reasonable risk of cancer to humans. A review of the minutes of the public meeting on October 30 makes clear that insufficient consideration was given to this question.

For example, as Dr. Samuel Cohen correctly observed in his letter to Dr. George Lucier, dated December 2, 1997, (copy appended) the amount of time spent on issues relating to the mechanism by which saccharin causes cancer and the lack of an in-depth discussion of the available data was surprising, especially since the Subcommittee was charged with the task of considering delisting of saccharin on the basis of such data. It is interesting to note that RG I focused significantly on the subject of mechanisms, Transcript, at 7, and that group voted 7 to 3 for delisting. Significantly, no new mechanistic data has been presented since the vote by RG 1 that might have led to a different conclusion. Moreover, it is important to note that the scientific literature about mechanistic effects discusses the similarity of action between sodium saccharin and sodium salts of other organic acids such as ascorbic acid. This issue was not discussed in any meaningful way by the Subcommittee during the public meeting. This lack of informed deliberation makes clear that the Subcommittee did not put emphasis on mechanistic analysis as it was explicitly charged to do by the NTP. Indeed, at the public meeting, Dr. Allaben commented that the Subcommittee was not addressing mechanistic information, but rather was incorrectly considering risk assessment. See Transcript, at 69, lines 12 - 21. Similarly, Dr. Hooper's comments during the public meeting reveal that he essentially ignored the usefulness of existing studies on mechanistic effects, contrary to the weight of the scientific evidence on the subject. See Transcript, at 72, line 23, and at 73, lines 1 - 15. In contrast to this, the 7 to 3 vote for delisting by RGI must be given considerable weight since that body fulfilled its mandate and "focused very heavily on mechanisms." Transcript, at 7.

## **6. The Subcommittee's Procedures Frustrated Informed Dialogue**

The public meeting held on October 30 did not enhance the public accountability of advisory committees established by the executive branch. First, all statements made by those wishing to participate in the public meeting were to be limited, individual, to five minutes in length. We submit that that is insufficient for a complete consideration of views, and encouragement of thoughtful dialogue on a complex subject. Second, substantive materials gathered by the NTP for the public meeting on October 30 were not provided sufficiently in advance of the meeting to allow members of the public to study the material, and prepare appropriate responses for the meeting.

The Federal Register notice announcing the public meeting stated that individuals wishing to make a formal presentation at the meeting must notify the designated official "no later than October 23, 1997," and provide a written copy in advance of the meeting. 62 Fed. Reg. 51,674 (October 2, 1997). The announcement further stated that "[w]ritten

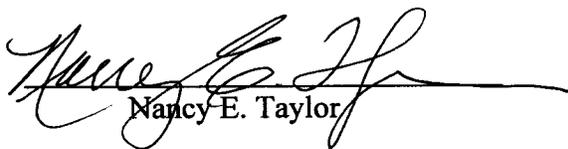
statements should supplement and may expand on the oral presentation, or may be submitted in lieu of an oral presentation, and should be received by October 27 so that copies can be made for distribution to Subcommittee members and staff and made available for the public." *Id.* Unfortunately, this procedure provided less than three days prior to the public meeting for the dissemination of materials on a highly complex, and controversial subject to the public. This can hardly be viewed as allowing for adequate preparation by those wishing to participate at the public meeting. At bottom, the lack of adequate time for dissemination of materials, and preparation for the public meeting amounts to a denial of an adequate opportunity to allow for a healthy dialogue for delisting of saccharin. That is clearly contrary to the underlying purposes of the FACA.

Aside from the lack of adequate preparation for the public, access by the members of the Subcommittee to materials submitted in response to the October 2, 1997 Federal Register notice simply did not afford adequate time for Subcommittee members to consider all aspects of the inquiry, be adequately prepared to lead a public discussion, and consider opposing points of view at the public meeting on October 30, 1997. These deficiencies foreclosed the kind of public participation in, and due consideration of the question of delisting of saccharin which a properly held public meeting would have provided.

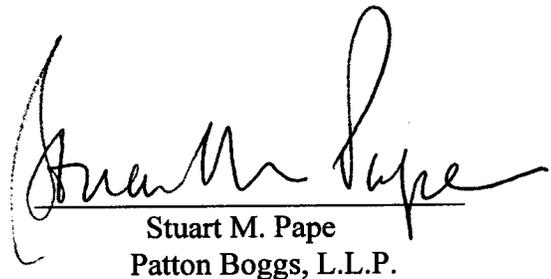
### Conclusion

Whatever the reason, the Subcommittee did not function as intended. Having failed to fulfill the public's legitimate and important expectations of careful scientific analysis, we believe that public confidence in the NTP's deliberative process can only be restored by reconsideration of the Subcommittee vote in context with the vote of RG1 and RG2 and the findings of highly respected public health policy bodies in the United States and around the world. In the interest of the effective marriage of science and public policy, the Subcommittee vote must be re-examined. We hope you concur.

Sincerely,



Nancy E. Taylor



Stuart M. Pape  
Patton Boggs, L.L.P.

Enclosures