

NATIONAL TOXICOLOGY PROGRAMPUBLIC MEETING OF THE REPORT ON CARCINOGENSOctober 21, 1999

DR. GOLDSTEIN: Let me introduce Dr. Kenneth Olden, Director of NIEHS.

DR. OLDEN: Good morning. I've been trying to convince the Department of Health and Human Services and the Environmental Protection Agency that they should buy a plane, and it would save the government a lot of money. This morning there were so many of us on the flight and it was late.

But let me say, first of all, thank you for taking the time to come here for a second time, and let me apologize for the fact that most of us were unable to get here three or four weeks ago. And I'm especially grateful to Bernie Goldstein because I called him after he had traveled halfway across the US -- he was out in the Midwest someplace -- to get here, and I reached him in the hotel after he had arrived telling him that we were going to be unable to get here, and we had to cancel this event.

So I really appreciate the fact that you've come here again to express your views about the

1 Report on Carcinogens. It is important to us and I
2 know it's important to you. So we regret the
3 conditions and certainly appreciate your
4 understanding and your patience.

5 Now, let me just spend a few minutes to
6 say that during my tenure as Director of the
7 National Toxicology Program and the NIEHS, I spent
8 an awful lot of time during the first year and a half
9 to two years having conversations with various
10 groups that are interested in the products of the
11 National Toxicology Program.

12 For example, we visited universities and
13 industry. We taught the university and industry
14 scientists. We talked to heads of environmental
15 groups, various industry groups, labor groups,
16 leaders at various government agencies, for
17 example, the Environmental Protection Agency, the
18 FDA, NIOSH, CDC, ATSDR, NCI, Consumer Products
19 Safety Commission.

20 We talked to an awful lot of people. We
21 talked to members of Congress. And, actually, we
22 had focus groups and town meetings around the
23 country, and the purpose was to talk to you to find
24 out what an agency like the NTP and all of its
25 responsibilities should be doing for you, the

1 American people.

2 I also convened a round table in 1993
3 where we brought together all the various groups
4 mentioned above -- industry, government,
5 environmental groups, academia -- to talk about
6 partnerships between NTP and the various groups.

7 I think it's fair to say that we've actually
8 reached out to the American people to hear your
9 concerns about the activities of the National
10 Toxicology Program.

11 Now, based on what I heard during those
12 first year, year and a half, we convened two panels.
13 The panels were composed, roughly, of 40 people
14 per panel, and one was to take a look at the
15 National Toxicology Program. The second panel was
16 to take a look at the Report on Carcinogens.

17 Now, many of the persons in attendance
18 here today were also parts -- members of those --
19 either one or both of those panels. Now, the
20 respective panels deliberated for more than a year.
21 They wrote a set of recommendations, and I can say
22 that the NTP and the Secretary of the department
23 accepted all the recommendations made by these
24 two review panels.

25 Now, the recommendations will be reviewed

1 shortly. The changes that we've made over the
2 years in the Report on Carcinogens will be reviewed
3 by Dr. Bill Jameson.

4 Now, let me make it clear. I think we
5 have a good process. Also, I am satisfied that we
6 have followed the process in the preparation of the
7 8th and 9th Report on Carcinogens. However, the
8 fact that we have a good process and that we
9 follow the process does not mean that the process
10 cannot be improved. And that is why we're here
11 today. We're here to get your advice and your
12 input.

13 Now, many of you have written to me. As
14 a matter of fact, maybe most of you have written to
15 me, and I can say that you've offered many good
16 suggestions. We will discuss -- we've already had
17 internal discussions about many of your
18 suggestions, and since we've gone through this
19 process now twice for the 8th and the 9th, we have
20 had internal discussions among the NTP Executive
21 Committee and the NTP staff about ways that we
22 realize and we believe that we can improve the
23 process.

24 Now, I anticipate that I will hear -- we will
25 hear many good suggestions offered over the next

1 two days. Maybe they'll be extensions of the good
2 ones that you've already offered.

3 In closing, let me say that I am 100
4 percent committed to sending the Secretary an
5 outstanding product, and that is the Report on
6 Carcinogens. I think everything that we have done
7 over the past eight years indicates exactly that. I
8 want to send the Secretary a report that is based
9 on the best science that is available at the time, a
10 report that is based on rigorous external peer
11 review.

12 I thank you for your input into the process,
13 and I thank you for your support over the years,
14 and I look forward to a productive discussion over
15 the next two days. Thank you very much.

16 **DR. GOLDSTEIN:** Thanks, Ken.

17 Our next speaker is Bill Jameson from NTP.

18 **DR. JAMESON:** I would also like
19 to welcome everybody to this meeting today and
20 tomorrow, taking the time to come here and share
21 your input with us about the Report on
22 Carcinogens.

23 I'd just like to emphasize that we are here
24 today to receive public comment on the criteria and
25 the process for reviewing the nominations for the

1 Report on Carcinogens. That's the purpose of our
2 meeting.

3 I'm Bill Jameson. I'm Head of the Report
4 on Carcinogens Group at NIEHS and responsible for
5 the coordination of reviews and the actual
6 preparation of the report.

7 This slide just shows that the RoC was
8 nominated as part of the 1978 Public Health Service
9 Act, which requires that the Secretary of Health and
10 Human Services to publish an annual report which
11 contains either a list of substances which are either
12 known to be human carcinogens or may reasonably
13 be anticipated to be human carcinogens and to
14 which a significant number of persons residing in
15 the United States are exposed.

16 This legislation was amended in 1993 to
17 make it a biennial report. So after the law was
18 amended in '93, it clearly states that this report
19 must be published every two years.

20 The latest report to be published was the
21 8th Edition, which was published in 1998. We are
22 in the final stages of completion of the 9th Report,
23 which will be submitted to the Secretary very
24 shortly. Reviews of the 10th Report will begin this
25 year, and we are working with a 2001 publication

1 date for the 10th Report.

2 The first set of nominations for the
3 10th Report will be reviewed in an open public
4 meeting by the Board of Scientific Counselors
5 Subcommittee, which is scheduled for December 16
6 and 17.

7 This slide shows the current criteria for
8 listing in the Report. I realize this is a difficult slide
9 to read, but you have copies as part of your
10 handout that are available where you signed in.

11 There are two categories for listing: Known
12 to be human carcinogens and reasonably anticipated
13 to be human carcinogens. The descriptive bottom
14 paragraph that follows pertains to both listing
15 categories of the criteria. This paragraph became
16 part of the criteria as a result of the public review
17 of the criteria, which was performed in '94 and '95,
18 which Dr. Olden alluded to earlier, and emphasizes
19 that "conclusions regarding carcinogenicity in
20 humans or experimental animals are based on
21 scientific judgment with consideration given to all
22 relevant information." This revision to the criteria
23 was one of the main reasons why the process for
24 reviewing the nominations was revised to include
25 external peer reviews in a public forum.

1 As you see, the criteria have two
2 categories. The first is known to be human
3 carcinogens, where agents, substances, mixtures, or
4 exposure circumstances for which there is sufficient
5 evidence of carcinogenicity from human studies are
6 listed. Human studies are not limited to human
7 cancer epidemiology studies, but also include
8 consideration of relevant information from human
9 metabolism, pharmacokinetic, or genetic toxicology
10 studies which relate to the mechanism of action for
11 cancer formation in humans.

12 The second category is reasonably
13 anticipated to be human carcinogens, where agents
14 are listed for which there is either limited evidence
15 of carcinogenicity from the human studies or there
16 is sufficient evidence of carcinogenicity from
17 studies in experimental animals, which could include
18 increases in malignant and/or a combination of
19 malignant and benign tumors in multiple species or
20 tissue sites, by multiple routes of exposure or
21 unusual incidence, site, or tumor type, or age of
22 onset, or there may be sufficient structure activity
23 or mechanistic data, which indicates that it should
24 be listed as a reasonably anticipated human
25 carcinogen.

1 Again, to emphasize, the conclusions
2 regarding either known or reasonably anticipated
3 human carcinogens are based on scientific judgment
4 with consideration given to all relevant information.
5 Relevant information includes, but is not limited to,
6 dose response, route of exposure, chemical
7 structure, metabolism, pharmacokinetics, sensitive
8 subpopulations, genetic effects, or other data
9 relating to mechanism of action or factors that may
10 be unique to a given substance.

11 This slide gives an overview of the review
12 process for the Report, and I will go through this
13 in detail. A one-page outline and a four-page
14 detailed description of the process is contained in
15 the handouts that were available to you when you
16 signed in.

17 We start here with the nominations. They
18 are routinely solicited by publication of requests for
19 nominations in the Federal Register and other
20 appropriate publications. The nominations come
21 from the public as well as State and Federal
22 agencies, industry, labor, academia, and are also
23 generated by review by the NTP of the current
24 literature to identify substances that may meet the
25 criteria for inclusion in the report.

1 Once a nomination is initially identified,
2 there is an announcement published in the
3 appropriate publications that solicits public
4 comment on the nomination.

5 The original nomination, with data provided
6 and/or supplemented by a limited literature search,
7 and all public comments received in response to the
8 announcement of our -- the intent of reviewing a
9 particular nomination, our initial review by the
10 NIEHS/NTP Review Group, which is referred to as
11 RG1, to determine if the preliminary information
12 available is sufficient to merit further consideration.

13 If the RG1 determines there is insufficient
14 information in the original nomination available to
15 warrant consideration by the NTP, the nomination
16 will not be considered further and will be returned
17 to the nominator, who will be invited to resubmit
18 the nomination with additional justifications.

19 A notice of this action will be published, and
20 the NTP Board of Scientific Counselors and the NTP
21 Executive Committee are notified of this action.

22 If it is determined that a nomination merits
23 formal consideration, that it contains sufficient
24 relevant information to go forward, we initiate our
25 own independent search of the literature and

1 prepare a draft background document, which
2 contains all of the relevant information and
3 addresses issues that have been identified in the
4 public comments that we receive in response to the
5 Federal Register announcement concerning a
6 particular nomination.

7 I must emphasize that the data concerning
8 the human and experimental animal studies that we
9 include in the background document must come
10 from publicly available, peer-reviewed sources.

11 The formal review of the nomination, again
12 referring to the RG1, is described in detail in the
13 handout. The original nomination and all public
14 comments received in response to a nomination are
15 formally reviewed by the RG1. The RG1 reviews all
16 relevant information available for each nomination
17 and makes its recommendation to the Director of
18 NTP for those nominations determined to contain
19 sufficient information for making a decision for
20 listing or delisting in the report.

21 Nominations reviewed by the RG1 for which
22 it is determined that sufficient information to make
23 a recommendation for listing or delisting could not
24 be obtained will not proceed further in the review
25 process. The other RoC review groups, as well as

1 NTP Executive Committee, will be informed of this
2 action.

3 The original nominator will be notified of
4 the RG1 action and be invited to resubmit the
5 nomination with additional justification for review
6 for either listing or delisting in the report. All
7 nominated agents, substances, or mixtures reviewed
8 by the RG1 that are not selected for listing or
9 delisting in the report will be included in
10 subsequent editions of the Report on Carcinogens
11 with the reasons why they were not considered
12 further.

13 Once the nomination has completed the
14 RG1 review, it goes forward to the Interagency
15 Working Group for the Report on Carcinogens, which
16 we'll refer to as the RG2. This is a committee
17 made up of representatives from the NTP Executive
18 Committee and includes the NCI, NIEHS, the
19 FDA/NCTR, NIOSH, NCEH, ATSDR, CPSC, EPA, and
20 OSHA. Again, the handout that you have describes
21 in detail the RG2 review.

22 After the RG2's consideration of all the
23 relevant information and the public comments, it
24 makes its recommendation to the Director of NTP
25 concerning the listing or delisting of the nominated

1 substance.

2 Following the RG2 review, the background
3 documents that are listed there is finalized and an
4 announcement is published announcing the meeting
5 of the Board of Scientific Counselors and the public
6 availability of the background documents as well as
7 solicit public comment. So at this point, again, we
8 actively solicit public comment on the nomination
9 and also make the background document that we
10 had prepared concerning the nomination available
11 for public distribution and comment.

12 So the notice also invites interested parties
13 to submit written or present oral comments at the
14 Board Subcommittee meeting -- during the public
15 meetings that are held.

16 Since the establishment of the new review
17 procedures for the Report on Carcinogens back in
18 '96, this announcement was published four weeks
19 prior to the Board Subcommittee meeting with a
20 deadline for submission of comments of the day
21 before the meeting, and this particular process has
22 caused some concern as it is felt that it does not
23 allow enough time for consideration of the
24 comments by the Board Subcommittee.

25 This is an issue that has been a topic of

1 many discussions by NTP staff, as Dr. Olden alluded to
2 earlier, and I'm sure will be discussed here
3 today. The NTP is considering several options
4 concerning this issue and following the input
5 received today will make changes in the process to
6 address that concern.

7 The NTP Board of Scientific Counselors, the
8 Report on Carcinogens Subcommittee, meets in an
9 open public meeting to review the nominations and
10 receive public comments concerning individual
11 nominations.

12 Again, details of the Subcommittee review
13 are contained in the handout. I won't take the time
14 to go through them now. Upon completion of its
15 review, the Board Subcommittee makes its
16 recommendations to the Director of the National
17 Toxicology Program concerning the listing or
18 delisting of material in the report.

19 Again, following the Board Subcommittee
20 meeting, we actively solicit public comments on the
21 final recommendations that were made by the three
22 scientific review groups.

23 There is an announcement published that
24 contains all recommendations of the three scientific
25 review groups and solicits final public comments

1 and input on the nomination. Following receipt of
2 the final public comments, the recommendations of
3 the RG1, the RG2, and the Board Subcommittee and
4 all public comments that have been received in
5 response to the various announcements concerning
6 review of the nominations are submitted to the
7 Director of the National -- are reviewed by the NTP
8 Executive Committee.

9 The NTP Executive Committee, made up of
10 the agencies that I pointed out earlier, reviews the
11 public comments and the recommendations
12 concerning the nominations and will make -- or,
13 actually, they provide their agency's opinion of the
14 recommendation of the nominations to the Director
15 of NTP.

16 Then all of the recommendations that have
17 been made by the various groups, the RG1, the
18 RG2, the Board Subcommittee and the Executive
19 Committee, plus all the public comments that are
20 received in response to our announcement, go
21 forward to the Director of the National Toxicology
22 Program, who reviews all of this information and
23 ultimately makes his final recommendation to the
24 Secretary of Health and Human Services for what
25 should be listed or delisted in the report by

1 submitting the final draft of the Report on
2 Carcinogens.

3 The Secretary of Health and Human
4 Services has the final authority for what is
5 contained in the final version of the Report on
6 Carcinogens. Upon review of the final draft
7 submitted by the NTP and approval of the report,
8 the Secretary forwards the report to Congress, and
9 a notice is published announcing the availability of
10 the final report, and this announcement also
11 identifies all newly listed or delisted agents,
12 substances, mixtures, or exposure circumstances in
13 that edition of the Report on Carcinogens.

14 So this is a rather extensive two-year
15 process to put together the final draft of the
16 report, which the NTP, as delegated by the
17 Secretary, submits to the Secretary for approval.

18 So that concludes my presentation. I tried
19 to make it short because of the time constraints,
20 and I'll be available if there are any comments or
21 questions.

22 **DR. GOLDSTEIN:** Thanks, Dr.
23 Jameson.

24 Dr. George Lucier is head of the
25 Environmental Toxicology Program for NIEHS/NTP.

1 DR. LUCIER: Thank you, Bernie.

2 One of the recommendations that we've
3 heard, really, on multiple occasions from you is
4 that we should hold these meetings in Washington,
5 our external peer review meetings. And based on
6 the level and diversity of the participation that we
7 have at this meeting, that seems like it might be a
8 good idea.

9 Given the lateness of our start and the fact
10 that you're here to present to us your ideas and
11 not here just to listen to us, I'll make my comments
12 very, very brief. Let me just say two things. One
13 is, as Dr. Olden said, we've worked very hard to
14 develop the process for the Report on Carcinogens
15 that's open and transparent and one that brings into
16 it all the best and relevant science that's available
17 to determine whether or not a substance should be
18 listed as a known or reasonably anticipated to be a
19 human carcinogen.

20 The second point is that, as Dr. Jameson
21 said, we have a number of review groups that look
22 at this. He just went through the details of the
23 process. We have an internal group at the NIEHS
24 affectionately called RG1. We have RG2, which is
25 the Interagency Working Group, and you recall the

1 Well, I agreed to do this only after having gotten
2 lots of reassurances from NTP and NIEHS that, in
3 fact, people were willing to listen and willing to
4 make changes. I think that that's crucial.

5 We really want to try, if we possibly can,
6 to focus on the changing issue: What can be done
7 with the process, if anything, that will change it in
8 the right direction? I think we'd all agree, as Ken
9 has told us, that any process can be improved.
10 Certainly something as complex as determining
11 carcinogenicity and where to put chemicals on --
12 where we have a continuum of evidence, but, yet,
13 we have to draw lines through that continuum and
14 put chemicals into a box and whether we call it
15 known or reasonably anticipated or A, B, C, or D or,
16 as some of our laws have it, we define the
17 difference between the probable and the possible
18 carcinogens.

19 It's a difficult situation because, inherently,
20 you're putting a line through a continuum, and
21 wherever you put that line, there will be some
22 chemical that is just above or just below that line,
23 and reasonable scientists will differ as to that. So
24 the process, inherently, is a difficult one. It
25 inherently can be improved and it inherently can be

1 made worse. Our goal is to focus on how to
2 improve it.

3 Many of the comments that I've seen in the
4 written documents have to do with individual
5 compounds. Now, each of the presenters will have
6 ten minutes. You can do with that ten minutes
7 what you'd like. I would urge you, however, not to
8 deal with the issues of the individual compounds,
9 whether or not they should have been interpreted
10 (inaudible), or any of the usual kind of things that
11 have to do with individual interpretation, that
12 simply isn't part of what we're discussing. It really
13 will be a loss of time, and we need to focus on
14 what the issue is here.

15 I'm actually going to demand that NTP
16 folks, when they have a chance to respond, not to
17 respond to these issues about the specific
18 compounds. It will just be taking away from the
19 time that we should be putting to talking about the
20 process and giving ideas in discussing the process.

21 We're in the discussion section, and this is
22 a different approach. The usual thing is to just
23 march people up, say your peace. We'll transcribe
24 it, and, eventually, something will happen. We're
25 going to try to help focus the discussion on

1 individual points that seem to be themes that are
2 emerging. For that, Clay Frederick of Rohm and
3 Haas Company and Lynn Goldman of Johns Hopkins,
4 recently of EPA, who are members of the Board of
5 Scientific Counselors, will be helping us focus that
6 discussion, trying to pick through the themes.

7 We're going to ask people to, at that time,
8 try to stick to those topics, and we're going to try
9 to ask those of you who haven't spoken before to
10 get a little bit of a preference in terms of making
11 comments. And I'll try to cut people's time so we
12 don't have any further speeches to be made but
13 really try to keep our focus.

14 It's an experiment. We don't know how
15 well it will work, but it is an attempt to try to get
16 at what is really the meat of this meeting and what
17 seems to be the request by people who have asked
18 for the meeting.

19 Let me emphasize that it should be ten
20 minutes and ten minutes only for the presentation.
21 That includes setup time. If any of you have
22 videos that you want to show or whatever, and it's
23 going to take you five minutes to set up, that's part
24 of your ten minutes. We will have folks here.
25 They're available to show the overheads, to show

1 slides. Please do get to them beforehand so that we
2 can really move this along.

3 Let me ask, as a personal favor, that when
4 you make your presentations, please avoid
5 abbreviations and jargon as much as possible. It
6 really will help. We've got a diverse audience
7 here. If you want to make a point, to try to get to
8 everyone, I think it's important that we speak a
9 language that we all can understand.

10 The discussion time is really going to be
11 our time. I mean, it's really an attempt to get
12 everybody -- to bring to a head where the
13 differences are while being, I hope, polite to
14 everyone. And, again, during that time I'm going to
15 ask the NTP folks please not to be defensive. This
16 is not an attempt to attack NTP. If it is, it's not
17 the point, and we missed the point if we're trying
18 to do that.

19 And, similarly, the NTP staff here, who
20 have worked very hard on this, inevitably, it's
21 human to be defensive about what they've done.
22 That's not the point here. There's no question.
23 Everybody is agreed that we could do a better job
24 if we just knew how to do it and could get the
25 ideas and discuss them well.

1 minutes flat. I'm going to do my best to be
2 evenhanded. I will make one exception. The first
3 speaker, Dr. David Guston, is from Rutgers. David,
4 you can have as much time as you want.

5 **DR. GUSTON:** My name is David
6 Guston. I'm an Assistant Professor of Public Policy
7 at Rutgers University. And for the past year, I've
8 been engaged in research sponsored by the
9 National Science Foundation on understanding how
10 scientific and political considerations are combined
11 in various decision-making arenas.

12 And before I go on, just let me say that
13 my opinions here are my own and in no way reflect
14 the representatives of Rutgers or NSF.

15 The National Toxicology Program and its
16 Report on Carcinogens have been part of that study,
17 which, unfortunately, is far from completed. I
18 would, however, like to present some preliminary
19 findings that may be relevant to some of the
20 discussions about the review procedures and listing
21 criteria for the report.

22 What led me first to investigate NTP in
23 detail was the apparently unique combination of
24 technical subject matter with explicit voting rules in
25 order to come to a policy-relevant conclusion.

1 Although there are no actual surveys of such
2 mechanisms, the predominant mode of decision
3 making in scientific advisory boards seems to be
4 consensus, meaning that the group continues to
5 deliberate until no explicit dissent is encountered.

6 A small study by the California
7 Environmental Dialogue, for example, found that
8 scientific advisory panels normally begin with
9 charges to seek consensus, and where consensus
10 cannot be reached, panels prefer to describe areas
11 of disagreement rather than to offer minority
12 reports. The National Academy Complex, for
13 example, works in this way.

14 Consensus decision making is notoriously
15 difficult to study, but votes are a gold mine of
16 empirical data to a political scientist like myself.
17 Table 1, if you would, please, shows the votes by
18 nominated substance and panel for the 9th Report.
19 You don't have to worry about reading that.

20 If you can flip to Table 2 now, what's
21 notable in this data is the level of consensus - here
22 meaning consensus as an outcome rather than a
23 process -- that's demonstrated. This consensus-as-
24 outcome can be measured in different ways. First, I
25 looked at the overall agreement within each

1 advisory panel across all substances. Table 2 shows
2 the percentage of 'aye' votes -- that is, votes in
3 favor of the proposal on the table -- cast in each
4 panel over all the substances reviewed, which is
5 uniformly high.

6 A second way to look at the level of
7 consensus is to examine the agreement within each
8 of the three panels. Votes can be categorized as:
9 Unanimous, meaning no one present voted against
10 the outcome preferred by the rest; strict consensus
11 -- unanimous means all present voted for the same
12 outcome; strict consensus, meaning that no one
13 present voted against the outcome preferred by the
14 rest, but may have abstained; supermajority,
15 meaning that two-thirds of those present voted for
16 the same outcome; or simple majority, meaning that
17 more than one-half of those voting voted for the
18 same outcome.

19 Of the 73 total votes, 35 were unanimous,
20 an additional 6 were strict consensus, 22 were
21 supermajorities, and only 10 were simple majorities.

22 A third way to look at the level of
23 consensus is to look across the three panels for the
24 24 substances. As Table 3 shows, three of the
25 substances were subject to all-unanimous

1 conclusions and three more to unanimous or strict
2 consensus conclusions. So for six of those 24
3 substances, no one in any of the panels dissented,
4 but perhaps some may have abstained.

5 A supermajority or more held in all panels
6 for 10 substances, and a majority held for an
7 additional four substances. For only four
8 substances was there any divergence, that is, a
9 majority or better of one panel voting in opposition
10 to the majority of another panel.

11 This level of consensus in itself seems to
12 me an important achievement. One might compare
13 it, for example, to findings by sociologists of the
14 seemingly surprising disagreements among reviewers
15 of research proposals to the National Science
16 Foundation or to general expectations of
17 disagreement within a highly politicized system,
18 perhaps comparing things that might go on with the
19 Report on Carcinogens to toxic torts, things that
20 are adjudicated in the courtroom.

21 My research intends to explore the reasons
22 behind this apparently high level of consensus,
23 particularly probing the hypothesis that the
24 consensus is a product of relatively strict
25 procedures and criteria and that divergence is at

1 least, in part, attributable to the characteristics of
2 the panelists and departures from the applications
3 of the criteria.

4 Preliminary analysis suggests that the
5 sectoral affiliation of members of the Report on
6 Carcinogens Subcommittee has an important role.
7 I'm not sure if you can actually make out the colors
8 from a distance here, but what Table 4 does is it
9 takes each member of the Report on Carcinogens
10 Subcommittee for the 9th Report and assigns to
11 that person a three-dimensional coordinate.

12 Where the vertical axis is the number of
13 times that a member voted the same as the majority
14 group, that it's as protective as the majority of the
15 substance was, where this axis is the number of
16 times the member voted in a less protective way
17 than the majority, this axis is in a more projective
18 way, and I've color-coded these individuals by their
19 sector of origin, university, labor, industry, and
20 government.

21 And I'm not sure if you can make it out,
22 but the sort of pinkish lines and boxes are the
23 university members, and they're somewhat clustered
24 around the as protective. The governing members
25 of the committee are, basically, on all corners.

1 There is one who's, if you will, the least protective,
2 one who's even on with the majority, and one who's
3 someplace over here, I think -- I can't see the
4 colors very well from the slide -- who is somewhat
5 more protective than the majority.

6 And the industry representatives, to the
7 extent that they deviate from the majority, are
8 uniformly less protective, the labor representative
9 uniformly more protective than the majority.

10 For those of you who picked up a copy of
11 my remarks, you will note that there is a Table 5 in
12 there. Please disregard Table 5 because there is an
13 error of aggregation there. I'm sorry about that.

14 One might think, for example, that because
15 of its more diverse public membership, the Report
16 on Carcinogens Subcommittee might be subject to
17 greater internal disagreement than the other two
18 committees.

19 There is, at best, slight evidence to
20 support this contention. For example, it had lower
21 overall levels of agreement, as Table 2 showed
22 earlier, but as shown on Table 3, it agreed
23 unanimously more than either RG1 or RG2 did.

24 The choice of using a voting rule rather
25 than a consensus rule may contribute to the

1 appearance of consensus. More than half of the
2 individual panel votes were unanimous or strict
3 consensus, and, therefore, one may judge their
4 conclusions to be independent or relatively so of
5 the mechanism of coming to a conclusion, but
6 almost half the panel votes were super- or simple
7 majorities, and, therefore, they may have reached
8 their conclusions only under conditions of voting,
9 and they may be very sensitive to the kinds of
10 procedures and criteria that are under discussion
11 here.

12 There are other ways that the procedures
13 and criteria influence the level of apparent
14 consensus. The current review process has only a
15 limited number of bins - known human carcinogen,
16 reasonably anticipated to be a human carcinogen, or
17 not listed - into which to sort nominated
18 substances.

19 These three bins may assist a convergence
20 of opinion, for example, by directing panel members
21 who have concerns about a substance to label it
22 reasonably anticipated to be a human carcinogen
23 because there is no other label other than delisting,
24 which they may interpret as meaning implicitly safe.
25 This came out of discussions between myself and

1 Dr. (inaudible) before this that the reasonably
2 anticipated to be a human carcinogen bin is
3 relatively large.

4 And an additional factor is that it may
5 differ in size depending on which side of it you're
6 looking at. It may seem relatively large when
7 considered on the side of the alternative of
8 delisting a substance. It may seem a different size
9 when looking at it from the side of the alternative
10 of being listed as a known human carcinogen.

11 There is -- adding bins, for example,
12 presumptive evidence of human carcinogenic activity
13 or laboratory animal carcinogen presumed not to be
14 a human carcinogen, which was suggested in the '95
15 review procedures, might spread the votes more
16 thinly and reduce the apparent consensus.

17 So, basically, the take-home point here is,
18 to some extent, the choice of procedures and
19 criteria is related to the degree of consensus. And if
20 this consensus is valued, and I think it should be
21 because there are too many other arenas in science
22 and policy that promote adversarial relations, there
23 is little reason to tamper with current arrangements,
24 and any proposed changes should clear a very high
25 hurdle.

1 Nevertheless, consensus is not an absolute
2 value, and the full information and the expression
3 of uncertainty deserve attention as well. As Table
4 4 describes, the current process does express some
5 of the uncertainty inherent in the deliberations --
6 expressing it through votes that are either more or
7 less protective than the majority opinion.

8 Allowing some more concrete expression of
9 minority opinion other than simply casting
10 dissenting votes might be productive because
11 without damaging consensus formation, it could,
12 first, help clarify how the procedures and criteria
13 are applied by individuals in specific circumstances;
14 (2), publicly commit individuals to neutral analyses,
15 potentially inhibiting the influence of economic or
16 other biases; (3), provide additional guidance to
17 future research on substances that might reduce
18 existing uncertainty or resolve existing conflicts;
19 and (4) provide a more coherent representation of
20 the conclusion of the scientific review by providing
21 more information about the range of beliefs of the
22 panel members.

23 I would thus endorse what NTP, in
24 describing some suggestions already received, has
25 characterized as a Comment Response Document or

1 a narrative justification - that would address these
2 four rationales - to accompany decisions.

3 Thank you.

4 DR. GOLDSTEIN: Thank you, Dr.
5 Guston. Our next speaker is Thomas Starr of the
6 American Forest & Paper Association.

7 DR. STARR: My name is Thomas
8 Starr. I'm an independent consultant for the practice
9 of risk assessment issues. I'm here today on behalf
10 of the American Forest & Paper Association. The
11 views I'm presenting are my own.

12 In spite of the admonition not to address
13 individual chemicals, I thought the comments I have
14 to present are well-characterized by the experience
15 the NTP has had with the consideration of Dioxin
16 for listing.

17 It has a fairly long history in consideration
18 for listing in the Report on Carcinogens. It was
19 first listed in the 2nd Annual Report in 1981 as
20 reasonably anticipated to be a human carcinogen.

21 Then in 1997 it was nominated internally
22 for upgraded listing as known to be a human
23 carcinogen by an RG1 vote of 10 to 0 and an RG2
24 vote of 8 to 0. Both voted to upgrade.

25 In the end of September of 1997, the TCDD

1 Background Document was issued, and a month
2 later, on Halloween, the Report on Carcinogens
3 Subcommittee voted 4 to 3 for an upgrade to known
4 to be a human carcinogen status. It was actually a
5 3-3 tie broken by the Chair.

6 After that decision created a great deal of
7 concern in interested parties, letters were written
8 to Dr. Olden protesting that the process was
9 defective and inadequate in consideration of Dioxin.
10 Dr. Olden determined somewhat later on that the
11 Report on Carcinogens Subcommittee Review may
12 not have been adequate and called for a second
13 review of by that Subcommittee in April of 1998.

14 In December of last year, the Subcommittee
15 voted 7 to 5 against upgrading the Dioxin listing.
16 The NTP Executive Committee vote has been taken.
17 We don't know that. The final recommendation has
18 not yet been made to Mr. (inaudible).

19 What specific problems are there in the
20 process that the Dioxin example illustrates? First
21 of all, the Background Document is inadequate.
22 There are significant factual errors in it. Just one
23 example, the Dioxin Background Document stated
24 that the IARC Working Group identified a causal
25 association with all cancer mortality among the

1 most highly exposed subgroups, but IARC concluded
2 that the human evidence was limited; that is,
3 "chance, bias, or confounding could not be ruled
4 out with reasonable confidence." In fact, the
5 Background Document, which I have here, is 99
6 percent the IARC document, and only two pages are
7 devoted to the human evidence that the NTP put
8 together.

9 So there's a problem in even interpreting
10 what other groups have done in the Background
11 Document. The problem with the Background
12 Document further is that no modifications are even
13 allowed after public release even though they might
14 be well justified.

15 The defective Background Document needs
16 to be improved, and I would recommend early
17 release of it by RG2 for review by the public and
18 selected outside experts with subject matter
19 specialties, modification by RG2 as appropriate,
20 including their recommendation of whether or not to
21 go forward.

22 The Report on Carcinogens Subcommittee
23 meeting, there are too many issues, too little time,
24 too little relevant expertise. There's insufficient
25 opportunity to explore the complex issues in depth,

1 both in preparation for and during the meeting.

2 The Background Document was issued just
3 30 days prior to the meeting. Public comments
4 were obtained right up to the beginning of the
5 meeting. There was no real opportunity for the
6 Subcommittee members to review carefully all of
7 that material.

8 There was insufficient opportunity for
9 public comment, just five minutes per individual,
10 and it was limited to one spokesperson per
11 organization. Unscheduled comments were not
12 permitted even though there were microphones in
13 the audience presumably to take unscheduled
14 comments.

15 There was insufficient expertise in
16 epidemiology, which is the critical subject area of
17 Dioxin. In the first vote, there were no
18 epidemiologists present when the vote was taken.
19 In the second vote, there was just one.

20 So the recommendation here would be to
21 limit the number of substances considered in a
22 two-day meeting to four, so you would have a
23 morning and afternoon -- a morning or an afternoon
24 for each of the substances for consideration.

25 Also recommending enlistment of multiple

1 outside epidemiologic experts. When Dioxin was
2 concerned in terms of the causal question, "Is there
3 a causal association between exposure and human
4 cancer?" when EPA was undertaking its reassessment
5 back in 1993, they employed eight outside
6 epidemiologists for a full day. When IARC
7 deliberated on this question in 1997, they employed
8 ten epidemiologists for a full week, yet we had
9 votes from either no or one epidemiologist present
10 in the RoCS meeting.

11 There's no explanation of votes given. No
12 rationale is provided for votes by the deciding
13 groups, so you cannot determine the reasoning
14 behind these votes. This is especially important
15 when votes are inconsistent, as they have been for
16 Dioxin, between and/or within groups, indicating
17 that reasonable doubts exist about classification.

18 So the recommendation here would be that
19 written explanations be provided for decisions by
20 RG1, RG2, and the Report on Carcinogens
21 Subcommittee as well as the Executive Committee,
22 including minority reports when votes are split.
23 Finally, transcripts should be taken of all group
24 meetings so that a full record is available to the
25 public.

1 Finally, I want to address a clarification
2 that Dr. Jameson did not reference that appeared in
3 the Federal Register in April of 1999, clarification
4 of the criteria for known to be a human carcinogen
5 listing. The clarification as it is worded is much
6 too vague and open-ended. There is an and/or
7 clause. Specifically, this can include traditional
8 cancer epidemiology studies, data for clinical
9 studies, and/or data derived from the study of
10 (inaudible) substance in question and useful for
11 evaluating one of the relevant cancer mechanisms
12 operating in people. This and/or clause will permit
13 listing as known to be a human carcinogen without
14 any direct evidence of carcinogenicity in humans.

15 What I recommend is that NTP follow the
16 advice it has received from two eminent
17 epidemiologists, Greenberg from the Medical
18 University of South Carolina and Richard Monson
19 from Harvard University, in a June 1, '99, letter in
20 response to this (inaudible).

21 They state: "A scientific judgment that
22 there is a known relationship of cause and effect in
23 humans should rely solely on the fact of exposure
24 and the fact of disease in humans."

25 "Sufficient evidence of carcinogenicity for

1 humans should derive from human epidemiology
2 studies alone."

3 Thank you very much.

4 DR. GOLDSTEIN: Thank you,
5 Dr. Starr.

6 Our next speaker is Jim Tozzi, representing
7 the Multinational Business Service.

8 MR. TOZZI: I try not to leave too
9 much of a record of what I say.

10 Good morning. I'm privileged to be here.
11 Mr. Chairman, distinguished members of the panel,
12 I'm Jim Tozzi with Multinational Business Services,
13 and I would like to compliment NTP for having this
14 meeting because Washington history is not replete
15 with agencies opening up their proceedings.

16 I also think they should be complimented
17 for their commitment to not only have the meeting,
18 but to review in some detail the comments people
19 make today. And there's going to be speakers more
20 knowledgeable on some of the technical processes
21 than I, both those preceding me and those that
22 follow.

23 So I'm not going to make any particular
24 points of those, but I want to make just one point
25 - most of my points are very easy, sometimes too

1 simple -- is that I think if you want to capitalize on
2 this process that you're having today, it's important
3 that you make one change in the procedures, and
4 let me go on to what I mean with that.

5 I'm most appreciative of what the Chair
6 said, that you're going to have a discussion after
7 the comments on these because I think that
8 ventilates them when they're warm.

9 Now, what is the only comment I want to
10 make today in all of this process? I mean, it's an
11 exceptional program. I think the only point I want
12 to make is sort of a question. That question is:
13 Why is the rush? What is the rush to publish the
14 9th Report? You may say, Well, that sounds sort of
15 (inaudible). Let me explain a little more on that.

16 First of all, you're way ahead of schedule.
17 You get an "A" on that. Some agencies (inaudible)
18 around 22 years. Of course, I used to be in
19 business, but -- so the first question is: Why not
20 sit back and take time on this? Because your last
21 report was in May of '98. If you add two years to
22 that, and I don't want to add to the technical
23 complexity of this topic, but you would have -- it
24 would be in the year May 2000.

25 So the first question is: Why this rush to

1 have the report done now? Seems to be a question
2 in my mind because (inaudible). Then you may say,
3 Well, let's look a little further. What was the
4 record of the agency in issuing reports in the past?
5 Well, the last report was in 1998.

6 Well, let's go back from there. Now, it's a
7 relationship (inaudible). So the report prior to that
8 should have been in 1996. Was it in 1996? No.
9 Was it in 1995? No. Was it in 1994? You win.
10 Four years. You may say, "Tozzi, you don't know
11 much about mathematics. That's just a point
12 estimate. You have to look at the whole data set."

13 Well, let's take 1991. That was -- 1994
14 was the last report. Go back two years. It would
15 be 1992. Was that report written in 1992? No. It
16 was in 1991. That was three years. Then they did
17 make it two years in 1989, but from 1989, back two
18 years is 1987. Did they make 1987? No. Did they
19 make 1986? No. 1985.

20 So what you see is, over a 15-year period,
21 only once did you make a two-year report. Most was
22 three to four years. So why the rush? It's not
23 clear given the kind of scientific evidence you're
24 going to hear today. What is this rush to publish
25 the report ahead of time?

1 Now, I'm not criticizing the agency for
2 taking four years because some of these are very
3 difficult issues. I applaud you. What I don't
4 understand is: Why the rush to publish?

5 Now, let me give you what I -- and this is,
6 most certainly, not specific, Mr. Chairman, to any
7 commodity on that list. These recommendations are
8 in keeping with what the Chair has said are very
9 generic. One, don't rush. And, second -- let me
10 give you the idea.

11 First, I think we should prepare a
12 transcript of this meeting, which Dr. Lucier said
13 you're going to have available in four to six weeks.
14 Second, I think you should analyze the comments
15 from this meeting and make them available to the
16 public, which I think the NTP staff is going to do
17 anyway or they wouldn't be able to benefit.

18 Now, here's where a little extra works
19 comes in. Third, I think you should give the public
20 an opportunity to comment on the agency's
21 responses to these proposed actions. Fourth, I
22 think you should assemble all this and put them out
23 for public comment, and then based on that record,
24 you all make the determination of what you want to
25 do in the 9th annual report.

1 Now, what I'm recommending differs a
2 little bit from what was in the NTP announcement.
3 How is it different? The NTP announcement says
4 that all these views are to be given in respect to
5 the 10th Report. My view is: Why waste a good
6 thing? Why not capitalize it now on the 9th Report?
7 Why wait two to three years to do it?

8 Mr. Chairman, I have four minutes left?

9 **DR. GOLDSTEIN:** Four minutes and
10 four seconds left.

11 **MR. TOZZI:** Thank you, sir.

12 So let me give you my views, a question:
13 What is the downside of taking slower (inaudible)?
14 What is the downside of ventilating these issues?

15 Well, I see a downside of not doing it. One
16 of the downsides are that there are many unsettled
17 issues here, and the resolution of which will have a
18 big impact only not on particular products in 9th
19 Report but what gets in the 10th Report and how
20 they're addressed.

21 I don't think these issues are going to go
22 away. You don't play to a packed audience like
23 this because there's no interest in this issue. And
24 to what extent are these going to go away ought to
25 be addressed in a formal way. I think they're not

1 going to go away.

2 Second, to those people that -- I'm hearing
3 repeatedly that this is just a hazard identification
4 and not a regulatory report. Let me just speak to
5 that. This report in draft form is used at the local
6 level by governments to ban products, and I'll be
7 glad to give you the localities. And they're acting
8 on the draft report, not even the final report. They
9 don't care that that little sign says Draft.

10 (Inaudible.)

11 So it has a big impact at the local
12 government. Forget inside the Beltway. It's
13 outside the Beltway where most people live, and
14 that's where it counts.

15 And, third, I think what you said in the 9th
16 Report are going to be precedential, and to have
17 these kind of precedences established without this
18 ventilation of issues I think is sort of sad.

19 So, in summary, I think Dr. Olden set it on
20 the right track. He said this morning: You want a
21 sound science report. And my only comment is:
22 The objective is to do it right. Don't do it fast.

23 Thank you.

24 **DR. GOLDSTEIN:** Thank you,
25 Mr. Tozzi.

1 Our next speaker is Stuart Cagen of the
2 Shell Chemical Company.

3 **MR. CAGEN:** Thank you.

4 I'm Stuart Cagen with Shell Chemicals. I'm
5 going to be speaking today commenting on the RoC
6 process, several items, that the process right now
7 has always had the best of intentions. However,
8 the intentions have not been actualized. There's
9 some additional difficulties beyond that. I'll
10 recommend quickly some process improvements and
11 recommend some implications for today.

12 As has been stated already several times,
13 NTP, of course, has the best of intentions,
14 especially, as Dr. Olden has pointed out since he
15 came on board, that there should be a correct and
16 defendable list of decisions by NTP that is
17 comprehensive and is an open discussion of current
18 science and has consistent application of sound
19 criteria.

20 However, many of these intentions were not
21 actualized. Has there been comprehensive and open
22 discussion of current science? Many times the
23 quality of the background document was a poor
24 reflection of science or out of date, and the
25 process itself had a limited ability to respond to or

1 even hear public scientific review and comments.

2 In that regard, there's a limited response
3 of the NTP process to the scientific comments, little
4 evidence that comments are reviewed or considered.
5 There's no documentation of why they were
6 accepted or rejected.

7 The peer review system does not have
8 adequate time or structure for scientific
9 interchange. Many times the review is not -- those
10 involved are not experts in those particular
11 chemicals, and there's very much a time-compressed
12 process for that expertise to be brought forward,
13 and, as I mentioned, there's little time for scientific
14 interchange with the peer review body.

15 Some additional difficulties: I think when
16 something is called known, that it has a special,
17 additional hurdle on it. When is known known
18 needs to be a little bit better defined. And many
19 times, as Dr. Jameson mentioned, there's exposure
20 criteria. I'm not sure whether that's consistently
21 applied.

22 Some suggestions on process
23 improvements: Invite the public and other experts
24 in early in the process. The process should allow
25 for modification of background documents when new

1 information is presented. Allow time for expert
2 review and scientific interchange. Document
3 reasons for accepting or rejecting the science
4 arguments. And more attention to criteria. Clarify
5 criteria for listing and make sure they are
6 consistently applied.

7 A little bit more detail. This can be
8 manifested in the fact that the RG1 prepares a draft
9 document, makes its listing recommendation with
10 the rationale. RG2 at that time invites comments
11 on the background document from the public and
12 experts and sponsors the workshop. RG2 then
13 would revise the background document and listing
14 recommendation, as necessary, and provide rationale
15 for its recommendation.

16 RG2 then forwards the revised document
17 and recommendation to the Board of Scientific
18 Counselors well in advance of the subcommittee
19 meeting. The board then conducts a review meeting
20 with adequate time to consider complex
21 scientific issues and engages in meaningful
22 scientific interchange with the public presenters.

23 The report then goes to the NTP Director,
24 including a recommendation on the listing proposal
25 with explanation of how the recommendation fits in

1 with the criteria as well as explanations of how
2 major scientific issues were resolved. And the
3 Director, in consultation with the NTP Executive
4 Committee, formulates a listing recommendation and
5 forwards the report to the Secretary of HHS.

6 Path forward, I definitely agree. There
7 needs to be process improvements, and they should
8 be considered in a formal manner. Suggest a blue
9 ribbon panel with experts on the outside.

10 And with all due respect to Dr. Goldstein's
11 discussion about whether we should discuss
12 chemicals on the 9th Report, I think many of the
13 specific examples are very relevant to how the
14 process has some problems and can be improved
15 and, in particular, several compounds on the 9th
16 list -- chloroprene, isoprene, (inaudible), nickel,
17 ethylene oxide, and Dioxin, which you're going to
18 hear or have already heard some discussion of
19 today -- are very relevant to these particular
20 comments and problems. And, in fact, what is the
21 rush? I think those, in particular, should be
22 reconsidered with the new and improved process.

23 Thank you.

24 DR. GOLDSTEIN: Thank you, Dr.
25 Cagen.

1 Our next speaker is Philip Leber, who is
2 speaking on behalf of Jim McGraw from the
3 International Institute of Synthetic Rubber
4 Producers.

5 **MR. LEBER:** Thank you very much,
6 Mr. Chairman.

7 Mr. Jim McGraw, who is the officer in the
8 International Institute for Synthetic Rubber
9 Producers, had prepared a presentation for
10 September and was not able to give it, so he asked
11 me to do so. I'm from the Good Year Chemical
12 Company and President of the Isoprene Toxicology
13 Committee within that organization, so he asked me
14 if I would make these presentations.

15 According to the Chair's request, I'm trying
16 to speak as generically as I can, but I think it's
17 illustrative to give some specific examples to lend
18 credence to the generic points to be made.

19 First of all, the first point I'd like to make
20 is that the people at IISRP and industry groups
21 have a very vested interest in these chemicals. We
22 consider ourselves major stakeholders from not only
23 economic perspectives but also from health, safety,
24 and environmental. And I was pleased, also, to
25 hear Dr. Olden use the term partnership as it

1 relates to the overall process.

2 We certainly have sponsored a significant
3 amount of research with several of the monomers
4 used in these rubber products. We all have MSPS's
5 and some substantial product literature that deals
6 with health and safety. Nobody, I don't think, has
7 more experience in terms of the uses and the
8 potentials and, subsequently, the potential exposure
9 scenarios that may occur related to these products.

10 Finally, we do have a specific toxicology
11 committee to address -- keep up with the literature
12 and try to provide comments when the opportunity
13 avails itself.

14 So I'm going to use isoprene as sort of my
15 prototype here of a situation that needs comment.
16 Back in '97, the NTP had a bioassay report which
17 indicated that there were three major tumor types
18 induced in rats and that they indicated that with all of
19 these tumors, there was an increase in the
20 benign variety.

21 However, the NTP went from the benign
22 increase to, quote, clear evidence based on these
23 incidences. It was acknowledged that both
24 testicular and kidney tumors were all benign, but
25 then it indicated that the mammary tumors were,

1 quote, neoplasms, and when you look at the table
2 within the report, it says, quote, benign or
3 malignant increases. Finally, the report indicated
4 that 3,700 people were potentially exposed to
5 isoprene in occupational settings.

6 Now, with regards to the evidence on
7 cancer, the text nowhere -- if you read the text
8 only, nowhere did it mention that all the increases
9 in tumors were of the benign variety. This is
10 important because the criteria for clear evidence,
11 one of them is there is an increase in malignant
12 tumors and then a second criteria is an increase in
13 the combination of benign and malignant tumors,
14 and there was a third, but nowhere is there an
15 increase in benign tumors only as a criteria, and,
16 nevertheless, the clear evidence was assigned.

17 Okay. On the third point, significant
18 exposed populations, and when I saw the figure
19 3,700 people, worker population, exposed, I
20 thought, now, this is going to be an easy one, a
21 noncontentious issue. We can work this out with
22 NTP.

23 So we did a survey of all our member
24 companies in the industry, and there was only 325
25 people who were employed in these environments,

1 either monomer or polymer environments.

2 So since we didn't know the definition of
3 what a significant number of exposure meant, we
4 went further and said: Maybe 325 people are being
5 exposed to very high levels. That then becomes a
6 significant number.

7 So we went further and we looked at the
8 workplace areas and found that 91 percent of all the
9 air exposures, PWA's, were less than one part
10 per million. 99 percent were less than 10 parts per
11 million, very low occupational exposure.

12 Then, finally, it was mentioned in the
13 document that most exposures were related to
14 residual monomer isoprene coming out, leaching
15 out, migrating from the polymers. So we went to
16 one of the final steps, and we looked at the
17 monomer residues in these polymers, and all of the
18 polymers that we looked at had less than 40 parts
19 per billion levels of monomer remaining.

20 So the point is that there just is virtually
21 no opportunity for consumer or other worker
22 exposure coming from these polymer residues. And,
23 overall, I would interpret that, anyhow, to probably
24 conclude that there is not a significant number of
25 exposed folks in the United States.

1 To summarize, the reports' texts are
2 selective in their discussion of the tox data
3 allegedly supporting the clear evidence. And when
4 you use terms like benign or malignant, if you look
5 deeper into the report and look at the tables, the
6 benign numbers and the benign or malignant
7 numbers are the same, meaning there is no increase
8 in malignant tumors, but when you read that kind of
9 text, you're led to believe something else. The
10 second point, exposure data demonstrates that there
11 is no significant exposure to isoprene in the US, so
12 the criterion were not met.

13 So, very broadly, I think the situation was
14 this. We offered NTP written comments and these
15 data on the worker exposure, and there was no
16 changes in the draft background document. We
17 then gave public comment at the Board of Scientific
18 Counselors orally, and what happened was, and this
19 is typical, you get an opportunity to speak for five
20 minutes. You sit down. There's no questions.
21 Nobody from the Board of Scientific Counselors
22 says, "NTP, are these new numbers correct or is
23 there a misunderstanding?" There's no dialogue.
24 There's no attempt to resolve differences.

25 And so what happens, no discussion.

1 Somebody makes a motion: "Let's vote on this
2 report as it now stands." People vote and end of
3 discussion, and this is how errors are incorporated
4 and are retained in these types of reports.

5 And I just might -- I'm very willing to be
6 called wrong. I get a lot of that from my kids, so
7 I'm somewhat used to it. I don't mind being told
8 that, "Leber, your 325 numbers there can be
9 updated. We've got recent information," and I say
10 "Okay. Let's talk," but there is no opportunity. And
11 if there's one message I think that we would like to
12 get across this week, today and tomorrow, is that
13 we give information. We put a lot of effort into
14 our comments, but there is no evidence that the
15 comments are considered.

16 Thank you.

17 **DR. GOLDSTEIN:** Thank you,
18 Mr. Leber.

19 Our next speaker is Dr. Emanuel Rubin
20 from Thomas Jefferson University.

21 **DR. RUBIN:** Thank you, Mr.
22 Chairman, members of the panel. I'm Emanuel
23 Rubin. I'm Chairman of the Department of
24 Pathology, Anatomy & Cell Biology at Jefferson
25 Medical College at Thomas Jefferson University in

1 Philadelphia. I've had a long-standing interest in
2 the adverse effects of environmental agents, and
3 I've been well funded by the NIH for over 30
4 years.

5 I previously provided written and oral
6 testimony to NTP at the request of the Beverage
7 Alcohol Industry in which I contested NTP's
8 proposed listing of alcoholic beverage consumption as
9 a known human carcinogen.

10 With regard to my oral presentation, I was
11 disappointed that after vigorous and even fractious
12 discussion, the Board of Scientific Counselors
13 Report on Carcinogens Subcommittee voted to
14 recommend this proposed listing. It is not my
15 purpose to discuss the specific errors underlying
16 this decision but, rather, to register my concern
17 about the process or lack thereof by which NTP
18 reached its decision.

19 Specifically, I wish to bring to your
20 attention three items: The scope of the review, the
21 decision-making process, and the need for more
22 transparent and public deliberations.

23 Let me go through the history a little. In
24 November 1998, I sent a letter to Dr. Larry Hart in
25 which I requested a number of items. I asked for

1 the selection criteria for literature citations since
2 only less than 20 percent of the 800 studies
3 identified by NTP were cited in its background
4 document.

5 I also requested information relating to the
6 criteria used by NTP for determining the causal
7 effect in this particular instance. Finally, I
8 requested abstracts of the papers identified by NTP.
9 None of my requests were honored, and this critical
10 information has yet to be released to the public.

11 Thus, the overall criteria for review
12 employed by NTP remain obscure. Moreover, other
13 than the discussion by the board, the public had no
14 opportunity to hear the deliberations of NTP's
15 various subcommittees. This lack of transparency
16 does not inspire confidence in decisions made by
17 the NTP.

18 Now, in March 1998, I filed comments with
19 Dr. Jameson of the NTP Report on Carcinogens
20 Program. In these communications, I emphasized a
21 number of items: The negative eugenicity studies
22 of alcohol, the failure to produce cancer by
23 administering ethanol to experimental animals, the
24 enormous differences between moderate alcohol
25 consumption and the various maladies associated

1 with alcohol abuse, and the importance of using
2 commonly accepted causation criteria, also known
3 as the Hill criteria, in evaluating the epidemiologic
4 evidence in this case. There was no adequate
5 response either to my written or to my oral
6 comments.

7 Now, neither the review panels nor the
8 Board of Scientific Counselors gave adequate
9 consideration even to the most important causation
10 criteria, which include strengthen (inaudible),
11 consistency, biological plausibility, dose response,
12 and exclusion of confounding factors.

13 For example, despite the fact that the
14 preamble to the Report on Carcinogens states that
15 dose response should be considered when
16 evaluating potential carcinogens, there is no
17 evidence that any attention was paid to this matter.

18 This omission is particularly relevant to the
19 issue of alcoholic beverages in which a high dose
20 actually defines a serious disease complex, namely
21 chronic alcoholism. This disorder introduces a wide
22 variety of potential confoundings. For example,
23 nutrition, metabolic changes, drug ingestion,
24 bacterial and viral infections, and concurrent
25 disease of many organs.

1 Let me just give you one example. The
2 NTP report actually accepts the original IARC report
3 on the supposed carcinogenicity of alcoholic
4 beverages, which they accept alcohol as a
5 carcinogen for the liver. All of those studies were
6 done without controlling for the most important
7 liver carcinogens in the world, namely Hepatitis B
8 and Hepatitis C.

9 Since the IARC report, it has been
10 demonstrated that there's probably 10 times the
11 incidence of Hepatitis C in alcoholics as in the
12 general population. So, clearly, this type of listing
13 is totally questionable, and far, far more studies
14 would have to be done to attribute any cancer of
15 the liver to alcohol rather than to Hepatitis B and
16 Hepatitis C.

17 Now, in December 1998, I testified orally
18 before the Board of Scientific Counselors Report on
19 Carcinogen Subcommittee and I supplied additional
20 written comments. With respect to my oral
21 testimony, the time allotted for my presentation
22 regarding alcoholic beverages which are consumed
23 in moderation by over 100 million Americans was no
24 different from the time accorded exotic industrial
25 chemicals.

1 The time constraints further precluded an
2 informed discussion of a topic that has the
3 potential for a significant negative impact on
4 public health. Moderate alcohol consumption has
5 been demonstrated to be beneficial in terms of
6 protection against coronary artery disease, stroke,
7 and osteoporosis, and overall mortality of social
8 drinkers is lower than that of abstainers.

9 Thus, think of the consequences. An
10 erroneous listing of alcoholic beverages as a known
11 human carcinogen is not simply an academic matter
12 but may have serious, albeit unintended,
13 consequences for public health.

14 Given the flaws in its review of alcoholic
15 beverage consumption, NTP should withhold the
16 decision on this nomination and should consider
17 some of the following recommendations:

18 One, NTP should adopt rigorous criteria for
19 review of epidemiologic evidence and should
20 disseminate this information to the public. Two,
21 the information upon which NTP relies together with
22 records of internal deliberations should be available
23 to the public.

24 Three, NTP should publicly respond to
25 written and oral comments as part of the

1 decision-making process. Four, the time allotted
2 for oral presentations and public discussion by the
3 committee should be proportional to the importance
4 of the topic and sufficient to facilitate scientific
5 interchange.

6 Thank you for the opportunity of
7 addressing this committee. I hope that my
8 comments will be helpful in improving the decision-
9 making process of NTP.

10 DR. GOLDSTEIN: Thank you,
11 Dr. Rubin.

12 Our next speaker is Dr. Peter Infante from
13 the Occupational Safety and Health Administration.

14 DR. INFANTE: Thank you very
15 much.

16 The NTP Report on Carcinogens is of vital
17 importance to citizens of the US as well as
18 governmental research and regulatory agencies. It is
19 the only governmental program in the US specifically
20 designed to inform the public about the occupational
21 and environmental causes of cancer.

22 OSHA specifically relies on the evaluations of
23 the NTP Report on Carcinogens. Under our Hazard
24 Communication Standard, the listing of a substance or
25 process in the Report is one tool

1 that's available to assist manufacturers in hazard
2 determination.

3 The Hazard Communication Standard
4 contains specific requirements that relate to the
5 information that must be provided to workers through
6 warning labels and material safety data sheets. These
7 warnings have the potential to inform millions of
8 workers about hazardous exposures of which they
9 might not otherwise be aware.

10 This information can result in more effective
11 control of the work practices to reduce exposure to
12 carcinogens on the job, particularly in exposure
13 situations where adequate workplace standards have
14 not yet been promulgated. My recommendation, in
15 general, is that more substances known to be
16 carcinogenic in humans or experimental animals be
17 added to the report.

18 An evaluation that leads to informing
19 workers about cancer hazards on the job is also an
20 environmental justice issue. The majority of
21 substances or exposure situations known to cause
22 cancer in humans have been identified by studying
23 blue-collar workers.

24 This legacy of identifying cancer-causing
25 substances by studying blue-collar workers simply is

1 a reflection of the relatively high exposure levels to
2 carcinogens that these workers disproportionately
3 experience.

4 Now responses to issues raised in the
5 NIEHS press release that announced the September
6 15th meeting. Industry representatives have asked
7 that their experts be involved earlier in the process
8 and have repeated opportunities to comment and
9 critique the data upon which decisions are made.

10 As is the case with IARC, scientists
11 representing those with economic interests in the
12 outcome of the cancer evaluations should not be
13 permitted to participate in the evaluations. The NTP
14 is a governmental scientific program that bears the
15 responsibility to make decisions on
16 carcinogenicity based on scientific data.

17 The current NTP review process allows for
18 all perspectives to be presented and considered. In
19 the interest of public health and the environment,
20 these evaluations cannot be encumbered with views
21 that are determined by economic rather than
22 scientific considerations.

23 Also, reviews of chemicals by others,
24 whether they represent industry or government,
25 should not be placed before the NTP. The NTP has

1 the obligation to review the data, not the opinions
2 of others, when it comes to evaluating chemicals
3 for carcinogenicity. This is also the policy of
4 IARC.

5 Now, should the NTP expand its database
6 for evaluation of studies to include unpublished
7 reports? Very emphatically, no. Unpublished reports
8 are not peer reviewed, and they should not
9 be included in these important cancer evaluation.
10 Furthermore, published reports that are not peer
11 reviewed should not be considered in the NTP
12 evaluations.

13 Regarding where these meetings should be
14 held, I suggest that NTP do a pilot by holding a few
15 meetings in the DC area, and the agency can then
16 decide which place affords more greater range in
17 public participation.

18 Other issues for NTP to consider: It's my
19 understanding that the NTP is considering a transfer
20 of the Report on Carcinogens to the National
21 Academy of Sciences. This would be a grave
22 mistake. The NTP has a delegated responsibility to
23 complete these Reports. It is demonstrated that it
24 has the expertise and ability to produce the Report
25 and has invaluable experience in doing so. No

1 other organization in the United States has
2 demonstrated this experience.

3 The staff of scientists at the NTP has
4 contributed to this success, and the removal of the
5 process from the NTP would impair the quality of the
6 Report because of diminished NTP staff
7 participation.

8 NTP has developed a very good review
9 process. The National Academy does not have an
10 established standing committee that could develop
11 the Report in the manner in which the NTP
12 has accomplished its goal.

13 Furthermore, it may be difficult to
14 determine the affiliation of committee members that
15 the NAS would select to participate on the review
16 committees. This could result in conflict-of-interest
17 situations that would not be apparent to the public.
18 Thus, it is of paramount importance that the
19 program be maintained in the scientific environment
20 of the NTP.

21 The carcinogenicity portion of the
22 summaries for the substances listed in the Report
23 on Carcinogens is usually two short paragraphs.
24 Often these summaries are the only part that is
25 read by the public. For this reason, I recommend

1 that the cancer evaluation portion of the summaries
2 be expanded to perhaps three to four times the
3 current length so that the reader will have enough
4 information to understand the basis for the NTP
5 cancer designation.

6 This expanded summary, however, should
7 focus only on the categorization of the substance,
8 as is currently done, and should not include
9 information on cancer potency or risk management
10 issues.

11 I also recommend that the major studies
12 that are relied upon for the evaluation of the
13 carcinogenicity be maintained in the docket at the
14 NTP in North Carolina and be made available to
15 public members who may request these studies.

16 In its Reports on Carcinogens, the NTP has
17 not listed a number of substances or agents found
18 in the occupational setting or the environment that
19 IARC has already classified as human carcinogens
20 and for which workers are at an elevated risk of
21 exposure and the subsequent development of cancer.
22 I recommend that the NTP place the listing
23 of these substances on a fast track so that workers
24 and the general population will be informed of
25 these cancer hazards.

1 In addition, IARC has listed 13 industrial
2 processes or industrial exposure circumstances as
3 known human carcinogens. NTP has placed these
4 13 industrial processes in an Appendix to the 8th
5 Report and simply states that IARC cites these as
6 known human carcinogens.

7 If IARC can list these substances as known
8 human carcinogens, then why is it that the NTP can
9 only place them in an appendix and state that IARC
10 has listed them? If the NTP chooses not to list
11 these exposure circumstances, it needs to provide
12 the basis for their not being listed. In the interest of
13 public health, they should be listed.

14 If these exposure circumstances have
15 changed such that they are no longer carcinogenic,
16 a petition to NTP can be made to delist them. In
17 the interim, I recommend that all 13 of these
18 exposure circumstances be removed from the
19 Appendix of the 8th Report and be added to the list
20 of known human carcinogens.

21 In addition to these 13 industrial
22 processes, there are several mixtures that NTP has
23 not listed as known human carcinogens that IARC
24 has classified as Category 1, known human
25 carcinogens. And I recommend that these mixtures

1 also be listed, and I nominate them for listing. For
2 example, wood dust. There are over 600,000
3 workers exposed to wood dust in the United
4 States, and it would be beneficial to these workers
5 to have wood dust listed as a human carcinogen.

6 In the listing criteria for carcinogens on
7 .Page 2 of the 8th Report, it states that evidence of
8 carcinogenicity in laboratory animals can be
9 downgraded if, quote, there are compelling data
10 indicating that the agent acts through mechanisms
11 which do not operate in humans.

12 NTP needs to establish criteria for
13 downgrading evidence of carcinogenicity.
14 Hypotheses related to downgrading need to be
15 tested to determine the merit of arguments being
16 used for downgrading evidence. It is not
17 scientifically objective or defensible for the NTP to
18 downgrade on the basis of uncontested hypotheses.

19 Furthermore, the NTP needs to state
20 explicitly that it will also use mechanistic
21 information to upgrade a substance. IARC has used
22 mechanistic information to upgrade substances to
23 known human carcinogens when epidemiologic
24 studies of cancer mortality provided limited
25 evidence of carcinogenicity to humans.

1 Therefore, I recommend that the listing
2 criteria be more scientifically balanced and state
3 that the evidence of carcinogenicity can be upgraded
4 if there are compelling data indicating
5 that the agent acts through mechanisms which are
6 thought to be similar to those that operate in
7 humans.

8 Thank you.

9 **DR. GOLDSTEIN:** Our next speaker
10 is Adriana Oller of the Nickel Producers
11 Environmental Research Association.

12 **DR. OLLER:** My name is Adriana
13 Oller, and I'm here representing NiPERA, which is
14 the Research Association for the Nickel Producers
15 (inaudible).

16 I would like to thank NTP for organizing
17 this meeting and giving me an opportunity to
18 illustrate some of the cause of the problems with
19 the RoC listing process as they apply to nickel
20 compounds.

21 In 1998, NTP announced that nickel metal
22 and all nickel compounds were considered for
23 listing as known human carcinogens in the 9th RoC.
24 Now, this meant an upgrade for a few nickel
25 compounds, but it was the first-time listing for the

1 majority of nickel compounds, which are in the
2 hundreds. The NTP Notices never distinguished
3 between these two groups.

4 The RoC Background Document was
5 prepared on all nickel compounds and public
6 comments submitted had indicated that the analysis
7 should be made for the different groups of nickel
8 compounds. This document became available for
9 commenting November of '98, and to put it politely,
10 again, the scientific quality left much to be desired,
11 and I'll be happy to give you examples of errors in
12 the document, data sets that were not considered
13 and biased analysis. Unfortunately, as mentioned
14 before, the reviews done by the groups 1 and 2
15 have already been made on this document that it
16 was not a (inaudible) document.

17 During a period of three weeks, the nickel
18 industry prepared lengthy and detailed comments on
19 this document and submitted them to NTP, and the
20 comments pointed out errors and deficiencies in the
21 document and also offered scientifically supportable
22 carcinogenicity assessments for the various nickel
23 species.

24 These comments were made available to the
25 Board of Scientific Counselors Subcommittee the

1 following week, which was Thanksgiving week,
2 allowing them very little time to review these
3 comments in preparation for their December
4 meeting.

5 At the Subcommittee meeting, the nickel
6 industry presenter was allowed just five minutes to
7 explain what was wrong with the Background
8 Document. This is to summarize 20 pages of
9 single-spaced comments and appendices and to
10 summarize the very extensive human, animal, and
11 mechanistic database for each group of nickel
12 compounds.

13 The five-minute limit for presentation was
14 particularly frustrating since it was clear that the
15 Subcommittee members had not had a chance to
16 review and be aware of the issues that were raised
17 in those comments. During the brief discussion
18 that followed, industry scientists were not allowed
19 to address any of the questions raised by the
20 Subcommittee members.

21 And, again, I can give you examples of
22 some of the issues that were raised but were
23 answered incorrectly or dismissed without
24 discussion. It was also clear that the Subcommittee
25 members did not know that metallic nickel was no

1 longer considered for an upgrade because it had
2 been removed earlier in the year from consideration
3 or that soluble nickel compounds had never been
4 listed before, and, therefore, this was the first time
5 they were going to be included in the list.

6 The change for metallic nickel was clarified
7 at the Subcommittee meeting, but the first-time
8 listing for soluble compounds was never mentioned.
9 And, indeed, in press reports that I've written, it's
10 mentioned -- it's written that nickel compounds
11 were just considered for upgrade.

12 So just to summarize the points (inaudible),
13 the confusing listing in the Federal Registry and
14 then to the BSC members as to how different nickel
15 compounds were considered. It was a poor quality
16 of the draft Background Document, which can
17 definitely benefit experts, part of the process of
18 writing this document and be involved early on in
19 the process and the fact that it was never revised
20 to respond to comments or correct errors.

21 There was a lack of timely and meaningful
22 opportunity for public comment, the lack of NTP
23 response to public comment, and the token public
24 participation at the meeting, which five minutes is
25 not a substitute for the lack of consideration of the

1 comments.

2 The fact that there was limited knowledge
3 of nickel-related epidemiology and toxicology by the
4 presenters and the BSC members, who, as I
5 mentioned before, are asked to do too much in too
6 little time. The superficial, confused, and hurried
7 discussions at the meeting where independent peer
8 review is supposed to occur and, finally, the failure
9 of the different groups that make recommendations
10 to explain the scientific basis for these listings and
11 how they fit the criteria that NTP is supposed to
12 apply.

13 And these are all things that I think were
14 mentioned for other compounds and, you know,
15 definitely can be corrected easily. And I think the
16 nickel industry has worked together with other
17 groups in making recommendations for
18 improvements, and some of them have been
19 presented already by Stuart Cagen and further were
20 presented by Phil Leber, and we'll be glad to work
21 with NTP on this.

22 Finally, the next slide and last slide, I
23 would like to illustrate how the procedural
24 differences can affect results. I would like to
25 compare two carcinogenicity assessments that were

1 conducted in parallel. One was the one conducted
2 by NTP on all nickel compounds, and the other one,
3 which was conducted for soluble nickel compounds,
4 was sponsored by US EPA, Health Canada, and
5 nickel industry.

6 This assessment was done by TERA, which
7 is Toxicology Excellence for Risk Assessment, an
8 independent group, and they were conducted at the
9 same time and looking at the same database.

10 The first big difference is that while the
11 document prepared by NTP, as I said, had certain
12 deficiencies and superficial data presentation, the
13 document prepared by TERA had exhausted data and
14 analysis. Both asked for public comment, but while
15 NTP did not respond to these comments, nor did
16 they incorporate the comments into the document,
17 TERA responded in writing to the main comments
18 raised by regulatory agencies as well as industry
19 and incorporated those comments into the
20 document.

21 Both had peer review meetings, and as you
22 can see, they were almost at the same time.
23 However, while NTP took less than two hours for all
24 nickel compounds, the TERA independent review
25 meeting took two days just for soluble nickel

1 compounds.

2 Public participation in NTP was limited to
3 five minutes presentation only. In the TERA peer
4 review panel, presentations by industry
5 representatives were allowed and participation was
6 sought for their expertise during the discussions.

7 The conclusions, then, could not be more
8 different. NTP concluded all nickel compounds
9 should be listed as known human carcinogens.
10 TERA concluded that carcinogenicity of soluble
11 nickel compound by inhalation and oral routes of
12 exposure cannot be determined, and this was based
13 on the fact that even though epidemiological data
14 demonstrated an association with exposures to
15 soluble nickel compounds, this was in the presence
16 of other nickel compounds, more insoluble, clear
17 carcinogenic compounds, and this association was
18 not supported by all the negative animal, inhalation,
19 and foreign studies and the mechanistic data. So
20 based on the conclusions that TERA reached for
21 soluble nickel compounds, this group of compounds
22 would not have fit the criteria for listing in the 9th
23 list.

24 So I think that NTP now being aware of the
25 problems with the process as they relate to those

1 compounds, we hope that this carcinogenicity
2 assessment will be reconsidered under an improved
3 process.

4 Thank you very much.

5 DR. GOLDSTEIN: Thank you,
6 Dr. Oller.

7 Our next speaker is Peter Lurie of the
8 Public Citizens Health Risk Group.

9 MR. LURIE: Good morning. Let
10 me offer a small correction. That's Public Citizens
11 Health Research Group. We're in the business of
12 minimizing risk, so I just wanted to correct that.

13 I want to start off with two historical
14 notes. First is a very nice, I believe, bit from the
15 New York Times reprinted (inaudible) talking about
16 the unfortunate death of Dr. David Rall. And he, as
17 all of you know, was former Head of NTP and was a
18 tireless advocate for reducing consumer exposure to
19 environmental and occupational chemicals, someone
20 who understood the importance of animal
21 carcinogenicity data.

22 I think there would be no greater tribute to
23 the work that he did and his legacy for this report
24 to continue to come out in an expeditious fashion,
25 as clearly written as it often is, publicly available

1 and so forth for the reasons that I will go on to
2 outline.

3 The second historical note is that in
4 preparing for my talk here, I took the occasion to
5 review some of the documents related to the 1995
6 reconsideration of the listing criteria for the annual
7 report -- or biennial report.

8 And I also compare it to the recent letter
9 from industry complaining about the problems they
10 see in the process for arriving at a listing in the
11 review of carcinogens, and what struck me was how
12 numbingly competitive the arguments offered in the
13 recent letter were to those same ones offered in
14 1995.

15 We heard again in this recent letter
16 complaints about the criteria. For listing, that is.
17 Much of that has been reiterated again in people's
18 comments today and no doubt will be over and over
19 again for the next couple of days.

20 We've heard about the importance of risk
21 assessment. We've heard about the importance of
22 considering mechanisms of action again, as
23 Dr. Infante pointed out in a kind of one-sided
24 direction for the purpose of downgrading, but
25 usually not for the purpose of upgrading.

1 We heard about the problems back in 1995
2 of introducing non-peer-reviewed data, and we saw
3 the same sorts of delaying tactics that are now
4 being recommended by the industry. How ironic
5 this is, complaints about process from industries
6 that are usually complaining about red tape,
7 arguments for transparency from industries that are
8 usually invoking trade secret exceptions to prevent
9 consumers from getting important information about
10 drugs and toxic chemicals. How unusual this is.

11 And as to the question of why the rush put
12 forward by Mr. Tozzi, well, (A), it's important, but
13 there's a simpler reason. It's the law. That's why
14 the rush. Every two years there has to be data to
15 be presented to show -- in fact, by and large, the
16 agency has not been consistent with the law. Very
17 often it's taken three years, not two. Why the
18 rush? Because it's the law. In addition, as I
19 pointed out, this is very useful information to
20 consumers.

21 One of the reasons that the reports do not
22 come out at the frequency required by law is
23 because, as no one has so far pointed out, very
24 often the report gets tied up in lawsuits from the
25 industry. First, there was dichlorobenzene. After

1 that, it was fibrous gloss, and now we're talking
2 about Dioxin.

3 These are some of the reasons that the
4 report keeps getting held up, and that's the reason
5 for the agency, I think, to get ahead of the
6 (inaudible), and so far have, and maybe we'll see
7 the report on time this time. And, again, as I've
8 mentioned, questioning of animal evidence was a
9 feature of the 1995 arguments and we're hearing it
10 all again.

11 Why is this report so necessary? Well, as
12 has been pointed out, it's the basis for regulation.
13 It's the basis for regulation by FDA, by OSHA, by
14 EPA, by the Agriculture Department, Consumer
15 Product Safety Commission. That's why it's needed.
16 Much of your objections -- let's be honest about
17 this -- is about the industry's efforts to avoid
18 regulation. That's what the objection is.

19 The second reason that the report is so
20 important is because many consumers, I believe,
21 labor under the misconception that, as the
22 expression goes in the popular culture, "Everything
23 gives you cancer," but nothing can be further from
24 the truth. Actually, it's a very limited number of
25 compounds that cause cancer, limited enough to

1 end up in a rather small book, as the report turns
2 out to be. That, I think, is reassuring to the
3 public, and so I think that that's sort of another
4 reason why it's such an important report.

5 There is substantial opportunity for public
6 input. As was pointed out by Dr. Jameson, there
7 are at least three opportunities for public input.
8 One can write a letter whenever one wants to. I
9 think the least of the problems faced by the NTP
10 has been the lack of opportunity for industry to
11 provide input. In fact, what has mostly happened
12 is that there's so much opportunity that it's led to
13 delays or particular lawsuits, and, as a result, often
14 the report has not been timely.

15 Now, Dr. Goldstein started off by asking
16 the speakers here not to speak to specific chemical
17 compounds, but, in fact, most of the industry has
18 been unable to resist this. Instead, we've got a
19 plethora of comments that amount to retrying
20 decisions that the industry is unhappy with. We've
21 heard about isoprene, Dioxin, alcoholic beverages,
22 nickel, and there will be more to come in the next
23 couple of days.

24 The fact is that these are complaints about
25 outcome that are masqueraded as complaints about

1 process. Sure there's some changes needed in the
2 process. The idea of moving the meetings to DC is
3 a good idea, especially for those of us on the Red
4 Line, but the fact of the matter is that, by and
5 large, the process is sound. The strength of
6 industry's opposition is the best evidence for the
7 usefulness of this report.

8 Thank you.

9 DR. GOLDSTEIN: Thank you, Mr.
10 Lurie.

11 The next speaker is Ellen Silbergeld. I
12 don't see her in the audience. I think that perhaps
13 she isn't here yet. We're a little early. I think
14 that perhaps the best way to deal with this is to
15 try to keep the schedule so that people who were
16 expecting to hear others or to be at certain points
17 would be able to keep to this schedule and know
18 where others are speaking.

19 So what I'm going to suggest we do is that
20 we take our 20-minute break now, reconvene at
21 11:30 rather than 11:45. If Dr. Silbergeld is here by
22 then, we'll start with her. If not, we'll just move
23 ahead. So until 11:30.

24 (WHEREUPON, a break was taken from 11:10 a.m. to
25 11:30 a.m.)

1 **DR. GOLDSTEIN:** Dr. Silbergeld,
2 unfortunately, couldn't be here. She has her written
3 comments, which will be part of the record.

4 I said this morning we're going to try a
5 little experiment here. We're trying to focus in on
6 some of the comments. Again, I would hope that
7 we could, by this, help illuminate some of the
8 issues.

9 We're asking the NTP folks to be listening.
10 Obviously, I think we're all familiar enough with
11 governmental processes that we're not asking for an
12 immediate response from NTP, yes or no, right now
13 on whatever idea they've heard. This is more to
14 put some breadth and some depth into some of
15 these ideas.

16 Let me start by first asking the NTP folks,
17 George Lucier, Bill, if there's anything you want to
18 say in terms of clarification.

19 **DR. LUCIER:** I'm glad to be part
20 of the experiment, Bernie. As I will throughout the
21 course of this meeting, I'll make my comments
22 relatively brief, and just issues of clarification is
23 what I'll deal with.

24 One of the things that came up this
25 morning was the composition of the Board of

1 Scientific Counselors and the external review group
2 and sort of the breadth of expertise on those
3 boards.

4 The intent, and I think it's pretty well
5 balanced at this time, is to have people who are
6 knowledgeable about animal cancer studies, have
7 people that are knowledgeable about mechanistic
8 studies, (inaudible) chromosomal changes and so
9 forth, and have people who are traditional
10 epidemiologists on the board as well. Right now I
11 think there are 12 people on the board, and it's
12 pretty well divided up into those categories.

13 I should also point out that some of the
14 board members would have a history affiliation that
15 they formerly are dealing as an independent
16 scientist for their activities on the Board of
17 Scientific Counselors, not as a representative of any
18 particular industry. So everyone functions as an
19 independent scientist on the Board of Scientific
20 Counselors.

21 The composition of the review groups, RG1
22 and RG 2, also involve people in those three major
23 categories: Mechanistic expertise, animal
24 toxicology expertise, and epidemiologic expertise.

25 Thank you. Anything else you think I

1 should --

2 **DR. GOLDSTEIN:** Well, I've got,
3 actually, a question that I think maybe -- I should
4 point this out. I really haven't been part of this
5 process except way back when sitting with the EPA
6 part of it about 15 years ago, so I'm not really that
7 familiar with it. I've been listening to it.

8 One of the things that I thought I heard
9 some of the commenters say was that the Board of
10 Scientific Counselors, in their voting, votes to
11 accept the background document. There's been a
12 fair amount of criticism of the background document
13 not always getting its facts right.

14 There are certainly EPA processes, other
15 government processes, the Clean Air Scientific
16 Advisory Committee, which I served on, where we
17 really feel, as part of the process, that we've got
18 to make sure that EPA gets its document correct.

19 Let me ask you whether or not the board is
20 being asked to vote up or down on the
21 recommendation in the document or on the entire
22 document itself. And, obviously, the key point is
23 that a board member could sit and listen to a
24 comment and say, "I agree with the comment. They
25 got that wrong in the document, but I still think

1 that the overall position is correct in terms of
2 where this is as a carcinogen."

3 **DR. LUCIER:** The vote is on the
4 level of carcinogenicity, either known or reasonably
5 anticipated to be a human carcinogen, or vote to
6 delist in some circumstances, if that's the
7 consideration under action. It's not a vote to
8 accept the background document. We've clearly had
9 cases where different review groups have voted
10 differently on the same background document, so
11 that's not the case.

12 So it's a vote on whether or not a
13 substance or mixture should be listed as known or
14 reasonably anticipated to be a carcinogen or
15 delisted, not on the report itself.

16 **DR. GOLDSTEIN:** Let me then
17 move this to –

18 **DR. FREDERICK:** Let me say
19 something on that specific point. Speaking as a
20 member of the board, my votes -- and I think my
21 votes are probably representative of other members.
22 My votes on the issue at hand, which is exactly
23 what George said, it's a recommendation to Ken
24 Olden, who actually is the ultimate decision maker
25 on the list that goes in to Dr. (inaudible), it's a

1 recommendation on what to do on the motion at
2 hand. It is definitely not an endorsement of the
3 booklet, per se. Happens to be a background
4 document.

5 The actual votes that are taken are
6 informed by the booklet from NTP, who have had
7 the different -- I'll have to say that I've dealt
8 personally. They vary sometimes. But it's informed
9 by that booklet, by external information that's
10 submitted in the course of the year prior to the
11 meeting, all written stuff, and I read every page
12 that's submitted, as well as the verbal comments,
13 as well as other peer-viewed scientific information
14 that happens to be in my purview as a professional.

15 So it's a fully informed document or
16 decision with regard to the body of information at
17 hand. It's a scientific recommendation -- that's all
18 -- on the issue of whether we should upgrade or
19 not, and I think we could get hung up about this,
20 that, or another phrase in one of these documents.
21 That is not the point. It's a scientific evaluation
22 on the overall body of information.

23 **DR. GOLDSTEIN:** That doesn't
24 mean that NTP couldn't change this around
25 completely and go over to an EPA process?

1 Frank, do you want to speak specifically to
2 that comment?

3 DR. MIRER: Yes. Absolutely. We
4 are, as reviewers --

5 DR. GOLDSTEIN: Let me say that
6 Dr. Mirer is a member of the BSC.

7 DR. MIRER: Yeah. As reviewers,
8 we're asked to critique the document itself, and if
9 you want to make a recommendation, we provide a
10 rationale -- for the primary and second review,
11 provide a rationale for their recommendation. I'd
12 like to believe it was taken into account. There's a
13 lot of -- five to ten pages of commentary in some
14 of my reviews.

15 So we do critique the document, and we
16 do -- or, at least, I read the material that is sent out
17 by the participants. There's no rule that they
18 have to give us the night before, and some seem to
19 get it to us two or three months before the actual
20 review occurs. At least, I take it into account in
21 doing my review, but we do critique the document.

22 DR. GOLDSTEIN: Thanks.

23 Before we get into comment time, we've
24 asked Dr. Goldman and Dr. Frederick to look for
25 themes and think of where they may be some issues

1 that we could particularly highlight during this
2 discussion section. So, Lynn?

3 **DR. GOLDMAN:** Yeah. I've heard
4 a few things, and one that I think is probably a
5 good starting point is, actually, the issues of the
6 process, of the peer review by the Board of
7 Scientific Counselors.

8 I'm a new member of the board, and,
9 actually, in my earlier life was part of the
10 Executive Committee for the NTP and, in fact,
11 chaired it during the time when these processes for
12 peer review were put in place. And I guess, you
13 know, no good deed goes unpunished. Now I have to
14 participate in this process.

15 But the -- I think that -- and there's been a
16 lot of email traffic among board members about
17 some of these same issues, and one thing I'm
18 encouraged by is some of the themes that are
19 pulled forward that are some things that board
20 members are concerned about, frankly, some of
21 them are kind of going the opposite direction, but I
22 think that they're issues that really need to be
23 talked through here very carefully.

24 And one has to do with, really, how
25 information is brought forward to the board and

1 discussed at the peer review meetings. There is a
2 tremendous volume, and what Dr. Frederick said, I
3 think that's shared by all the members, and that is
4 that there's a tremendous volume of information
5 that's provided in advance that because of the
6 earlier comment processes gives a very good flavor
7 for the views of scientists coming at the issues
8 from different perspectives, not just the NTP and
9 the other government scientists but, also, those
10 who have commented from industry and elsewhere.
11 And the members do read all of that material.

12 And hearing the discussion this morning, I
13 almost wish that there were tests so that people
14 could feel some faith or trust that that material has
15 actually been read by the principal reviewers
16 because those who are assigned with those
17 reviewing responsibilities, from what I can see, take
18 those responsibilities very seriously and feel that
19 it's a very difficult and serious task being involved
20 in that.

21 And there is frustration, though, and I
22 think I've heard it here, too, and I think NIEHS is
23 already trying to take steps to fix this with -- when
24 there are last-minute materials that want to be
25 provided, that perhaps, you know, there's new

1 information or maybe people feel they just want to
2 say it again to make sure that they've been heard,
3 and there certainly is a lot of that in this process,
4 that that will come sometimes just within a matter
5 of a couple of days of a meeting.

6 And even if it's something that is a
7 reiteration, you have to read it to make sure that
8 that's what it is, and that's a lot of last-minute
9 effort. And so -- and I think that that's already --
10 there's already a decision on the part of NIEHS and
11 the NTP to change that process so that there isn't
12 the possibility of getting a barrage of last-minute
13 material to wade through, and that's a good thing.

14 And I think then what has happened
15 sometimes in some of these public meetings is that,
16 you know, you see people just throwing their hands
17 up in frustration about having this huge pile of
18 material to read on an airplane or something and --
19 but, you know, I think people do agree that rarely
20 has there been anything truly new in that and that
21 that could have been done in advance and that that
22 would probably be a better process.

23 The other thing is that the nature of the
24 oral interactions that happen in those meetings and
25 if -- you know, that in these formal oral

1 presentations that are given that are often, really, a
2 reiteration of the materials that were provided in
3 advance of the earlier comments and so are issues
4 that have already been in much more detail because
5 reading is a much more efficient way to get
6 information than listening and so in much more
7 detail have been heard.

8 In sake of fairness, to make sure people
9 are heard, that's a good thing, but on the other
10 hand, some of the members of the board sometimes
11 feel that then there's not very much time to
12 actually have scientific exchange and discussion
13 because time is spent going -- you know, listening
14 -- actually listening, and that's not maybe the best
15 engagement of the brains of the people around the
16 table, and that kind of -- so something, maybe, is
17 lost in that.

18 And I guess the other thing that I've heard,
19 and Dr. Frederick might want to, you know, enlarge
20 on this a little bit, is that sometimes members of
21 the Subcommittee would like to see more back-and-
22 forth exchange between the scientists who are
23 coming in with points and the scientists from the
24 NTP, but on the other hand, they don't want to get
25 into kind of a, you know, debate of free-for-all.

1 So how do you engage those meetings so
2 that there can be some exchange without it being
3 just a matter of, say, one party being on attack and
4 the other one on the defensive, which isn't
5 necessarily the way good science really happens.
6 And so these are not easy issues at all, but, you
7 know, those are some issues that could be involved in
8 terms of improving the process.

9 The second issue that I've heard very
10 clearly and I think at some point would be worth
11 talking about is, really, a whole suite of concerns
12 related to dose and whether the exposures in the
13 population should have any bearing on listing,
14 whether dose-related effects should have any
15 bearing on the classification, and there are a
16 number of people who made comments kind of
17 around that issue.

18 Another one having to do with the process
19 of using data other than direct human studies for
20 making that determination of whether a substance is
21 a human carcinogen or sometimes referred to as
22 upgrading or downgrading the classification based
23 on that. And, you know, the view of the BSC is
24 that the data can be used to drive a classification
25 decision in one direction or the other, either to

1 upgrade or to downgrade.

2 And there were comments this morning
3 that -- you know, in both directions, one comment
4 that, you know, they're only used to downgrade, but
5 I think there's plenty of evidence that they've been
6 used to upgrade, both ways, and, second, that they
7 should only be used to downgrade.

8 And I think that a sense by the BSC is that
9 if you're going to bring in those considerations,
10 that the science can point in either direction and
11 that you have to let the chips fall where they may
12 in terms of the science.

13 And then a final issue that I picked up
14 and, really, because of one of my inherent biases,
15 which is just the need for better epidemiological
16 input into the process when there are a lot of
17 human studies involved. And I recognize that that's
18 an issue that the NTP is trying to address by
19 bringing more epidemiologists into the process early
20 on and by bringing people into the peer-review
21 process, but it does seem to be an issue that was
22 raised a lot this morning.

23 **DR. GOLDSTEIN:** Thank you.

24 **DR. FREDERICK:** Yes. I'd just like
25 to pick up on some points from the presentations

1 this morning, and I'd like to go through those in
2 sequence, if I could, and then we can discuss those
3 if they look like they bear more discussion.

4 On David Guston's presentation, there are
5 two points I want to make. One is the Board of
6 Scientific Counselors does not strive for consensus
7 in any aspect. The individual members of the
8 board both are conscious on the issue at hand and
9 reflect their professional judgment. And it's my
10 feeling that there's actually no -- as opposed to
11 committee situations where you're moving for a
12 consensus decision, I don't feel like that's the
13 dynamic of the committee at all.

14 The second thing is there were a lot of
15 unanimous votes there, but it's biased by exactly
16 the point that David noted. There's a fairly low
17 threshold for listing materials as probable human
18 carcinogens, and most of the unanimous votes are
19 in that area.

20 In the area where you're moving to known
21 human carcinogen with regard to delisting votes,
22 there are many more mixed votes in that area, and
23 I think a reanalysis of the data on that basis would
24 provide a different perspective that's probably more
25 reflective of the dynamics of the voting in that

1 particular group.

2 The second issue from Dr. Starr's
3 presentation is that these votes are advisory, and
4 the real message on a mixed vote -- in the case of
5 Dioxin, we voted twice, and there happened to be
6 mixed votes in both cases. And it turns out I
7 voted both sides of that issue. I hadn't really
8 noticed until Tom put the slide up there. I was
9 on the losing side both times.

10 But the point isn't exactly what the vote
11 was. The point is that it was a mixed vote. And
12 the recommendation to Ken is there is a mixed
13 scientific opinion on this specific issue from this body
14 of people, and the fact that I voted both sides
15 of it says that, you know, I've been swayed. I've
16 been kind of on the borderline. I am trying to vote
17 exactly what the science is, and I've been swayed
18 by the body of information, which has changed
19 somewhat.

20 It doesn't matter what I believed when. The
21 point is, in trying to vote exactly what the science
22 is and the message to the agency, to Ken Olden, is
23 that there's a mixed scientific opinion on this, and
24 I think that's reflective of the consensus (inaudible).

25 If we move to Dr. Leber's talks, he feels

1 frustrated for the lack of dialogue, but this is a
2 straight scientific evaluation. It's up or down on
3 the science, and dialogue doesn't really do any good
4 for that.

5 Quite honestly, the written information
6 that's submitted covers the points. In dialoguing
7 on it, it doesn't move anywhere. It doesn't make any
8 difference if 3,000 people are exposed or 300
9 people are exposed. The law that drives this
10 process says there's a significant number of people,
11 and we aren't going to quibble over the exact
12 number. That goes in the risk assessment arena.
13 This is a hazard identification process.

14 The concern is: Is there a substantive --
15 enough of a level of concern based on the body of
16 science, basically, to look at the degree of the
17 concern, but that's handled somewhere else. It's
18 just with regard to the hazardous identification
19 issue.

20 The issue on benign or malignant, that sort
21 of thing, and how the group gets into the nuances
22 of the science discussion, which we don't want to
23 get into other than to say that, we look at the
24 whole body of information, including all the
25 mechanistic information, to try to reach the best

1 decision and recommendation for society.

2 Moving to Dr. Rubin's talk, Dr. Rubin's talk
3 was very interesting because it's a very good
4 example of something we've run into a couple of
5 times where an individual comes in as an advocate
6 for an industry or a group and, in fact, the
7 message is not exactly what was intended. We
8 discussed this when Dr. Rubin gave his original talk
9 at the meeting, so I'll reiterate this.

10 In his published papers, he's shown and
11 argued quite conclusively that excessive alcohol
12 consumption causes (inaudible) -esophagus and is
13 directly responsible for esophageal cancer. And he
14 says that very clearly in his written documents, A
15 to B to C, and there's direct correlation between
16 excess alcohol consumption and esophageal cancer.
17 And, you know, those documents were submitted to
18 us, and I confirmed it verbally with him at the
19 meeting.

20 And it doesn't matter what the mechanism
21 is. If you have linkage of exposure and the
22 ultimate effects there, that's sufficient for the needs
23 that we have on the table. And to a certain extent,
24 his publications were part of the reason my vote
25 went the way it did, and we gave explicit advice to

1 NTP staff to say that moderate alcohol consumption
2 had not been shown to correlate with excess cancer
3 risk, and we want the list to reflect that. It is
4 only excessive, and that's the way the study showed
5 it, and we wanted that reflected in the
6 documentation.

7 So that was the advice we gave, and that
8 was my perception of the advice we gave, and it
9 was very strong, very direct and reflective of the
10 science and reflective of where we were on the
11 issue.

12 If we now move to Dr. Infante's comments,
13 even as Lynn said, we use mechanistic data and the
14 full body of information to upgrade and downgrade
15 equally. It's an overall package of information.
16 We're trying to get the right answer with regard to
17 the body of science.

18 And Dr. Oller's presentation with regard to
19 nickel, it's illustrative of a very good problem that
20 you run into when you serve as an advocate for an
21 industry. Part of the package that was submitted to
22 us invoked Dr. Max Costa's work, who's Head of the
23 Environmental Toxicology Program at NYU, a very
24 distinguished scientist in metal toxicology.

25 And as we read and evaluated that

1 information as well as all the other information,
2 then you may come to a different position than
3 what might be presented at this particular meeting.

4 I would point, for example, to a recent
5 publication of Dr. Costa's, and he starts out -- the
6 first sentence of this publication says: Nickel
7 compounds have been well established as human
8 carcinogens. Well, that creates a problem with an
9 (inaudible) industrial presentation. And then he
10 goes on to talk about the difference in potency
11 between insoluble and soluble forms.

12 So it reflects the fact that by looking at
13 the overall body of information and all of the
14 published papers of the people cited in this body,
15 then you may come to a different conclusion than
16 what might be presented in one of these meetings.

17 So I think I've brought up enough issues to
18 fuel a lot of fire for discussion.

19 **DR. GOLDSTEIN:** Let me do it this
20 way. Unfortunately, some of Clay's issues and
21 some of your issues are issues which, again, get us
22 to specific chemicals. I've just been sitting here
23 doodling some things about the BSC, which I think
24 is perhaps the first place we ought to try to focus
25 on.

1 I'd like to -- again, I apologize if I've got
2 this wrong. I've left out -- I'd like to get us to
3 focus on the recommendations part. What we've
4 heard, we've heard denied. It's unimportant as to
5 whether it's right or wrong so much as: What are
6 the recommendations to deal with this perceived
7 issue?

8 We've heard that the BSC is hurried. It's
9 hurried in terms of the members. Maybe it is.
10 Maybe it isn't. We've heard there's too much
11 material, too little time. It's hurried in terms of
12 the public. You only got five minutes to make a
13 presentation and sure that what happens there is
14 really transparent. Is there enough information? Is
15 there not enough information as to what the
16 decisions were made on?

17 And some people are concerned that it's
18 not iterative enough. You make the presentation to
19 the public. You don't find out -- there is no
20 specific response. It's not an EPA kind of record
21 where every public comment gets a written response
22 to it. It's done in a completely different way.

23 These are the kind of differences of
24 opinions that we've heard. We've heard some
25 people say, you know, "There's no need for all of

1 this iteration or written record. Let's just go
2 forward. This is something that's been built on a
3 couple of previous approaches, and this is just, yet,
4 a final approach."

5 So I'd like comments on what is clearly a
6 difference of opinion here from folks, hopefully
7 restricted to that. I know people will want to go
8 beyond these, but just to start with.

9 And, please, when you do make a comment,
10 please tell us who you are and who you work for.
11 We're trying to record this, so we'd appreciate it.

12 **DR. BACAU:** I'm Dr. Bacau
13 (phonetic), and I'm representing (inaudible). And
14 the reason -- one of the things that you have on
15 the list that probably -- it's the impression that the
16 audience had that by the time that public meeting
17 occurs, every one of those members has already
18 made his mind up or her mind. This is the distinct
19 feeling I received when I listen to the deliberations
20 in the BSC meeting.

21 Every one -- on every compound -- wasn't
22 limited to one compound. On every compound I
23 listened, I felt that all this was -- the message I
24 got, it was a show, that we -- they gave an
25 opportunity to the public to come, give a five-

1 minute presentation, then the members already had
2 made up their mind way before that, maybe
3 unjustified. It might not be the true feeling, but
4 this is the message I received. I don't know how
5 many people who were in that meeting received the
6 same message.

7 I feel that one of the recommendations we
8 can make is that these meetings should be held not
9 once, but twice, because I think if we have one
10 meeting where the public can make this five-minute
11 presentation or ten-minute or whatever the number
12 of minutes is, and then the Board of Scientific
13 Counselors sit down, address those issues and so
14 on and then have another meeting where we can
15 listen to some of the issues that were brought and
16 their reaction to it, I think that will convey a better
17 feeling in the sense that, "Yeah. I had an
18 opportunity to make a comment. Somebody heard
19 me, and this is their answer to my comment." I
20 know it might create a major problem for the
21 timing, but I think that's the best recommendation.

22 DR. GOLDSTEIN: There's a
23 comment over here.

24 MR. KELLY: I'm Bill Kelly with
25 Federal Focus, which is not a newsletter. It's a

1 research organization. I've been an observer
2 at the last two RoC Subcommittee meetings, and I
3 was very interested in Dr. Lucier's comment and
4 Dr. Frederick's comment, also, that the
5 Subcommittee is not voting on the background
6 documents, which -- and those background
7 documents are the only written record. We have
8 this up here as one of the issues. I think it's an
9 important issue.

10 I mean, when the recommendation goes to
11 the Subcommittee, there's a certain rationale stated,
12 and it's stated only in that one document. And,
13 certainly, as an observer, I was surprised today to
14 hear that because I had the distinct impression
15 that, basically, the Subcommittee was voting on the
16 rationale stated in the background document.

17 And I was also surprised to hear from
18 Dr. Frederick that they had a kind of -- what would
19 you call it? -- a change to suggest with regard to
20 alcoholic beverages, but that -- I don't think it
21 showed up in the subsequent record like in the
22 Federal Register notices where they record the
23 various votes. You just see the numbers.

24 So something is not actually changed in
25 the background document in the Subcommittee

1 meeting, give the impression it's been approved,
2 and then that's not the end of the process. That
3 document goes forward at least through three more
4 steps: The Executive Subcommittee, then to Dr.
5 Olden, and then to the Secretary. And, finally, it's
6 my understanding it gets, basically, printed in that
7 form in the final report.

8 So if the Subcommittee does have
9 something in there that it feels is wrong or that
10 needs to be qualified or changed, a record needs to
11 be made on that, and it needs to be passed up the
12 line to the Executive Committee and to Dr. Olden
13 and to the Secretary because it's certainly not -- I
14 appreciated the clarification, but it certainly wasn't
15 a clarification that was needed. I have to admit
16 that even after the clarification, I'm still a bit fuzzy
17 on it.

18 You know, that document goes forward. It
19 states a certain rationale, and if everybody is
20 voting in favor of it or so many votes against it or
21 there's a significant split on it, you don't know
22 what it is that people are descending from or what
23 they're disagreeing with. The document just goes
24 forward unchanged.

25 That goes to this whole issue of, you

1 know: Is there an adequate written record of what
2 people have actually thought about the scientific
3 evidence here?

4 **DR. FREDERICK:** Let me clarify
5 the recommendation. The recommendation is what
6 goes in the final report that's published for the
7 public to see, and we, as a body, recommend to
8 the NTP staff what the final publication -- assuming
9 that Dr. Olden took the recommendation of the
10 Board of Scientific Counselors, that the text that
11 actually goes out to the public in the listing would
12 reflect the scientific evaluation of the board, that
13 moderate consumption of alcohol -- I just use that
14 by example. It doesn't make any difference, but
15 moderate did not carry a risk. It was only
16 excessive carried a risk. That's sort of the gist of
17 the --

18 **DR. GOLDSTEIN:** We have a
19 comment as to what actually goes forward.

20 **DR. BUCHER:** I'm John Bucher of
21 NTP. I'd like to clarify exactly what the background
22 document is and what we consider the entire body
23 of information that's used here.

24 The background document is comprised of
25 two parts, generally. There's the information on

1 which the whole listing is -- the recommendation
2 for listing is based and then there's a summary
3 statement that appears in front of that background
4 document that is what we intend would be going
5 into the report itself.

6 So the background documents are a living
7 document in that they are changed in response to
8 comments of RG1 and RG2, and they go to the
9 Board of Scientific Counselors Peer Review
10 Subcommittee. The background document is not
11 changed beyond that because we want to have a
12 record, a solid record, of what the information was
13 that was presented to the board for them to reach
14 a decision at that point.

15 All of the information that we receive as
16 comments is considered part of that background
17 information and it's added to the background
18 documents. So when all of the information goes
19 forward to the further steps, we say background
20 document plus all the comments that have been
21 received.

22 So make sure that you understand that.
23 There will be changes to the wording of the
24 summary statements based on the conclusions at
25 each stage of the review, and what appears in the

1 final book may differ slightly or substantially from
2 what appeared in the Board of Scientific Counselors
3 Review Panel.

4 DR. GOLDSTEIN: Just to be clear,
5 when this gets to Secretary Shavel (phonetic),
6 you're saying it's got the original background
7 document that is seen -- word for word is seen by
8 the Board of Scientific Counselors, plus it's got all
9 of the comments that have been received, and they
10 all go to Secretary Shavel that way?

11 DR. BUCHER: The actual document
12 that is submitted to Secretary Shavel is only the
13 final Report on Carcinogens. All the information
14 that Dr. Olden uses to make a decision about listing is
15 the entire file of information that has been
16 collected from the very beginning in consideration
17 of that -- of the information.

18 DR. GOLDSTEIN: So all of the
19 information, including the public comments, go as
20 far as Director Olden?

21 DR. BUCHER: Yes.

22 DR. GOLDSTEIN: And at that
23 point, there may be changes in the summary
24 statement?

25 DR. BUCHER: Yes.

1 DR. GOLDSTEIN: And there may
2 also be changes in the summary statement at the
3 level of the Secretary's Office?

4 DR. BUCHER: I would -- that's
5 possible, but I'm not sure that that's happened.

6 DR. GOLDSTEIN: Thanks, Doctor.
7 Dr. Oller?

8 DR. OLLER: I would like to make
9 a couple of quick comments. One is, again, I want
10 to reiterate I think it's very important that the
11 background document be a high-quality document,
12 and I think when the reviewers of the Board of
13 Scientific counselors, which is where the peer
14 review occurs, when they get this document, this
15 may be the first time they become familiar with the
16 literature in a particular compound. And, therefore,
17 what the document is saying and what
18 recommendations have been made up to that point
19 will be the basis for the decision that they're going
20 to make.

21 Now, then a few days before the meeting,
22 they get comments, comments that may disagree
23 with what's in the document. How can they judge
24 who is right and who is wrong unless NTP takes the
25 time to answer to the comments that I submitted

1 and said, "We disagree with your comments because
2 of this and this and this reason," or, "We -- okay.
3 We agree with part of your comments," and that
4 may not have been clear in the document. That has
5 to be done. Otherwise, I cannot see how the Board
6 of Scientific Counselors can really take these
7 comments and understand the issues that are
8 raised.

9 I also would like to point out that as an
10 industry scientist, we have recommended that the
11 listing of certain nickel compounds be upgraded to
12 known human carcinogens. So we're not here just
13 saying everything has to be downgraded. It's just
14 that we think that there are differences in the
15 behavior of these compounds that are supported by
16 the data, and there are some of them which are
17 clearly carcinogenic and others that are not.

18 Furthermore, you may not be aware that
19 Dr. Costa and I have written papers together, and
20 he agrees with the concept that soluble nickel
21 compounds are not carcinogenic.

22 Thank you.

23 **DR. GOLDSTEIN:** I should have
24 made the point that that's Dr. Adriana Oller of the
25 Nickel Producers Environmental Research

1 Association.

2 **DR. FREDERICK:** Bernie, let me
3 respond. I don't want to talk about the specifics of
4 nickel, but I just want to -- with regard to
5 particular scientists and how we can be affected by
6 a number of inputs, but the real point is I think
7 you're taking far too narrow a view of our role.

8 Each of the members of this committee are
9 scientists in the absolute sense of the word, and
10 we don't -- if you think we just look at the input
11 that comes in one document from NTP, you're
12 sorely, sorely mistaken. And if industry waits until
13 the last minute to submit their comments, they're
14 making a really big mistake.

15 Those comments should be going in a year
16 ahead of time. They should be sending in a
17 package that would be a part of what comes to us,
18 and then you only tailor that at the last minute if
19 you've got, you know, something that you want to
20 change with regard to some specific points. Then
21 those come out three weeks ahead of time or
22 whatever it might be.

23 But the point is, waiting until the last
24 minute to get your comments in is not an effective
25 way to present information for scientists to

1 evaluate. This is a scientific exercise. You get the
2 fullest body of information on the table.

3 MR. LEBER: Philip Leber, Good
4 Year. I agree implicitly with what Clay is saying,
5 and I think hidden in that message was comments
6 and so forth have to -- and input have to be made
7 much, much earlier in the process.

8 But as it currently stands, Clay, we see a
9 draft document weeks -- one to two weeks before
10 the hearing. We can give comments, but we don't
11 know what we're commenting on. We just unload
12 our database as -- on isoprene or whatever. What's
13 going to happen with it? We have no clue at that
14 point, so there's no comments to be given earlier.

15 Secondly, on the issue of -- oh, the
16 background documents and just tweaking at the last
17 minute, I have one here that says: Chemical X is a
18 reasonably anticipated human carcinogen based on
19 evidence of benign and malignant tumor information
20 in multiple organ sites and multiple species. For
21 Chemical X, that is a false statement.

22 And that comment was made in writing.
23 On the day of the Board of Scientific Counselors'
24 meeting, it was not acknowledged that this was a
25 false statement, and, therefore, board members were

1 voting on the assumption that this is a multi-
2 species, multi-organ carcinogen, and that's not true,
3 but what they're voting on is not that point but
4 that it's reasonably anticipated. Now, if you take
5 away that information or you correct it, is it still
6 reasonably anticipated to be a human carcinogen? I
7 have some serious doubts.

8 So, you know, that's why this iteration and
9 the complaints of legal action and so forth occur,
10 folks, because, you know, we give comments and
11 we give input, but, you know, if it's being heard,
12 there's no acknowledgment that it's being heard,
13 and there's no attempt to correct the bona fide
14 errors that are clearly in there.

15 **DR. GOLDSTEIN:** Let me pursue
16 that with you a bit just so we have some
17 clarification. There's two issues I think you're
18 asking there when you're talking about the --

19 **DR. FREDERICK:** Phil, don't leave.

20 **DR. GOLDSTEIN:** We've got two
21 issues. We've got process issues and we have, if
22 you will, factual issues. Are you saying that, in
23 fact, there are multiple tumors caused in multiple
24 species, and because there is scientific debate and,
25 in fact, the scientific debate was something that

1 you did not have a chance to present because the
2 process was too slow or was it -- is it something
3 that just there was an absolute misreading of
4 everything?

5 If it's a question of just there's differences
6 among the scientists and you think they're wrong
7 and they think they're right, and the board got an
8 opportunity to hear both sides of it, that's -- I
9 mean, that's a little different from saying that the
10 board didn't have an opportunity to hear that
11 point.

12 **DR. GOLDMAN:** Well, (inaudible)
13 debate, Bernie, because, I mean, we can't get away
14 from the fact that there's a tremendous amount of
15 hearing through reading that's going on in the
16 process.

17 **DR. GOLDSTEIN:** Hearing because
18 it was too hurried or that there wasn't enough time
19 to put this data together. And then, of course, one
20 issue I haven't heard yet or I did hear once, but
21 it's buried in some of the writing we'll hear later
22 is: Was this published or unpublished data?

23 So could you respond to that instance? Are
24 you talking about a situation where you think they
25 had enough time and they just disagreed with you

1 or they --

2 **MR. LEBER:** I'd be pleased to.

3 In this particular case, there is definitely
4 multi-organ, multi- -- I'm sorry -- multi-organ
5 malignant tumors in one species. In the second
6 species there was only benign tumors. And the way
7 this reads is you're supposed to believe that there's
8 multi-organs, multi-species carcinogenic benign and
9 malignant tumors. Now, in that second species
10 there was only benign tumors. Okay?

11 This was commented on at the draft stage
12 in writing. The Board of Scientific Counselors
13 meeting, we did not hear anybody from NTP say,
14 "We've got to make a change here on the basis of
15 what we're going to be voting for reasonably
16 anticipated to be a human carcinogen. There's an
17 error there." That was not changed, so I repeated
18 it verbally that day and got no comment there
19 either. The vote was taken, reasonably anticipated.

20 **DR. GOLDSTEIN:** Let me pursue
21 this. Is it conceivable that the scientific members
22 of the panel voting up or down on the issue of the
23 classification believed completely what you said,
24 agreed with you completely, but still voted the
25 classification the same way? They still think.

1 DR. FREDERICK: The answer is
2 yes, Bernie.

3 DR. GOLDSTEIN: Is that the issue
4 here? Try to get your focus on the issue.

5 MR. LEBER: That may be, but,
6 Dr. Goldstein, I would assume that if you're
7 presenting -- or NTP is presenting a statement,
8 given the basis for why it is a reasonably
9 anticipated, that there would be a correct statement
10 for that basis.

11 DR. GOLDSTEIN: Here's a question
12 of the record, not so much that the facts were not
13 able to get to the board. Those are two different
14 issues, important issues. I just wanted to get it
15 clarified.

16 Dr. Mirer?

17 DR. MIRER: Frank Mirer again,
18 from UAW, and also a member of the Report Review
19 Committee and past member of the Report Review
20 Committee and present member of the Report on
21 Carcinogens Subcommittee.

22 First of all, let's go to the background
23 document. I would say about 80 percent, 85
24 percent of the content of the background document
25 typically is the IARC review of the material, which

1 is the most prestigious and complete document
2 available. There's a veneer on top of it which
3 reviews additional information that's developed
4 since the IARC review and contains some of the
5 other material required for the report.

6 We also receive what are perceived to be
7 the key papers underlying the IARC review and
8 subsequent to the IARC review, and we can request
9 additional papers if we think they're relevant. So
10 the BSC members have the complete record in front
11 of us. There's no rule that says the new stuff has
12 to come in the night before, and, typically, it
13 comes in months before to our offices. Those of
14 us who are involved in the material go through it.

15 The five-minute summary, in my view, the
16 oral comments at the meeting, basically, truncate
17 the discussion of the board members who are
18 reviewing the material. The reasons why people
19 take a position if you disagree with the critique,
20 you have to state the reasons you disagree with the
21 conclusion. I guess people who don't disagree
22 don't usually write down reasons why they agree,
23 but the record is completely there.

24 And I resent the notion that we're
25 incompetent to review that material and render an

1 opinion on it. So I think we do critique. At least,
2 I view my role as critiquing that report and
3 suggesting changes in it. So I don't really accept
4 the criticism.

5 **DR. GOLDSTEIN:** Let me raise a
6 different issue about the BSC. And I should have
7 -- Tom brought this up, Tom Starr: Is the
8 composition right? I will point out that none of
9 you, as far as I can hear, claim that the group is
10 biased one way or the other. There is, at least in
11 one of the written comments, some passing
12 comment about academics, and I will not respond
13 that one, but let me raise that issue.

14 Is there anyone who would like to comment
15 on the composition of the BSC in any way? Again,
16 having already heard something about the need for
17 more epidemiological expertise from the point of
18 view of Dr. Starr. Any other comments in that
19 way?

20 **MR. LEBER:** At the tox forum,
21 again, there was a comment made that, certainly,
22 the Board of Scientific Counselors was --
23 represented a political cross-section, and I think --
24 that was not an industry person, however, and then
25 I think it does also represent the wide range of

1 expertise from statisticians, MDs, and so forth.

2 One of my concerns, though, is that so
3 much of the data that is applied to carcinogenesis
4 comes from bioassay data, and the bioassay field is
5 sort of a unique, somewhat capsulated --
6 encapsulated realm within the field of toxicology.

7 You have a lot of issues, such as high
8 historical incidences of certain tumors, testicular
9 and so forth. You have a lot of chemistry that's
10 involved in the generation of atmospheres and
11 inhalation studies.

12 And many of the people who are
13 represented on the boards are mechanistic people
14 or they're people who don't have very much
15 experience in the bioassay field. That's one of my
16 biggest concerns. And epidemiology. I think you
17 definitely need bolstering in that arena.

18 **DR. GOLDSTEIN:** Other comments?

19 Dr. Guston, please introduce yourself.

20 **DR. GUSTON:** Dave Guston from
21 Rutgers. You heard about me before, and I put the
22 little graph of the people's votes in the
23 three-dimensional spaces.

24 When you aggregate those data, and I
25 won't show you on the overhead because, like I

1 said, there is an error of aggregation there, but
2 when you aggregate those data, it appears that the
3 people with university affiliations are normally
4 distributed around the majority opinion. The people
5 with government affiliations seem to be similarly
6 normally distributed around the majority opinion.
7 Again, these are aggregating all of the individuals
8 with those affiliations.

9 The people with industrial affiliations, and
10 here I'm going to add the people with labor
11 affiliations because that seems to be part of the
12 idea, and even with the addition of the labor
13 affiliation to the industrial affiliations, you get
14 something that is shaded more than the university
15 and government folks toward less protective.

16 Now, I'm not going to say that that makes
17 the committee biased or not because you can't say
18 where the meeting ought to be, necessarily, but it's
19 based on where the majority is. That's the way
20 these people with these substances ended up
21 coming up.

22 I can't say for anything other than these
23 substances, and I don't think that necessarily
24 implies bias in the committee, but that's the
25 aggregation.

1 DR. GOLDSTEIN: I can't wait for
2 the word to get out about that.

3 DR. GOLDMAN: I just want to ask
4 you a question, if you could come back up to the
5 mike, because one of the things that I was
6 wondering about in hearing your analysis and just
7 speaking about the process, in a way, you could
8 think of this process as kind of a quality control
9 step, in a way, of -- which is coming off a
10 conveyor belt and assembly line, except they're not
11 all the same.

12 And some of these are very complex,
13 difficult decisions, and some of them are much
14 more straightforward, and I think, as Dr. Frederick
15 pointed out, that, particularly, the ones where
16 you're talking about listing something as a known
17 human carcinogen or, conversely, when you're
18 talking about a delisting decision, that those tend
19 to be particularly controversial.

20 And I guess one thing I want to put to you
21 is: Is there a way that you could look at, say, the
22 type of decision, the type of product that's coming
23 forward, and perhaps not -- should we be
24 considering having a different process design for
25 the reviews that are going to be more complex,

1 more difficult on priority, you know, like listing a
2 known carcinogen?

3 DR. GUSTON: Yeah. That's part
4 of the difficulty of presenting stuff in the middle of
5 the research program, but I just had to take
6 Dr. Frederick's suggestion seriously to decompose
7 the data and to look at the decision based on which
8 bin you're sorting. The idea -- just sort of offhand,
9 the idea of a different process for a different bin
10 strikes me as potentially problematic. I --

11 DR. GOLDMAN: Well, then you get
12 into other issues like: Then do the people who
13 have the less special cases feel they're not getting
14 as much of a hearing or as much of a discussion?
15 So, I mean, you could have an appearance of
16 inequity, but --

17 DR. GUSTON: That might be a
18 way to priority sort.

19 DR. GOLDSTEIN: Couple of
20 comments? I would -- we've got about five minutes.
21 Please come up and make your comment.

22 I would like -- I'm surprised we haven't
23 heard anything about the written record issue
24 among us. I'd appreciate comments on that. I
25 think among all of the things that are up there,

1 that the idea of a written record that gets
2 responded to is perhaps more central to changing a
3 process than almost anything else that's there.

4 **MR. KELLY:** I thought that was
5 the first thing I came up here to talk about.

6 **DR. GOLDSTEIN:** Okay.

7 **MR. KELLY:** Bill Kelly with
8 Federal Focus. If the Subcommittee disagrees with
9 something in the background document, in other
10 words, it's voting to go along with the classification
11 decision but on a different rationale, that should be
12 documented, or if there's a mistake that could be
13 significant in the background document, that should
14 be documented. That's the written record.

15 **DR. GOLDSTEIN:** What about the
16 issue, though, of all of the comments that come
17 from the public should be responded to in writing
18 and become part of the record? Which is what I
19 think I heard some people suggest. That makes
20 that -- that's obviously a much more of an iterative
21 process. It gets people to respond to the record.

22 **DR. FREDERICK:** That's not, from
23 my perspective, the whole philosophy of this
24 process in the sense of going through the
25 regulatory process of an EPA risk assessment or

1 something like that. That has a whole different
2 protocol associated with it, using the scientific
3 advisory opinion of a group of scientists who have
4 looked at a big body of information. Not all of it
5 is going to be consistent, generally, but you're
6 trying to get out the signal from the noise with
7 regard to what the scientific issue is, to make a
8 health recommendation for the public.

9 People look at that body of information and
10 they provide their opinions by way of a vote, and I
11 think that's -- that's it. That's the punch line.
12 And I think getting into a long iterative-type
13 process as you're going through, you know, like, an
14 air pollutant standard or something like that, that
15 totally misses the point of this.

16 **DR. GOLDSTEIN:** I think that's a
17 key issue that was raised by a number of speakers,
18 and I'm offering the opportunity for people to talk
19 about it now. We can talk about it later as well.

20 **MR. KELLY:** What I would -- that's
21 not what I really got up here to address, but I
22 would say if you're going to handle that, it should
23 at least be handled in a separate section of the
24 background document. At that point, the agency
25 already has a set of comments from the industry on

1 its original listing proposal even though it didn't have
2 a rationale at that point.

3 I think, at a minimum, the background
4 document should set aside a brief section where it
5 addresses the principal comments and what the --
6 how the agency -- what the agency's responses are
7 that are relevant to what's going in the background
8 document.

9 DR. GOLDSTEIN: You had
10 something else to say?

11 MR. KELLY: That had to do with
12 composition, which was the next subject,
13 composition of the Subcommittee. And that's
14 something nobody's mentioned, is that sometimes,
15 on some of these substances, we're dealing with a
16 huge and complex database, and I don't think
17 anybody needs to impugn or denigrate the scientific
18 expertise of the members on the Subcommittee, but
19 I find it difficult to believe that members of the
20 RoC Subcommittee in a couple of days or a couple
21 of hours -- I'm not sure what -- can get completely
22 up to speed on some of these huge databases.

23 And, for example, in the case of nickel
24 compounds, I heard a dispute developing here over
25 just what was said by a couple of experts in the

1 field. Shouldn't we have -- when we're dealing with
2 very complex issues, call in some of the people
3 who have special expertise on those substances?

4 As the process works now, the people who
5 come in and comment always have a vested
6 interest, and so they're tainted with a color. This
7 person represents industry. This person represents
8 a public interest group or whatever, and that, I
9 think, taints the consideration to some degree.

10 There's an EPA model, and I know it
11 complicates the situation, which Dr. Frederick
12 doesn't like to hear, perhaps, and that's of calling
13 in a subgroup of consultants who are experts in
14 that particular field or on that particular substance
15 to offer their views without being associated with a
16 particular industry or a particular company, and
17 that's actually the IARC model, which NTP relies on
18 to a great extent in their deliberations.

19 IARC will go out of its way to pick people
20 who are experts with regard to that particular
21 substance to develop the IARC views on that, but
22 NTP does not do that. It's a very generalist
23 approach, and I think the process suffers as a
24 result. And it may just be that Congress has given
25 the agency an impossible task here, and maybe that

1 needs to be addressed, too.

2 **DR. GOLDSTEIN:** Thank you.

3 Again, we've got some -- I'm happy to have
4 had some very specific recommendations, and,
5 obviously, we won't mention them all, but
6 subgroups, two meetings, whatever that had come
7 out for NTP to be considering.

8 **DR. GOLDMAN:** Bernie, just to
9 add to that idea, actually, what NTP often does is
10 not set up a new subgroup but, rather, bring in
11 specific consultants to add to, say, the science
12 advisory board, a standing advisory committee.
13 There will be ad hoc consultants brought in to
14 participate in reviews where you need that, you
15 know, area of specialized knowledge and it isn't
16 present already on the advisory committee, which is
17 a little different than setting up a whole new
18 committee. It's more like adding to the discussion.

19 **DR. FREDERICK:** There's an
20 underlying philosophical problem here that I think
21 kind of permeates this that I'd like to get at. I
22 work for industry, and I think I understand how
23 industry works in terms of the culture, and I've
24 been a part of this board for a while, and I think I
25 understand the culture of this group.

1 Industry likes to comment on documents.
2 They like to have a target, something to work off
3 of. And I think industry has been frustrated
4 because they haven't had this document early in the
5 process to comment off of, to work on.

6 And it's a rare day -- well, I'd say it's
7 atypical for industry early in this process, a year
8 ahead of time, when these notices go out, to send
9 in a really good comprehensive package of an
10 industry position. That's what the -- if industry, in
11 general, understood this process, that's what they
12 could and should do. That is atypical.

13 Independent of whatever is going on at
14 NTP in terms of the development of their document,
15 industry presents their position. And then only
16 later, when you actually get this document, then
17 you respond to it, but that's just not the way the
18 culture works. The culture is you get the
19 document, whatever is being developed in
20 government, and then you respond to it. You
21 attack it. You deal with weaknesses and errors and
22 all that sort of thing.

23 I think that fundamental cultural difference
24 is the primary problem, if I can say there's a
25 problem here, from my perspective, and I think

1 there are a variety of ways of addressing that, but
2 I think that's the principal source of concern.

3 **DR. GOLDSTEIN:** My target right
4 now is lunch. We'll have an opportunity for
5 discussion later. I'm sure a lot of the speakers will
6 bring up much the same points, and we can go back
7 over these. There are other areas, such as
8 mechanistic research, that were raised before.

9 So we'll start again at 1:20 sharp. Let me
10 thank you all for your participation.

11 (WHEREUPON, a lunch recess was taken from 12:30
12 p.m. to 1:20 p.m.)

13 **DR. GOLDSTEIN:** Our first speaker
14 this afternoon is Susan Nathanson of the Y-ME
15 National Breast Cancer Organization. Again, for
16 those of you who hadn't heard before, we're going
17 to try to stick to the ten-minute time period for
18 each of the presentations, and, again, we ask the
19 presenters to try to stick to the process rather than
20 to the individual chemical. Thank you.

21 **MS. NATHANSON:** I want to thank
22 the Chairman and the panel for allowing me to
23 speak. My name is Susan Nathanson, and I'm the
24 Executive Director of the Y-ME National Breast
25 Cancer Organization, and I appreciate the

1 opportunity to share our concerns with you
2 regarding the classification of Tamoxifen in the
3 Report on Carcinogens.

4 Briefly, the Y-ME National Breast Cancer
5 Organization is a patient advocacy group that was
6 formed 21 years ago by two women with breast
7 cancer to educate and support other women and
8 their families in our communities who also are
9 dealing with breast cancer.

10 Basically, our mission is to try to decrease
11 the impact of breast cancer and create an
12 increased breast cancer awareness and through
13 information and the interpretation of science that's
14 available and evidence to provide a mechanism for
15 women to be empowered to ask their health care
16 providers the right questions and determine what is
17 best for themselves in partnership with those
18 providers and do that so that, essentially, no one
19 faces breast cancer alone.

20 We achieve this mission in several ways.
21 We educate, inform, and support women diagnosed
22 with breast cancer through the provision of two
23 24-hour, seven-day-a-week hotlines, which at the
24 moment receive well over 31,000 calls a year, plus
25 a web site that gets, in mid year this year, over

1 half a million hits and over 2,500 direct questions
2 about various treatments and diagnoses with regard
3 to breast cancer. We do that both in Spanish and
4 in English.

5 We have support groups around the country
6 in over 25 chapters in the United States, and we do
7 it through annual and biannual educational
8 conferences on numerous topics. Last April, in
9 particular, we had a conference on breast cancer in
10 African-American women.

11 We also provide workshops to raise
12 awareness about breast cancer in topics such as
13 early detection of breast cancer through breast
14 self-exam, age-appropriate mammography, and
15 clinical breast exams. We also have a national
16 bimonthly newsletter that carries critical up-to-date
17 information to over 15,000 individuals on recent
18 findings on breast cancer diagnosis and treatment.

19 I am here today to urge the NTP to
20 consider listing the pharmaceutical product
21 Tamoxifen in a different manner than with other
22 human carcinogens. We are not here to dispute
23 that Tamoxifen is associated with an increased risk
24 in endometrial cancer in women taking this drug,
25 and we realize that this is a serious side effect.

1 On the other hand, we have 25 years of
2 information collected about the use of Tamoxifen
3 for the treatment of breast cancer that indicates that
4 for women taking this drug for treatment, the
5 benefits outweigh the potential risks of endometrial
6 cancer.

7 Y-ME believes that women should know the
8 risks and benefits they incur by taking any drugs.
9 Many of the drugs that they take are cardiotoxic,
10 and some of them lead to other malignancies as
11 well, but these are the treatments that are available
12 today for breast cancer.

13 We feel strongly that these risks and
14 benefits need to be communicated in a responsive
15 and responsible manner, and we try very hard to
16 make sure that the women understand the science
17 behind the -- the scientific evidence behind the
18 risks and benefits that we tell them about.

19 The fact that the FDA has fully evaluated
20 this product and approved its use for the treatment
21 of breast cancer we feel should be taken into
22 account, along with the fact that the risks and
23 benefits are included in the product information.

24 Y-ME is here today because we are
25 concerned that the release of this list with the

1 inclusion of Tamoxifen as a human carcinogen, a
2 known human carcinogen, without a strong,
3 balanced statement about both the benefits and the
4 risks will frighten hundreds of thousands of women
5 currently taking Tamoxifen for the treatment of
6 breast cancer and could result in unnecessary
7 confusion as well as women stopping the treatment
8 they're involved in.

9 Therefore, we are asking that the NTP
10 release the information about Tamoxifen so that
11 both the benefits and the risks are included with an
12 advisory to women who may be concerned about
13 this listing to contact their physicians for details
14 and advice.

15 We are especially concerned that the media
16 will release this information in such a way as to
17 sensationalize to list Tamoxifen as a human
18 carcinogen without information about the full
19 benefits as well as the risks associated with taking
20 this drug.

21 As you know, people diagnosed with cancer
22 of any type are fearful, not only for their lives but
23 especially for their choices in the kind of treatment
24 that they engage in. On the hotline, we try to give
25 reasoned responses to questions regarding any

1 treatment, including the risks and benefits of all,
2 but when a story is reported in the media, we hear
3 about it from thousands of women. We can barely
4 handle the calls that come in.

5 For example, when the media reported that
6 there was fraud found in some of the results of the
7 NSABP trial for Tamoxifen, even though those
8 investigators were exonerated, thousands of women
9 called our hotline because they were terrified by
10 the possibility that they had made a mistake in the
11 choice of treatment that they had taken.

12 The same thing occurred when the whole
13 issue of silicone breast implants were reported and
14 were listed as a cause of systemic and immune
15 system disease. Women were unnecessarily
16 frightened by all of that, and these were women
17 who had -- many times had had silicone implants
18 and went through the surgical procedure of having
19 them removed where, in most cases, it might not
20 have been necessary. And, again, women are really
21 afraid of the fact that they are choosing the wrong
22 treatment or choosing -- making the wrong decision
23 with regard to how they live their lives following a
24 diagnosis of breast cancer.

25 So, basically, we are here today to urge

1 public health officials to take great care in how
2 this information is released and to consider listing
3 this drug in a separate category to allow the NTP
4 to better communicate the risks and benefits of the
5 drug therapies involved.

6 **DR. GOLDSTEIN:** Thank you. For
7 those of you who don't know, that organization is
8 one of the most effective ones out there.

9 Our next speaker is William Kennedy from
10 AstraZeneca.

11 **MR. KENNEDY:** Thank you,
12 Mr. Chairman. First, a personal thanks to you in
13 my own risk management. Your strict adherence
14 to the program allowed me the opportunity to push
15 away from the luncheon table, getting the benefits
16 of nutrition and avoiding the risk of overindulgence.
17 I wish more of these things that I went to I would
18 have these things.

19 Good afternoon. My name is Bill Kennedy.
20 I'm a Vice President in the Drug Regulatory Affairs
21 Department at AstraZeneca. I'm pleased to have the
22 opportunity to share my thoughts with you
23 regarding the classification of pharmaceutical agents
24 in the Report on Carcinogens.

25 I commend the committee for holding this

1 public meeting to discuss the procedures used to
2 prepare the Report, and we appreciate NTP's
3 thoughtfulness as you review the complex issues
4 surrounding the inclusion of pharmaceutical therapies
5 in the Report.

6 The Report on Carcinogens is an important
7 function of the NTP and reflects Congress's
8 honorable intention to protect the health of the
9 American people by providing information about
10 possible health risks. Our concern is that the
11 report may have the unintentional result of
12 confusing and potentially hurting the public.

13 All pharmaceuticals inherently have health
14 benefits and risks that must be carefully and
15 consistently communicated to consumers. Because
16 the Report on Carcinogens does not contain this
17 important benefit information, it has the significant
18 potential, as Susan has already pointed out, to
19 confuse rather than inform patients about their drug
20 therapies.

21 It's our belief that this confusion will
22 cause patients not to take important lifesaving
23 medications that their doctors have prescribed for
24 them. Our concern is heightened because the most
25 serious life-threatening diseases are the cancers

1 that are treated with some of the medications that
2 are included in the current report.

3 Every day real people affected by serious
4 illnesses must make important decisions regarding
5 their medical treatment. Patients deserve clear and
6 comprehensive information about the medications
7 that have been prescribed by their physicians.

8 We recommend that the NTP seriously
9 consider the proposal that has been made by the
10 FDA to establish a pharmaceutical category in the
11 Report on Carcinogens. Currently, listings in the
12 report do not distinguish between a pharmaceutical
13 product that the FDA has fully evaluated and
14 concluded that it confers a benefit to human health.
15 They don't distinguish this from any other substance
16 in the clinical -- in the carcinogenicity report.

17 A pharmaceutical category would list
18 pharmaceutical agents separate from non-
19 pharmaceutical agents and provide the public with
20 the information about FDA approvals for drugs as
21 well as potential side effects. Most importantly,
22 such a category would list benefit and risk
23 information together for comparison. Without a
24 separate category for pharmaceuticals, patients and
25 their doctors could become confused about the

1 magnitude of the risk versus the benefit from a
2 medicine or treatment.

3 When the U.S. FDA approves a
4 pharmaceutical, it evaluates its benefit and risk and
5 decides if the availability of that medicine is in the
6 best interest of the public health. A pharmaceutical
7 category would acknowledge FDA's critical role and
8 better serve the public by providing complete
9 information about listed drugs. A pharmaceutical
10 category would continue to serve the Congressional
11 intent of the report but acknowledge that the U.S.
12 FDA has determined that the benefits outweigh the
13 risks.

14 This new category would be highly
15 appropriate for therapies like Nolvadex, our brand
16 of Tamoxifen, a breast cancer therapy that is also
17 credited with reducing the incidence of breast
18 cancer in women at high risk and reducing the
19 incidence of recurrence and second breast cancers
20 in survivors.

21 The incidence of endometrial cancer,
22 pulmonary emboli, and deep vein thrombosis is very
23 rare. While women must be monitored for possible
24 side effects, the FDA and other world health
25 organizations have determined that the benefits far

1 outweigh the risks of women who are at high risk
2 of developing breast cancer, have breast cancer, or
3 are breast cancer survivors.

4 We cannot ignore the risks in favor of the
5 benefits; nor should we ignore the benefits in favor
6 of the risks. To focus on one and not the other
7 does a great disservice to the hundreds of
8 thousands of women who are fighting breast cancer
9 today.

10 We appreciate and respect NTP's mandate
11 to inform the public about potential health risks,
12 and in the case of pharmaceutical drugs, it must be
13 done without frightening patients away from the
14 medicine that can successfully treat their serious
15 diseases. We at AstraZeneca call upon the NTP to
16 enhance its mission by accepting the FDA
17 recommendation to create a separate pharmaceutical
18 category in the Report on Carcinogens.

19 Mr. Chairman, thank you.

20 **DR. GOLDSTEIN:** Thank you.

21 Our next speaker is Michael Bird of the
22 Exxon Biomedical Sciences, Incorporated, and the
23 Butadiene Work Group of the Olefins Panel of the
24 Chemical Manufacturers Association.

25 **MR. BIRD:** My name is Michael

1 Bird, and I'm here today on behalf of the Chemical
2 Manufacturers Olefins Panel, and this panel
3 comprises the US producers and some of the users
4 of butadiene. The panel's been involved in health
5 research for butadiene for about 20 years
6 (inaudible) with others in the generation of
7 (inaudible).

8 Just by way of brief background, butadiene
9 is listed in the 9th Report as a human carcinogen.
10 Butadiene in combination with styrene makes up
11 SBR rubber, which you find in the majority of the
12 car tires, but it's also a product of auto emissions
13 as well.

14 Now, some of what I have intended to say
15 has been adequately covered, and I certainly don't
16 want to numb my audience. Being Speaker No. 13
17 in the afternoon, I have some trepidation, but there
18 are some points that I want to go over.

19 First of all, this all important key
20 background document is, essentially, prepared in a
21 closed process. Now, there's nothing intrinsically
22 wrong about a closed process, but it doesn't
23 include outside input and especially that from those
24 who have been involved in the business of
25 generating much of that data.

1 And what we found in the case of
2 butadiene, and I'm going to illustrate some of my
3 process comments with butadiene, is the fact that
4 this particular background document didn't include
5 some important studies, both epidemiologic and
6 mechanistic, and, also, there are a number of
7 factors there which we felt were given more weight
8 than, perhaps, they should have been.

9 The net result is that RG1 and RG2 had at
10 their disposal -- the only document they had for
11 their review was this background document. The
12 first opportunity for industry to view or input --
13 and not only industry, by the way. A number of
14 the academics involved in generating the data was
15 given two or three weeks before the RoC
16 Subcommittee review.

17 We also note that the document tends to
18 advocate a particular position rather than presents
19 the evidence, and I submit to you that other
20 organizations tend to have a rather more balanced
21 document and tend to only develop the position
22 after they've had adequate discussion and
23 assessment. I've given you a technical example
24 there. I'm not going to get into that.

25 There's no mechanism to revise the

1 background document, as we've heard this morning,
2 and it's fine to have public comment in parallel,
3 but, boy, I'd like to see some integration and, also,
4 some of that addressed.

5 Now, in the case of butadiene, again,
6 Dr. Frederick, it would be nice to have one year. In
7 fact, we had three months from the time of first
8 notice in the Federal Register that butadiene was
9 going to be upgraded to your meeting, and, in fact,
10 we had three weeks prior to your meeting to review
11 a 60-page background document. So more time,
12 please.

13 And, again, we submitted, and others from
14 academia, detailed comments to the RoC, and I
15 submit to you that we really do need to have
16 discussion and adequate deliberation of those
17 comments. As Phil Leber said this morning
18 (inaudible) in response to comments provided, I too
19 have children, four of them. They often say, "Hey,
20 it's not right," or "No" to me, too, but, boy, it's
21 sure nice to hear from them because at least it means
22 that they have heard me. I'm not sure that
23 we have been heard.

24 I'm going to skip right way down. You've
25 had more than enough of the first two bullets.

1 Need chemical-specific expertise on
2 subcommittee. We've heard about epidemiology, but
3 with butadiene a lot of the material was
4 epidemiologically related. There are a lot of
5 subtleties in that data. And we've heard reference
6 today already about IARC, the SAB, the Science
7 Advisory Board of the EPA. Both IARC and EPA-SAB
8 reviewed butadiene within two or three months of
9 the NTP RoC review. I'll get into that in a minute,
10 at least the (inaudible) views. And they had
11 extensive and different compositions on their review
12 boards.

13 Dr. Goldstein, if I could be (inaudible) this
14 afternoon just to make sure I have an audience.
15 It's important to have epidemiologists, and you need
16 more than one. Okay? They're good buddies and
17 friends. I work with them real hard, but I
18 recognize (inaudible) that you definitely need,
19 because they can't agree on a cause of death, and
20 that's why you need debate and adequate time for
21 debate.

22 And when we get involved in some of the
23 reviews by IARC and EPA, IARC for instance had a
24 separate epidemiology subgroup of some ten
25 epidemiologists, and they took several days to talk

1 about the butadiene epidemiology.

2 Now, I'm not suggesting -- Dr. Infante, you
3 made the point. I'm not suggesting NTP mimics
4 IARC or EPA-SAB, but I think it's important, with
5 the reviews being so close, they should take note
6 of why they are so different and examine why the
7 difference in interpretations because, otherwise, it's
8 a very confusing message to the public and to
9 others involved.

10 One of the facts involved in the EPA-SAB
11 and IARC reviews was the fact that the
12 epidemiology data is derived from the SBR,
13 styrene-butadiene, rubber process as opposed to the
14 monomer industry, and all the leukemia we've seen
15 with butadiene could be derived from that
16 industry.

17 And there's a lot of discussion and a lot of
18 developing data pointing to the fact that when they
19 did (inaudible) work, that these can't be excluded.
20 We also had further data in metabolism, and I hear
21 -- NTP might stand up and say, "We've got to draw
22 a line somewhere," but, on the other hand, we have
23 very new, critical data in a time (inaudible). It's
24 very important, I think, to be flexible and at least
25 have some footnote in your report that this is a

1 variable. So I submit that, currently, the
2 background document as it stands is outdated and
3 doesn't represent the scientific data as we stand at
4 the moment.

5 If we look at the reasons why IARC and
6 EPA-SAB might be different from the NTP, at the
7 bottom line we'll see two different conclusions. For
8 IARC and EPA, it's probable, implying some doubt.
9 For NTP, it's known, and that's a pretty certain
10 category. I divided it on the left in two aspects,
11 the evidence, or data, and, also, the process.

12 Well, as I've mentioned, there's a lot of
13 human data available for butadiene, which is why
14 you need those epidemiologists, plural, but both
15 IARC and EPA said that the human data wasn't
16 consistent. One of the things they recognized was
17 that monomer workers don't have leukemia. The
18 SBR workers do.

19 They also recognized that there wasn't
20 sufficient human data. They classed it as limited
21 because the data really derived from one study,
22 albeit very large. That study is just now being
23 revised. It's now out, as I speak, and I think we'll
24 be finding that the conclusions are rather different.

25 Also, IARC and EPA found that there wasn't

1 enough mechanistic data or there was mechanistic
2 data to suggest there wasn't a parallel between
3 some of the rodent findings and the human studies.

4 Now, NTP came to different conclusions,
5 which is fine, I guess, but the NTP review process
6 was very hurried and, I submit, different address
7 the similarities of the IARC and EPA decision; nor
8 did they address some of the critical new data.

9 And as you can see, I'm being critical here
10 perhaps as to process. The quality review
11 document for the IARC and EPA was very high.
12 With the NTP, it was variable. There were some
13 portions which were excellent and there were some
14 portions which weren't so good, particularly the
15 epidemiology. Peer review process, extensive for
16 IARC and EPA. The NTP, limited. As you can see,
17 if you have problems with the evidence and the
18 process, that's just one of the reasons I submit you
19 come to a very different conclusion.

20 Recommendations. First of all, I submit
21 that we obtain input to and revise the Draft
22 Background Document prior to submitting it to the
23 RoC Subcommittee, and I mean well prior, and let's
24 have adequate time and input even along the RG1
25 and RG2 so that those committees know and have a

1 complete database to work with.

2 Also, let's have a realistic period. Let's
3 give us more than three months to review this
4 complex subject from start to finish. Let's have
5 adequate discussion. So far in the last 12 years,
6 we've had four international symposiums. There's
7 going to be another one next year on butadiene,
8 isoprene, and chloroprene. None of those issues
9 are dead. There's much scientific debate. Certainly,
10 I wouldn't want to put any of those chemicals into
11 the known category.

12 Let's provide adequate rationale for
13 recommendations at each stage of review, and I
14 suggest that if there's new information, which there
15 is with butadiene, that we reopen the debate. Let's
16 not just put out a document (inaudible) which is
17 out of date. So my suggestion would be to take
18 butadiene and consider it for re-review.

19 I think I'm finished. Thank you very much.

20 **DR. GOLDSTEIN:** Thank you.

21 **DR. FREDERICK:** Bernie, quick
22 clarification point from Bill. Typically, they do --
23 there's a year's notice on the upgrade or downgrade
24 or whatever. Was this one an exception to that?

25 **DR. JAMESON:** It turns out for

1 this particular one, which was reviewed in 1997, the
2 Federal Register announcement announcing the
3 nominations we were going to review that year did
4 not come out until late June of that year. So in
5 this particular case, that's correct. That is an
6 accurate statement.

7 **DR. FREDERICK:** Okay. I just
8 wanted to be sure on that.

9 **DR. GOLDSTEIN:** Our next speaker
10 is Lee Coogan of Sorptive Minerals Institute.

11 **MR. COOGAN:** Good afternoon.
12 My name is Lee Coogan, and I'm the Executive
13 Director of Sorptive Minerals Institute, or SMI, the
14 national trade association representing the
15 manufacturers and marketers of sorptive mineral-
16 based products. These product are widely used as
17 pet litters, filtration aids, and industrial floor
18 absorbents. They're composed primarily of clay
19 minerals with trace amounts of quartz. It is this
20 occurrence of quartz as a minor component in these
21 products that led to SMI's participation in the
22 National Toxicology Program's Board of Scientific
23 Counselors Subcommittee review process for the 9th
24 Report on Carcinogens. These comments are based
25 on that experience.

1 On October 26, 1998, the NTP announced
2 that the Board of Scientific Counselors' Report on
3 Carcinogens Subcommittee would be meeting on
4 December 2nd and 3rd of 1998. The stated purpose
5 of the meeting was the peer review of substances,
6 mixtures, or exposure circumstances nominated for
7 listing in or delisting from the 9th Report on
8 Carcinogens and the provision of the opportunity
9 for public input. While the stated purpose for the
10 December meeting was clear, SMI believes that the
11 NTP process failed to adequately address that
12 purpose.

13 In order for an independent peer review to
14 be full, fair, and effective, a review panel must
15 consider all of the available scientific information,
16 including those materials submitted by outside
17 parties. Only after carefully reviewing and
18 considering all the relative scientific information
19 can the panel make a truly informed decision. SMI
20 believes that the process used in the 9th RoC did
21 not meet the requirements that ensure an informed
22 decision on these issues for the following reasons.

23 Prior to the meeting of the Board of
24 Scientific Counselors Subcommittee, the NTP
25 published a notice in the Federal Register soliciting

1 comments and input from interested parties and
2 promised, and I quote, "another independent peer
3 review group that assesses whether the relevant
4 information available is sufficient for listing in or
5 delisting."

6 Given the date of the Federal Register
7 announcement for the 9th RoC meeting and the time
8 frame for submitting comments, a fair and effective
9 peer review of all the submitted information was a
10 virtual impossibility.

11 NTP requested that comments from outside
12 interested parties be received by November 30th,
13 1998. This was only 39 hours prior to the start of
14 the Subcommittee meeting. As a result, the
15 members of the Subcommittee had little or no time
16 to read the information that was submitted and give
17 the information the kind of careful and critical
18 assessment that is an essential part of a scientific
19 peer review. This fact was confirmed when during
20 the course of the proceeding at least one
21 Subcommittee member commented that they had not
22 had time to review all of the materials.

23 Additionally, presentations made by the
24 NTP staff that had obviously been prepared well in
25 advance of the meeting failed to address or even

1 acknowledge the issues raised in the written
2 comments. SMI has done a great deal of research
3 on crystalline silica over the past 13 years. This is
4 what was submitted (indicating). Due to the timing
5 of the NTP notice, the Subcommittee was given one
6 working day to consider that material. It is not
7 unreasonable to believe that careful consideration
8 of this information may have had a substantial
9 impact on the final Subcommittee recommendations.

10 In SMI's opinion, the peer review process
11 used for the 9th RoC was inadequate and
12 incomplete. The process failed to provide the
13 Subcommittee members with enough time for careful
14 and critical review of the comments received from
15 outside interested parties.

16 It is particularly troublesome that despite
17 their obvious failure to consider all of the available
18 scientific information, the Subcommittee felt
19 compelled to proceed with a vote to upgrade
20 crystalline silica to a known human carcinogen.

21 Due to the significance of this activity, SMI
22 urges NTP to build more time into their peer review
23 process. All of the available scientific material
24 must be carefully reviewed and considered and
25 understood by all of the Subcommittee members

1 prior to the Subcommittee making its final
2 recommendations.

3 Members of the Subcommittee should
4 receive copies of the written documents a minimum
5 of two weeks prior to the scheduled meeting date.
6 This will allow the members a reasonable amount of
7 time for a thorough evaluation of the materials
8 presented. It will also enable them to discuss the
9 material both among themselves and with the
10 presenters during the Subcommittee meeting. Only
11 by making these changes will the NTP process
12 provide the kind of thorough, critical peer review
13 mandated by the Department of Health and Human
14 Services. Without these changes, the review process
15 is, at best, misleading, and the conclusions reached
16 by the Subcommittee will be based on incomplete
17 and poorly understood information.

18 In addition to the submission of written
19 comments, the review process invites interested
20 parties to make oral presentations to the
21 Subcommittee. Unlike the presentations made by
22 the NTP staff members, who were under no time
23 constraint, presentations by interested parties were
24 limited to five minutes. As a result, years of
25 research and pages of scientific information had to

1 be distilled into a five-minute talk. This brief time
2 period is woefully inadequate to discuss complex
3 scientific material.

4 In short, I've been given ten minutes today
5 to tell you what I think is wrong with the NTP
6 process. I was given five minutes to distill this
7 (indicating).

8 SMI recognizes the necessity for time limits
9 on the oral presentation phase of the review
10 process. Nevertheless, the serious nature of the
11 process warrants that presenters are allowed more
12 than five minutes to present their material. If, as
13 SMI believes, the purpose of the review process is
14 to ensure that the members of the Subcommittee
15 clearly, accurately, and completely understand all
16 the information being presented, then additional
17 time must be allowed for questions, answers, and
18 discussion.

19 SMI recommends that the Subcommittee
20 allow a minimum of ten minutes for each party to
21 present their remarks followed by a minimum of five
22 minutes for questions and discussion.

23 Upon the completion of the oral
24 presentations, there is a discussion among the
25 members of the Subcommittee. In the case of

1 crystalline silica, there was a lengthy debate
2 focusing upon concerns raised by two of the
3 Subcommittee members. During that discussion,
4 additional questions were raised that fell outside
5 the scientific expertise of the Subcommittee
6 members. Three experts, who moments before had
7 completed their oral presentations, attempted to
8 answer these questions or provide clarifying
9 information.

10 Their attempts to provide this information
11 was silenced by the Chairperson. In so doing, he
12 effectively indicated that participation in the
13 discussion was limited to the members of the
14 Subcommittee regardless of whether the information
15 being discussed was correct or not.

16 Such an exclusive discussion at this crucial
17 point in the process is unacceptable. It increases
18 the probability that the final vote of one or more of
19 the Subcommittee members will be influenced by
20 inaccurate information. SMI believes that it is
21 essential for the process to allow dialogue between
22 Subcommittee members, NTP technical science staff,
23 and others with technical expertise on the subject
24 under discussion. The Chairperson of the
25 Subcommittee must allow, within reasonable time

1 limits, such relevant dialogue.

2 In terms of the criteria used for listing --
3 and, Mr. Chairman, I'll have to be somewhat more
4 specific here -- in the case of crystalline silica, the
5 NTP nomination to reclassify was based on the
6 recent IARC listing of October 1997. However, the
7 NTP background document failed to accurately
8 represent the IARC finding. An important statement
9 in the IARC listing recognizing the differences in
10 crystalline silica and its potential carcinogenicity
11 was inexplicably omitted from the NTP nomination.

12 The IARC listing included the following
13 statement, and I quote, "In making the overall
14 evaluations, the Working Group noted that
15 carcinogenicity in humans was not detected in all
16 industrial circumstances studied. Carcinogenicity
17 may be dependent on inherent characteristics of the
18 crystalline silica or on external factors affecting its
19 polymorphs," end quote.

20 In the presentation on behalf of NTP, the
21 presenter failed to mention this extremely important
22 qualification. Instead, the presenter stated that,
23 and I quote, "their (IARC's) conclusion was,
24 'Crystalline silica inhaled in the form of quartz or
25 cristobalite from occupational sources is

1 carcinogenic to humans (Group 1)," closed quote.

2 Therefore, while using the IARC listing as
3 the criterion for considering the classification of
4 crystalline silica, the Subcommittee chose to ignore
5 IARC's conclusion that all forms of respirable
6 crystalline silica may not be carcinogenic.

7 While two members of the Subcommittee
8 raised this issue after hearing the oral
9 presentations, the majority of the panel chose to
10 ignore this glaring omission. In the end, the
11 Subcommittee went ahead with a vote to upgrade
12 respirable crystalline silica to a known human
13 carcinogen, without qualification. By so doing, the
14 Subcommittee, unlike IARC, indicted all forms of
15 crystalline silica, including that found in common
16 soil and beach sand.

17 The stated criteria used by NTP for
18 reclassifying crystalline silica was the 1997 IARC
19 evaluation, yet the Subcommittee selectively ignored
20 an extremely important qualification, that
21 evaluation. If the criterion for listing is to be the
22 IARC evaluation, then NTP is obligated to consider
23 that evaluation in its entirety.

24 In collusion, for the reasons I've outlined
25 above, SMI believes that the NTP process failed to

1 fulfill its stated purpose of performing a full, fair,
2 and independent peer review on the nominations for
3 the 9th RoC. It is SMI's hope that as a result of
4 these public meetings, the NTP review process will
5 be improved to allow for a more balanced and
6 thorough evaluation of all the relevant scientific
7 information.

8 Until those thanks can be implemented,
9 however, SMI requests that all previous work on the
10 9th RoC be discarded and that the process begin
11 anew under the improved procedures.

12 Mr. Chairman, thank you.

13 **DR. GOLDSTEIN:** Thank you,
14 Mr. Coogan.

15 Our next speaker is William Kelly from
16 Federal Focus, Incorporated.

17 **MR. KELLY:** Good afternoon. I'm
18 Bill Kelly for Federal Focus. We're a nonprofit
19 research foundation. We're not here on behalf of
20 any particular industry. I want to speak on just
21 one subject, and that's the -- what Congress
22 expected from this document and whether what's
23 being produced is what Congress originally
24 expected.

25 I happened to be a part of the Aspen

1 Toxicology Forum in July, and this issue came up
2 very briefly. I think Roger McClellan actually raised
3 it, if I'm not mistaken.

4 And in the last few weeks, I've gone back
5 and -- gone to the Library of Congress and taken a
6 look at the Congressional background materials
7 there. And I don't have any neat slides or
8 overheads, but I did take the time to set out what
9 we found in a written presentation that's on the table
10 out there. And I'm not going to read that
11 presentation, but I would encourage you all to pick up
12 a copy of it because the attachment to it
13 actually has the language of what we found.

14 And I'm careful to say in there that we're
15 not sure we got everything because when I was there,
16 I noticed that there were hearings materials,
17 for example, in connection with the 1978
18 legislation. There was testimony in hearings
19 presented by NCI and NIH. I took a quick look at
20 that, and I did not see anything on this, but my
21 experience with Congressional materials is that
22 there's usually a lot more there than you get out of
23 just the reports or the floor debate.

24 The primary -- what comes across as a
25 whole when you look at the Congressional materials

1 indicating what their intent was is really an intent
2 that this be a consumer-oriented document. This
3 was intended to be not just a technical document
4 for academics or something that would be done as
5 an exercise for government agencies. It was
6 intended to be something useful to the general
7 public.

8 And the report and the debates talk,
9 actually, about this document allowing people to
10 make decisions about what they would avoid, what
11 exposures they would avoid, what they might be,
12 where they might go. In fact, as far as saying, you
13 know, it should enable them to be able to know
14 that they've had a significant exposure to
15 something, they should go in for medical screening
16 before they get cancer.

17 Now, in order to do that, you have to know
18 what you're looking for and you have to know
19 whether you have actually received a significant
20 exposure to something. That's the conclusion you
21 immediately draw from those sort of statements.

22 So it's surprising when you pick up a copy
23 of the Reports on Carcinogens and right in the
24 preamble you see a listing here -- a statement that
25 a listing here is not intended to indicate that a

1 substance poses a risk for people in their daily
2 lives.

3 Well, I think everybody here knows the
4 difference between the terms hazard and risk, but
5 I'll bet if you went out and asked the man on the
6 street what the difference is between hazard and
7 risk, they'd know that about as readily as they'd
8 know who the 23rd President of the United States
9 was. And I don't know that. Maybe somebody will
10 tell me.

11 So the whole object of the report is to
12 give useful information, and I don't -- I think
13 somebody said it at Aspen. In fact, I think it was
14 somebody from FDA. You could not write in big
15 enough and bold enough issues across the front of
16 the report that this is about hazard only, not about
17 risk, and have people understand that.

18 You need to provide information that will
19 really alert people in a user-friendly way to what it
20 is that's the type of risk. You know, is this
21 dangerous? You know, if they barbecue a piece of
22 meat, is that dangerous, you know, if they eat it? If
23 they go out in their car and if they drive on the
24 road, is this dangerous?

25 Is this only really known to be dangerous

1 for chemical workers in a particular occupation or
2 people who have been exposed in an industrial
3 accident or, you know, miners who have worked at
4 least 20 years under certain conditions? that sort of
5 thing.

6 And when you look at the Congressional
7 history materials, you see that Congress was
8 actually very aware of this, and I was very
9 surprised, given what's in the preamble to the
10 reports about this being only a hazard document,
11 not a risk document, that everything in the
12 Congressional history materials talks about risk.

13 They talk about wanting information on
14 magnitude of risk. They talk about wanting
15 information on significance of exposures, on
16 subpopulations that have unusual exposures. And I
17 think it's quite clear from the context there that
18 they're not talking about subpopulations that have
19 some unusual genetic susceptibility. They're talking
20 about -- and actually give examples, as I recall, like
21 chemical factory workers or workers in the nuclear
22 industry or people who eat fish out of a particular
23 river that has been contaminated with something.

24 So they want information given to the
25 public. Should I really be afraid of this? And if I

1 should, under what conditions should I really be
2 afraid of it? And I think the agency really needs to
3 confront this issue. I've never seen anything from
4 the agency that's confronted this issue.

5 Granted, when you read the specific
6 language of the legislation -- I mean, it certainly
7 can be interpreted to allow the agency to do a report
8 the way the agency has done, a simple list
9 with just known or reasonably anticipated followed
10 by a compendium of information, but I don't think
11 there's enough information, either in the listings or
12 in the -- what they call the profiles later on in the
13 report, to really alert the public and give them the
14 information they need.

15 I think the industry needs to take a really
16 hard look at that, and they need to think about --
17 and they need to respond to it, you know, in a
18 public way and say, "We've looked at this. Here's
19 what we think. We're going to keep doing it for
20 these reasons," or, "We're going to change it for
21 these reasons."

22 Although I don't want to get into specific
23 substances, I would note that just this morning I've
24 heard references to several substances where this
25 type of thing was an issue. This thing is really

1 only a significant risk under certain circumstances
2 or very high exposures or they didn't differentiate
3 between this particular exposure circumstance and
4 that particular exposure circumstance.

5 So I would encourage the agency to
6 confront this issue, and I would encourage them to
7 actually consult what we put together on the
8 legislative history materials, and I would also
9 encourage them, perhaps, to dig a little bit deeper
10 and see if there's anything else there that needs to
11 be compared with what we have dug up so far.

12 Thank you.

13 **DR. GOLDSTEIN:** Thank you,
14 Mr. Kelly.

15 Our next speaker is Richard Carchman from
16 Philip Morris.

17 **MR. CARCHMAN:** Thank you,
18 Mr. Chairman, members of the committee, the
19 audience. Good afternoon. My name is Richard
20 Carchman. I'm here at the behest of Philip Morris,
21 and I think this is a wonderful opportunity for
22 people interested in this area to have time for the
23 kind of participation that I was listening to this
24 morning.

25 I, working for Philip Morris, submitted

1 scientific information to NTP regarding one of the
2 materials that was on the list, and I thought that
3 was a very important process, and I was involved in
4 the December presentation at Research Triangle
5 Park, and I thought, again, this was a very
6 important aspect.

7 And I'm only here not to -- trying not to
8 reiterate many of the things that I've heard already
9 but to try to highlight some points with regard to
10 the process that may not have been touched on, at
11 least as I understood it. So, again, the purpose is
12 for people like myself and the company that I
13 represent to express their views about the process
14 and evaluation criteria.

15 The fact that the NTP may initiate an
16 independent search of the literature and prepare a
17 draft background document, I've heard a lot of
18 commentary in terms of this particular process.
19 And the components of the draft background
20 document, I don't think that I have any difficulty
21 with it. I think it's the right kind of bullets to try
22 to address in arriving at the conclusion based upon
23 some consideration of these types of facts.

24 Now, with regard to the review steps, the
25 primary and secondary reviewers examine the

1 nomination, the literature citations, and the
2 document for completeness and accuracy. Now, the
3 conclusions regarding carcinogenicity in humans or
4 experimental animals are based on scientific
5 judgment. So it's not simply a regurgitation of
6 what some study says or some body or other
7 organization says, but it requires an assimilation of
8 the relevant information.

9 Completeness and accuracy are clearly the
10 foundation for scientific judgment, but integral to
11 that is an ability to critically analyze the
12 information once you have some assurance that it is
13 both complete and accurate because when you have
14 completeness and accuracy and critical analysis, it
15 gives you the best opportunity to apply the best
16 scientific judgment in arriving at a conclusion.

17 Now, I was somewhat bouyed listening to
18 Dr. Frederick when he alluded to the fact, as I
19 heard it, that he simply doesn't rely upon the
20 background document, that he embraces materials
21 that may not have been included, that may be more
22 current. I said: That's good news.

23 Unfortunately, the potential downside to
24 that is that the people out there like myself and
25 others may not have access to that kind of

1 information, nor the process by which Dr. Frederick
2 and/or his colleagues may have used in arriving and
3 utilizing that particular information. With respect
4 to human studies, we provided comments with
5 regard to environmental tobacco smoke, and I won't
6 really spend any time talking about that.

7 I'd like to use as examples within that
8 report some data that was provided in the
9 background document on animal carcinogenicity
10 studies. As it was pointed out by one of the NTP
11 scientists this morning, the background document
12 contains a body of information. There's a summary
13 on the first page that then is a distillation of the
14 background document.

15 If you look at the ETS document from NTP,
16 it speaks to the epidemiology and it speaks to one
17 of the several kinds of animal studies that were
18 referenced in this document, and that was the
19 A/J mouse. Within the background document but
20 not within the summary were two other studies that
21 the background study referred to, some studies by
22 Dr. Hans P. Witschi and from Finch and colleagues
23 at Lovelace.

24 So you have the mouse skin painting, in
25 summary, which is a particulate smoke condensate,

1 the Finch study, which is inhalation of mainstream
2 smoke with tobacco-specific nitrosamine, NNK, and
3 the Witschi study, which is a sidestream/mainstream
4 inhalation study.

5 All three studies had important and vital
6 scientific information in drawing a conclusion. The
7 mouse skin used the smoke condensate. The Finch
8 study used tobacco smoke. The mouse skin
9 condensate was carcinogenic when applied the way
10 it was done there.

11 In the Finch study, NNK was carcinogenic in
12 that mouse model. Tobacco smoke didn't do
13 anything. In fact, at high enough levels, there was
14 a suppression of the NNK-induced lung
15 carcinogenicity, but there was no real discussion of
16 that. The Witschi study was fascinating because
17 this is the first study to demonstrate, by inhalation,
18 increase in lung tumorigenicity in animals with a
19 tobacco smoke surrogate. So you have these three
20 studies.

21 What was missing was a critical analysis of
22 just what was going on because if you look at the
23 Witschi studies, he was able to demonstrate that
24 the gas phase of this tobacco smoke material was
25 totally and wholly responsible for the increase in

1 lung tumorigenicity.

2 Juxtapose that with the mouse skin
3 painting, which is tobacco smoke condensate, which
4 is a totally different material. Though they're all
5 true, true, in some sense, related, any reasonable and
6 thorough scientific analysis would have pointed out
7 some of the difficulties here.

8 So, indeed, if Witschi's work is somehow
9 related to the human smoking experience, it turns
10 on its head the last 50 years of tobacco smoke
11 carcinogenicity. No comment at all on this critical
12 analysis.

13 What was missing from the background
14 document? A publication by Dr. Maronpot, an
15 NIEHS scientist that reviewed the strain A mouse
16 work, an A/J mouse, the model that Witschi used,
17 and Witschi's a coauthor of the Maronpot paper.
18 And they did this review for the NTP, and the
19 conclusion is pretty clear that they think it's an
20 unreliable test to use as a decision-point approach
21 for carcinogen testing. It was not cited in the
22 background report.

23 Within the Witschi study, the background
24 report mischaracterizes the overt toxicity. It said
25 there is no overt toxicity. In the exposure aspect

1 of Witschi's studies, the body weight gain
2 depression was at or above 20 percent, which
3 normally would have invalidated it in an NTP study.

4 Putting that aside, the exposure levels in
5 Witschi's study were 1,000 to 10,000 times higher
6 than anything reported in the EPA ETS Risk
7 Assessment Document, and the A/J mouse -- the
8 animals died from adenocarcinoma of the lung just
9 sitting in the cage, i.e. no exposure. There is no
10 discussion of this at all.

11 And as I said in the last bullet point, the
12 attribution of increased lung tumorigenicity to the
13 gas phase of smoke, in fact, Witschi measured
14 benzo (a) pyrene and NNK, a tobacco-specific
15 nitrosamine, and he basically found and concluded
16 that these could not possibly be responsible for the
17 increased lung tumorigenicity he was seeing.

18 Now, Dr. Steven Hecht, who was a
19 participant in this committee and present at the
20 December meeting and probably one of the world's
21 experts on tobacco-specific nitrosamines recently
22 published a review in JNCI, and this is a quote in
23 reference to the Witschi work:

24 "It was concluded that the vapor phase of
25 ETS is as tumorigenic as full ETS and the

1 responsible agents are not NNK or BaP." These
2 studies require confirmation. That's my
3 highlighting, not his.

4 Remarkable. Again, no discussion, no
5 commentary. These things are included as if
6 they're used in some sort of meaningful, supportive
7 way. Any kind of critical analysis of this would
8 raise some very interesting and important questions.
9 That was not evident at all.

10 Recommendation - that for the background
11 report, we need to make sure it's both complete
12 and accurate. Somehow we need to have critical
13 analysis, a response to the submitted information,
14 which seems to fall into a vacuum, and then
15 justification for the classification system. Since it's
16 not simply based on the background document, what
17 is it based on?

18 Thank you very much.

19 **DR. GOLDSTEIN:** The next speaker
20 is Stephen Lester of the Center for Health,
21 Environment, and Justice. And, again, I'll
22 recommend to the speakers that we stick to general
23 points, not the specific chemicals or specific
24 studies.

25 **MR. LESTER:** Good afternoon. My

1 name is Steve Lester. I'm the Science Director of
2 the Center for Health, Environment, and Justice.
3 Our organization was founded in 1981 by Lois
4 Gibbs, the woman who organized (inaudible) Niagara
5 Falls. Since that time, we've worked with a large
6 network of community-based groups of over 8,000
7 groups. Our primary works involves (inaudible).
8 Before I begin, I'd like to thank the NTP for the
9 opportunity to make these comments and for having
10 this meeting here in the Washington, D.C., area.

11 Like others before me, I'm here today to
12 talk about the listing and delisting procedures, but
13 unlike many others this morning, I'm here to say
14 that I think this is a good process. I think it's a
15 scientifically grounded process, one that is fair, one
16 that is open, and one that provides opportunities
17 for comment. I don't think this process is broken
18 and I don't think it needs any major changes.

19 The most important elements of this
20 process is the need for impartiality and for
21 transparency. The NTP needs to maintain an
22 objective, science-based approach for considering
23 and deciding on the carcinogenic status of a
24 substance.

25 The NTP staff must operate independently

1 and use the best science available to review their
2 chemicals, and they must report results of their
3 evaluation in an open manner that includes
4 providing the basis for their decisions, the
5 information they used for making their decisions,
6 and the process by which they went through to get
7 there. It is our opinion that the current process
8 currently embodies these basic elements and
9 principles.

10 The American people, public interest
11 community, government at the federal, state, and
12 local levels all rely on the decisions made by NTP
13 in deciding the carcinogenic status of a chemical. If
14 this information is questionable or tainted by a
15 relationship with a company or special interest,
16 then the credibility of the agency and its work will
17 be seriously damaged.

18 The NTP staff should examine all of the
19 scientific data and relevant information in deciding
20 whether a substance is a carcinogen. This review
21 should be based on published scientific, peer-
22 reviewed information. There is no place in this
23 process for unpeer-reviewed information or
24 unpublished information.

25 The NTP should explain their decision, list

1 the papers that were relied upon in making their
2 decision, and provide the public with an opportunity
3 to review and comment on this process. We believe
4 the process, as it's currently structured, works and
5 does not need to be changed.

6 We also believe it's important that the NTP
7 staff not make themselves available to special
8 interest groups who have a favorite chemical up for
9 review. There should never be private meetings
10 between NTP and consultants for private companies
11 or industries or special interest organizations.
12 There is no need for it and there's no place for it.

13 Staff at NTP are perfectly capable of
14 deciding, based on the best scientific information,
15 whether a chemical is capable of causing cancer in
16 animals or humans. The decision should not be
17 decided by the pressures applied by industry or
18 pressure applied by special interest groups.

19 The situation that currently exists at EPA
20 should be a lesson learned for NTP. Over the
21 years, the EPA has bent over backwards to work
22 with industry to allow special interest meetings and
23 to allow opportunities for industry to meet with the
24 staff. As a result, the agency has reached a point
25 where they're afraid to make a decision without

1 first speaking with these special interests. I don't
2 think this is in the best interest of the public. It
3 is not how government is supposed to work, and
4 it's certainly not how scientific decisions are
5 supposed to be made.

6 The situation with Dioxin is a perfect
7 example of this problem. In the Fall of 1944, EPA
8 released a health assessment document on Dioxin.
9 At that time, they were deluged and overwhelmed
10 with information from industry and special
11 interests about this report. Since that time, the
12 agency has continued to receive comments and
13 continued to work with all of these special
14 interests. As a result, more than five years later,
15 there is still no final reassessment on Dioxin.

16 The NTP will suffer the same fate if they
17 are not careful. If industry and special interests
18 are allowed routine access to the staff, the process
19 of listing and delisting chemicals will come to a
20 crawl or come to a complete stop.

21 Public interest groups like CHEJ do not
22 have the staff or budgets, as many companies and
23 special interest organizations do, to dedicate to
24 lobbying the scientists at NTP as they try to decide
25 whether a chemical is a carcinogen or not.

1 This decision should not depend on
2 whether someone or some company gets to speak
3 directly with the staff and present special data that
4 only they have access to. The decision on whether
5 to list or delist a chemical should depend on the
6 peer-reviewed, publicly available literature and on
7 the scientific integrity of the staff to examine this
8 information and analyze it and make a decision. As
9 we understand it, this is generally how decisions
10 are now made at NTP, and we would suggest that
11 NTP not change this process.

12 Although there are many aspects of the
13 process that are working well, we have several
14 recommendations. First, we'd like to see more
15 scientists with public interest background and
16 experience be part of the panels and the review
17 committees that are part of this process.

18 We also suggest that the NTP consider
19 involving community activists at some level in these
20 reviews, including, in particular, in terms of priority
21 setting and research recommendations. NTP should
22 not lose touch with the people who are directly
23 exposed to these chemicals.

24 Second, we'd like to see these meetings
25 continue to be held in Washington or perhaps other

1 cities such as New York or Los Angeles or Chicago.
2 NTP should consider having some (inaudible)
3 meetings to see how well this might work. Our
4 organization could not have been here if this
5 meeting wasn't held in this area.

6 In closing, the NTP process for listing and
7 delisting chemicals is a good process. It does not
8 need any major changes. Most importantly, it
9 needs to remain divorced from the influence and
10 lobbying efforts of industry and special interest
11 groups.

12 Thank you.

13 **DR. GOLDSTEIN:** Thank you,
14 Mr. Lester.

15 Our next speaker is Jackie Warren. And,
16 Ms. Warren, I'm sorry. I don't have your affiliation
17 listed.

18 **MS. WARREN:** I'm a member of
19 the public.

20 **DR. GOLDSTEIN:** A member of the
21 public.

22 **MS. WARREN:** Thank you.

23 Ten years ago, I represented the Natural
24 Resources Defense Council and the Environmental
25 Defense Fund as Intervenor in support of NTP when

1 a group of the Synthetic Organic Chemical
2 Manufacturers Association and other industry groups
3 sought to enjoin the publication of the 5th Annual
4 Report on Carcinogens, to stop it from being
5 published. That case raised many of the same
6 issues that are being raised here today. There
7 were then and there still remain very serious
8 questions of public health protection and debate in
9 these issues.

10 And I'm here today just as a private citizen
11 to ask that the NTP give very careful consideration
12 to the adverse impact on the integrity of its
13 scientific judgments that would necessarily follow
14 from the adoption of many of the procedural
15 changes that are being demanded by industry
16 participants at earlier points in this process as well
17 as here today, the kinds of demands that are either
18 blatantly threatening future legal action or by
19 implication doing the same thing.

20 The Sofa (phonetic) case was decided
21 before NTP's criteria for listing were amended the
22 last time around, three years ago. That process
23 has been expanded and opened up since that time.
24 Nevertheless, at that time, the judge in the Sofa
25 case concluded that NTP's then process, which

1 provided multiple levels of review, which is the
2 case now even more, and continuing opportunities
3 for public input was completely consistent with
4 their responsibilities under their statute, was
5 appropriate, and declined to enjoin the publication
6 of the report.

7 But here we are ten years later hearing
8 many of the same kinds of complaints and the same
9 sorts of arguments in suggesting that NTP's process
10 must, in every way imaginable, become a carbon
11 copy of the regulatory process that EPA and OSHA
12 and other regulatory agencies go through in their
13 risk management balancing under their
14 administrative actions.

15 Now, Congress apparently did not disagree
16 we the Soffa Court's decision back in 1989 because
17 (inaudible) NTP's statutory mandates in 1993, they
18 didn't say, "Your process is wrong. It's warped. It's
19 fatally deficient." They said, "Publish your report
20 every two years instead of every one year." That's
21 all they said. You cannot draw a conclusion that
22 the NTP's process is in some way failing this law
23 when Congress so recently took a look at the
24 process and didn't reach that conclusion.

25 Therefore, I think that when NTP listens to

1 what I view as a deja vu kind of attack on the
2 agency's process that they should bear in mind that
3 a process that wasn't as open as this one is passed
4 judicial muster and, also, Congressional scrutiny
5 within the last ten years and that they're under no
6 legal obligation to provide the kind of line-by-line
7 written response to everybody's comments, to
8 provide ever-increasing earlier (inaudible)
9 intervention in the process so that the particular
10 special interests who want to protect their
11 chemicals and keep them, at best, from being listed
12 in the annual report will have even more
13 opportunities to come forward and do that.

14 The purpose of the annual report is
15 informational. If you look at the language of the
16 legislation, you can see that what Congress had in
17 mind was the provision of a source of objective,
18 peer-reviewed information for the public, for
19 government agencies, for health professionals.

20 The statute itself that was enacted in 1978
21 was intended to increase the number of
22 environmental chemicals that were being tested for
23 carcinogenicity. The agency that was given that
24 responsibility is not simply another group of
25 political appointees and career bureaucrats who

1 don't really know what they're talking about.
2 Therefore, we need some outside, very well-
3 informed scientists to tell them what they should
4 do.

5 I mean, these are highly skilled technical
6 professionals whose life's work is the testing of
7 substances for carcinogenicity. When they sit down
8 to look over the list of nominations, they're not the
9 man in the street or the woman in the street.
10 They're people who have a lifetime of
11 carcinogenicity testing behind them to look at, and
12 their conclusions with respect to the substances
13 that they review, I believe, and the court agreed at
14 that time, is entitled to its degree of deference,
15 which we're not seeing in this room, I must say,
16 and I didn't particularly see in the comments.

17 Now, what NTP regards as its particular
18 role is the hazard identification step of risk
19 assessment, but not the risk assessment itself. The
20 Court specifically upheld the propriety of that role
21 under the statute so that NTP is not required to do
22 the quantification or to do the kind of balancing
23 that says, yes, this may be a carcinogen, but let's
24 look at every little aspect that might say it isn't,
25 and, therefore, the benefits don't outweigh the

1 costs that might be imposed on a manufacturer if
2 this would be regulated. Those kinds of arguments
3 are absolutely appropriate at the regulatory
4 agency's venue, but they are not appropriate in
5 front of NTP.

6 I think that the extent of the intrusion of
7 economically motivated pressures into NTP's
8 process, which should be, really, a purely scientific
9 process, has been a subtle but gradual shift of the
10 burden of proof away from the chemicals and onto
11 the public. The result of this is that many
12 substances to which people are presently exposed
13 continue not to be either listed or, therefore,
14 regulated or the exposures continue. And that, to
15 me, seems to be the antithesis of public health
16 protection.

17 It may be that some statutes exist that say
18 when NTP puts a substance on their list,
19 informational requirements have to be taken under
20 OSHA or (inaudible). Those are informational
21 requirements, however, but the actual regulation
22 requires that these regulatory agencies do a cost
23 benefit analysis and take into account all of the
24 kinds of factors that are not appropriate for
25 deciding whether the hazard exists in the first

1 place.

2 And over the ten years, watching what's
3 been happening here, it seems to me that NTP is
4 really not resolving the (inaudible) uncertainties in
5 favor of protecting public health anymore, that
6 when a substance is reviewed and mechanistic
7 information is brought forward and there's
8 controversy among the scientists, why should that
9 substance be delisted when there's a debate in the
10 scientific community?

11 Seems to me that once they're on the list,
12 once there was a consensus that a substance posed
13 a threat of cancer to humans, there ought to be
14 compelling evidence that it is not to be a human
15 carcinogen and will not be rather than taking it off
16 on the basis of unproved theories for which there
17 isn't a consensus in the scientific community and
18 then simply waiting until the human data come in
19 15 years from now showing that, in fact, it was a
20 human carcinogen.

21 Many of the substances that are known
22 human carcinogens were positively carcinogenic in
23 animals before we had human data. All of the
24 substances which we know are human carcinogens
25 are also positive in animals. That's the reason for

1 the whole premise of the NTP's criteria, which is if
2 the substance causes cancer in animals, it is likely
3 to cause it in humans. And to err on the side of
4 the chemical in the face of questionable and
5 controversial information seems to me to be a
6 retreat from the obligation and the mandate that
7 NTP has had in the past.

8 In my testimony, I spoke to some specific
9 substances, which I won't do here, but I will say
10 that I feel really strongly that NTP should not
11 further compromise the scientific objectivity of its
12 process. Just to look at the list of speakers today
13 indicates who is knocking on NTP's door regularly,
14 has already been allowed into the process more
15 than I personally think they have a right to be and
16 want to be even further involved.

17 They already have multiple levels of public
18 opportunity. They'll have another opportunity at
19 the regulatory agency if and when the substance is
20 regulated, but they certainly have already, in my
21 opinion, adversely affected the perceived scientific
22 objectivity of the NTP to some extent, and that is
23 because of the adoption of criteria which are based
24 on unproven theories and controversial approaches
25 to interpretation of data.

1 That kind of involvement has already
2 seriously compromised the public credibility of the
3 National Academy of Sciences. Now, their review
4 panels have conflicts of interest which are not
5 public and which occasionally get out into the
6 press, doing great damage to the objectivity of the
7 National Academy of Sciences. I would not like to
8 see this process (inaudible) at all, but I think that
9 it's very important that NTP do everything it can to
10 avoid that same kind of result.

11 I also think that the industries potentially
12 affected by the proposals within the 9th Report
13 have readily acknowledged in one of the ten
14 signature letters that went to Dr. Olden that the
15 potential marketplace impacts of these decision
16 weigh heavily in the balance for them. Well, the
17 potential public health impacts weigh heavily in the
18 balance for all the rest of the people in this
19 country who deserve to have these reports prepared
20 and circulated around to them, the way Congress
21 intended.

22 One of the speakers said, if you looked at
23 the legislative history, if you look at what the
24 statute says and what the last judicial review of the
25 agency's mandate showed, NTP is doing its job

1 properly and it should continue to do so.

2 **DR. GOLDSTEIN:** Thank you.

3 Our next speaker is Carolyn Nunley of
4 Consumers Union, Public Service Projects.

5 **MS. NUNLEY:** My name is
6 Carolyn Nunley, and I'm with Consumers Union, an
7 independent, nonprofit testing and consumer-
8 protection organization and publisher of Consumer
9 Reports Magazine.

10 In the 14 years that I've worked on toxics
11 issues, I've conducted substantive research on the
12 toxicity of commercial chemicals, how they're used,
13 and the level of exposure that such use generates.

14 I'm continually struck by the lack of
15 publicly available information on both use and
16 exposure and toxicity. The Report on Carcinogens
17 is one of the few readily available sources that
18 offers a broad, independent view of the extent of
19 knowledge that exists on potentially carcinogenic
20 compounds.

21 A chemical's listing is not an end but a
22 beginning, a place to start if you're looking for
23 information on the risks associated with a chemical.
24 The Report on Carcinogens flags those chemicals
25 that may pose cancer risks so that agencies charged

1 with managing such risks and members of the
2 public can map a course for whatever further action
3 may or may not be warranted, be it further
4 investigation, regulation, or other types of action.

5 I have three basic points to make in my
6 comments today. One, the Report on Carcinogens
7 in its current form works well and should not be
8 significantly changed. Two, as its mission is to in
9 form and educate rather than manage and
10 regulate, the listing process ought not be
11 encumbered by stakeholder involvement of the
12 nature that is more appropriate for regulatory
13 decisions.

14 While we are among the strongest
15 advocates for openness and transparency, we
16 believe that the process already allows for a
17 tremendous amount of public participation in a
18 manner that's both efficient and sufficient given the
19 fact that risk management decisions are made
20 elsewhere.

21 And, finally, because the Report on
22 Carcinogens is such an important resource for the
23 public, to subject it to the bias of parties that have
24 a commercial interest in spin-doctoring chemical
25 listings would, essentially, destroy one of the few

1 useful resources whose purpose is solely to inform
2 the public.

3 With over six trillion pounds of some
4 77,000 chemicals in US commerce today, almost
5 none of which have been adequately characterized
6 as to their potential toxicity, it's critical that we
7 haven't an efficient, expedited means for identifying
8 the known and possible cancer hazards that
9 selected, well-tested chemicals may pose.

10 Many of us in the public interest
11 community count on NTP to provide a document
12 that reflects the scientific landscape in a way
13 that's not censored by those who have a commercial
14 interest in minimizing or obfuscating the evidence.
15 This is particularly important since to develop such
16 a compilation from the literature would be
17 impossible for most public interest groups that have
18 limited staff, resources, and access to the
19 literature.

20 The proposal put forward by some industry
21 representatives to expand the level of review and
22 reporting to include more active participation of
23 affected industries in the listing decisions is
24 disconcerting.

25 Looking back to the time when

1 carcinogenicity of chemicals like asbestos and vinyl
2 chloride were the subject of debate, the affected
3 industries repeatedly refused to face the
4 uncomfortable fact that these chemicals caused
5 serious health effects in humans as well as
6 laboratory animals. Nonetheless, industry already
7 has a place at the table with at least one
8 representative on the Board of Scientific
9 Counselors, and we feel that's more than sufficient.

10 With all due respect to the need for
11 scientific debate, we believe the strongest impulse
12 of economically affected parties is to emphasize
13 uncertainties and block consensus, delaying listings
14 and the associated bad PR for as long as possible.
15 The plain truth is that for most substances listed in
16 the Report on Carcinogens, there's already
17 consensus, at least among non-economically
18 interested experts. There comes a time when
19 enough debate is enough.

20 Unlike regulatory decision-making, the
21 decision to list a chemical in the Report on
22 Carcinogens does not in itself constitute a
23 regulatory action. Often, experts within the
24 regulatory agencies have already developed
25 extensive risk assessments on chemicals before they

1 are listed in the Report on Carcinogens.

2 It's up to other agencies and their
3 respective risk management decision-making
4 processes, which are political as well as scientific
5 in nature, to decide what action to take. Congress
6 no doubt recognized this distinction when it chose
7 to place the listing authority in the hands of NTP
8 scientists rather than a regulatory agency.

9 Interested parties should lobby the specific
10 regulatory agency about whether or not action
11 should be taken on the basis of the facts
12 referenced in the Report on Carcinogens, not the
13 NTP, about whether the chemical should be listed in
14 the first place.

15 The Report on Carcinogens listing process
16 is one of hazard identification, not risk assessment.
17 It is simply an admission of research findings that
18 suggest that a chemical may cause cancer. Given
19 that any method for identifying potential
20 carcinogens necessarily reflects the many
21 uncertainties in the existing data, it's critical that
22 those engaged in the activity are not influenced by
23 commercial interests in delaying or preventing such
24 a conclusion.

25 Congress knew what it was doing when it

1 made government, and government alone,
2 responsible for hazard identification, thereby
3 drawing a distinct boundary between the scientific
4 process of reviewing the knowledge base and
5 summarizing it for public consumption and the
6 political process of deciding what action such
7 information warrants.

8 It's interesting to note that so many
9 petitioners who expressed a problem with the
10 current NTP approach are those organizations that
11 have a commercial interest in keeping chemicals off
12 the list. We, therefore, strongly object to any
13 changes that would be made solely for their
14 benefit.

15 Let us not forget that the Report on
16 Carcinogens is a product of Congress's passage of
17 the Toxic Substances Control Act in 1978, following
18 on the Nixon Administration's War on Cancer
19 launched in 1972. As that war is still far from
20 won, we need to maintain, if not strengthen, our
21 vigilance to identify and characterize compounds
22 that may be contributing to this trend.

23 The Report on Carcinogens in its current
24 form is one important tool that helps us bring
25 chemicals that may be harmful into focus, just as it

1 helps steer us away from wasting precious research
2 and regulatory dollars on controlling substances for
3 which the evidence suggests no risks.

4 In our view, this review process must not
5 be hindered. The more chemicals that undergo NTP
6 review the better. The Report on Carcinogens
7 offers an efficient approach to identifying chemicals
8 that warrant further action. It's also a flexible
9 document that allows for listing decisions to be
10 revisited in light of new information.

11 To subject this process to more lengthy,
12 encumbered politics of further committees and
13 analysis would defeat its purpose in being a
14 reliable, timely report with which to begin the more
15 political process of deciding how to assess and
16 manage risk.

17 Just a few years ago, these listing criteria
18 were reviewed and changed. Presumably that
19 process was open and transparent and enjoyed
20 broad participation from a wide range of
21 stakeholders. Yet, somehow we find ourselves here
22 again, just three years later, to reopen the debate
23 simply because a group of economically affected
24 parties don't agree with some of the new listings.
25 It makes one wonder if we will all find ourselves

1 here again after the next Report on Carcinogens is
2 issued, suffering through this time- and resource-
3 wasting debate endlessly, unless or until no
4 commercial chemicals remain on the list.

5 But as we've learned from chemicals like
6 asbestos, PCBs, and lead, an ounce of prevention is
7 worth a pound of cure. It's society that has to pay
8 for that pound; yet it's often industry that refuses
9 the ounce. That's why we need tools like the
10 Report on Carcinogens to identify carcinogens, if
11 possible, before they saturate the chain of
12 commerce.

13 The information in the Report on
14 Carcinogens isn't earth-shattering. It's, basically,
15 information the government and the scientific
16 community already know. The public has a right to
17 this information as well. The Report on
18 Carcinogens provides it in a clear, digestible, not-
19 hard-to-understand prose with appropriate caveats
20 as to its tentative nature. For the public and
21 Congress, this is no small benefit. To quote
22 Thomas Jefferson, "Only an informed public can be
23 trusted to govern itself."

24 What we think we see here is the affected
25 economic interests objecting to the bad publicity

1 attendant to seeing their chemicals listed this way.
2 Their tactic is to attack the basis of the listing as an
3 unfair result of a flawed process. We think the
4 words of another president probably fit the
5 industry's campaign here: Self-delusion in face of
6 unpleasant facts is folly, Ronald Reagan.

7 Regardless of how noble and reasonable
8 they try to make it sound, good science, peer
9 review, open process, transparency, let's not forget
10 that the goal of the petitioners here is to prevent
11 the public from getting information. That's
12 profoundly undemocratic, and NTP should resist the
13 impulse to go along with this unreasonable request.

14 Thank you very much.

15 **DR. GOLDSTEIN:** Our next
16 speaker, our last speaker before the break, is Barry
17 Castleman, who will be taking the place of Jane
18 Williams of California Communities Against Toxics.

19 **MR. CASTLEMAN:** Thank you. I'm
20 an environmental consultant. My background is in
21 chemical engineering, and I'm here to speak with
22 the people from the various public interest groups
23 and consumer protection groups to urge that the
24 Report on Carcinogens be kept where it is, where
25 it's least endangered by improper corporate

1 influence.

2 The pressure to move this to the National
3 Academy of Sciences or the EPA Science Advisory
4 Board or the International Agency for Research on
5 Cancer that's coming from the industry and public
6 interest groups are consistent in wanting the
7 current process retained and protected. NIEHS has
8 a more open process than groups like the National
9 Academy of Sciences and, certainly, the
10 International Agency for Research on Cancer.

11 In the case of butadiene, the International
12 Agency for Research on Cancer meetings were
13 highly improper. There were two votes held on the
14 classification of carcinogenicity of this major
15 industrial chemical. The first vote, by one vote it
16 was decided that butadiene would be graded as
17 Class 1 by IARC as a human carcinogen.

18 Subsequent to that, one of the people who
19 was present -- one of the experts who was present
20 had to leave. That evening, a bunch of lobbying
21 went on and an additional vote was held the next
22 day, and at this point the votes were by one vote
23 in the other direction. One person, I believe, was
24 persuaded to change his vote. When the Chairman
25 of the IARC panel asked that this be disclosed in

1 the IARC publication on butadiene, this was
2 disregarded by the staff at IARC, including
3 Americans who happened to be on the staff at
4 IARC.

5 So I don't think that this is a model that
6 we want to follow or rely upon too much if we
7 have more open and public process for evaluating
8 carcinogens. The meeting at IARC was also heavily
9 loaded with people who were representing the
10 affected industries who were there as observers by
11 IARC.

12 There have also been criticisms about
13 IARC's handling of (inaudible), another major
14 industrial chemical used in gasoline, and the
15 deletion of certain important animal studies in the
16 IARC review on that chemical. Conflict-of-interest
17 information received by IARC, by the experts who
18 serve on IARC panels, is not publicly available.

19 I've been following these kinds of activities
20 with the international agencies, the World Health
21 Organization, the International Labor Office, the
22 International Program on Chemical Safety, and with
23 Dr. Richard Lemmon I've authored an editorial called
24 "The Manipulation of International Scientific
25 Organizations" that was published last year in the

1 International Journal of Occupational and
2 Environmental Health. And it's usually the process
3 that is at issue where the process is being grossly
4 manipulated by financially interested parties, as Dr.
5 (inaudible) used to call them.

6 At the EPA Science Advisory Board, I
7 understand that participants disclose their potential
8 conflicts of interest and then go ahead and vote
9 anyway. I think that the industry preference for
10 the National Academy of Sciences, for the EPA
11 Science Advisory Board, and the International
12 Agency for Research on Cancer, as venues preferred
13 for evaluating carcinogenicity, reflects that the
14 industry has greater ability and access to influence
15 those so-called expert panels in those other venues
16 than they had with the civil service and open
17 public process of NIEHS.

18 And I guess I would only have to conclude
19 that it's a shame that David Rall can't be with us
20 today because I believe that he would also agree
21 that this is yet another wave of corporate influence
22 trying to overwhelm our democratic processes and
23 expose the public to more carcinogenic agents for
24 financial reasons.

25 Thank you.

1 DR. GOLDSTEIN: Okay. Well,
2 we've got a break coming up, and we're scheduled
3 to come back at, I guess, 3:20. Our first speaker
4 may or may not be here. Is Joe Shapiro here?
5 We'll be --

6 SPEAKER: I could probably do it
7 for him.

8 DR. GOLDSTEIN: You have his
9 material?

10 SPEAKER: I do.

11 DR. GOLDSTEIN: Okay. So we
12 will start at 3:20 with --

13 DR. FREDERICK: -- with a
14 discussion. We're doing the discussion first.

15 DR. GOLDSTEIN: I'm sorry.
16 You're right. We will start at 3:20 with discussion.
17 (WHEREUPON, a break was taken from 3:00 p.m. to
18 3:20 p.m.)

19 DR. GOLDSTEIN: Let me make a
20 couple of points about the discussion. I think the
21 format -- from talking to people around in a very
22 informal way, the format seemed to have worked
23 reasonably well this morning, so we'll try to
24 reproduce that.

25 We're going to first ask the NTP folks if

1 they have any real clarifications. Then I'll turn this
2 over to Clay and to Lynn to see if they've got some
3 specific themes they think they want to go over.
4 I've got a whole bunch that seemed to have been
5 developed, but we'll primarily depend upon the
6 discussion here.

7 Let me make a few points about that
8 discussion. Again, I would hope that we do not get
9 into the chemical-specific, study-specific kind of
10 issues. We really are focusing on a process here,
11 and the motive of what we're doing is to improve the
12 process.

13 I think that's the only motive that ought to
14 be discussed here. I don't think it's helpful to
15 discuss or try to impugn motives to everyone as to
16 why they're doing this or not doing this. So let's
17 focus it on the motive of trying to get things
18 better.

19 Let me turn it over to George. Do you
20 have any comments at all or any clarifications?

21 DR. LUCIER: None.

22 DR. GOLDSTEIN: Fine.

23 Okay. Lynn, Clay?

24 DR. GOLDMAN: Okay. I thought,
25 actually, in the last series of comments -- probably

1 many of you appeared to be sleeping (inaudible),
2 but I thought in the last series of comments there
3 were a number of speakers and, really, coming from
4 different points of view, on the one hand from the
5 point of view of the tobacco industry in terms of
6 the listing for tobacco smoke, on the other hand
7 from the point of view of some of the public
8 interest groups, that there was some interesting
9 issues that I'd like to hear more discussion on with
10 respect to the whole -- kind of the guts of what the
11 process should be about in terms of not only
12 documenting the initial scientific analysis that is
13 done, which is clearly done very well, that, you
14 know, that is provided, not only providing the
15 comments that are received from members of the
16 public at all stages, and, clearly, that's provided,
17 but also then whether or not the process should
18 include, you know, the kind of process that you see
19 in rule making, for example, where then each of
20 those comments is formally responded to and
21 there's an opportunity for everybody to get kind of
22 a formal response back.

23 And I really was very interested and it
24 made me realize there really is a difference
25 between an agency like the NIEHS that's a part of

1 the NIH Scientific Research Agency and, you know,
2 obviously, Congress putting this process there and
3 not at the individual regulatory agencies.

4 It didn't say: EPA will do this for the
5 ones it regulates and FDA for the ones it regulates
6 and OSHA for the ones it regulates. It said that
7 this would be, really, housed in or coordinated by,
8 because there's a lot of participation from any of
9 those other agencies, the NIEHS.

10 And, you know, when you do science in a
11 regulatory context -- and when I was at EPA, it was
12 in the context of, for my office, either the Toxic
13 Substances Control Act or (inaudible). You not
14 only have to get the science side, but there's also
15 a tremendous amount of process and procedure that
16 you have to get right.

17 And we knew, for example, under TSCA
18 that if we did a rule where -- I mean, all the
19 science might be correct in the rule, but we failed
20 to, say, respond to every comment or we failed to
21 have proper docketing of every study, even if those
22 comments or those studies were not even germane
23 to the decision, even if, from a scientific
24 standpoint, those were not important in terms of
25 the ultimate judgment, that could have returned the

1 decision because in a legal context, and which is
2 where you operate with rule making, in a legal
3 context, I hate to say this, but, you know, process
4 is actually sometimes more important than the
5 substance, but that's not where this activity was
6 placed. It was placed in an agency where, you
7 know, substance wins out over process in a sense
8 where science comes first.

9 So in listening to discussion, I really had
10 -- you know, I didn't have any question at all,
11 especially after Jackie Warren's presentation about
12 what the intent of Congress was to have been,
13 because she gave a very compelling argument, and
14 maybe there are other lawyers here who could
15 argue against, but she gave a very compelling
16 argument that, in a sense, it had already been
17 argued out whether or not, you know, a regulatory-
18 type process is required, and it's not, but then even if
19 it's not required legally, what would be the
20 benefits of having, you know, a process that looks
21 more like that, and, also, what would be the
22 problems with it?

23 And I guess one thing I really worry about
24 a lot, from some of the things I heard, particularly
25 from some of those on the industry side, is just,

1 you know, my sense that it's a tremendous amount
2 of time and resources to do those very meticulous
3 kinds of notice and comment processes.

4 At EPA, one of the major costs in rule
5 making was just that piece of, you know, every
6 single comment that came in, you know, docketing,
7 responding, having lawyers review it, frankly, you
8 know, and all of that is an enormous amount of
9 effort.

10 And I just thought it would be useful to
11 hear a little more from people about, you know,
12 why -- you know, if that's what they're looking for,
13 why they'd want something like that, how they think
14 it would actually improve the scientific process. As
15 you can probably hear, I'm pretty dubious about
16 that, but, you know, whether this would truly be
17 enough addition of value in that that it warrant the
18 effort.

19 **DR. FREDERICK:** Let me pick up
20 on what Lynn was saying. This process is clearly
21 focused on the substance of the science. And I
22 participated in the reevaluation of the listing and
23 delisting guidelines a few years ago, and we
24 intentionally wrote those -- the group worked with
25 George and others, (inaudible), who we wanted

1 these guidelines to be guidance to bring in the full
2 body of information.

3 Quite honestly, from industry's perspective,
4 there's a real opening there for doing good-quality
5 science to effect these listings. It's not taken
6 advantage of nearly as often as it should by
7 industry. There's a clear opening there to put
8 good-quality science on the table to support
9 the position that industry is taking, and this could
10 involve very new technology.

11 It wasn't even in -- it was not more than a
12 twinkle in our eyes back when we wrote those
13 listing and delisting provisions years ago.
14 (Inaudible) technology certainly holds a lot of
15 power with regard to the (inaudible) expression of
16 many genes at the same time as a manifestation of
17 a toxic response or to say that there's not a toxic
18 response, either way.

19 But the point is that this is a scientific
20 evaluation. It's not a rule-making process. I've
21 participated in EPA peer reviews from time to time.
22 That's a very different sort of thing. Takes a lot
23 more time. There's a lot of wordsmithing involved
24 and all those sorts of thing.

25 In this process, you look at the body of

1 information and you form an opinion, yes, no, up or
2 down. We don't wordsmith. We don't get into all
3 the nuances of what goes on in a regulatory
4 agency. It's just a recommendation (inaudible) on
5 what the clear scientific signal is on the motion on
6 the table. Is it a probable human carcinogen? Is
7 it a known human carcinogen? That's all.

8 Now, I'd like to come back to a couple of
9 the comments that were presented because they
10 bring up some important points. Michael Bird's
11 presentation -- Michael, the background document is
12 not an all-important document. It may be an
13 all-important document to some people on the
14 outside who are looking at it and want to focus on
15 it and obsess on it, but it's not an all-important
16 document. It is a part of the information on the
17 table that's evaluated with regard to the decision-
18 making at hand.

19 There is a full body of information there,
20 and it includes all the outside comments that come
21 in and all the papers we look up, all the peer
22 review papers, the full listing of the IARC listing, if
23 we want of go back and look at that. It's the full
24 body of information on the table. There's not one
25 piece that's all-important. It's the full body of

1 information on the table, and I think it would be
2 inappropriate to describe the background document
3 as being all-important.

4 And this is really highlighted when we get
5 to Richard Carchman's comments with regard to
6 picking one element of the background document on
7 one specific listing discussion, which happened to
8 be on environmental tobacco smoke, and what you
9 did there was focus on one aspect of the animal
10 data that, from my perspective, was totally
11 incidental to the meat of the discussion at hand.

12 It's well acknowledged that the animal
13 models are very poor with regard to tobacco smoke
14 for a variety of different reasons, which I won't go
15 into, but the point is that the meat of discussion
16 really related around other aspects of the scientific
17 information.

18 And to focus on not only -- you know, just
19 one aspect of this background document and say
20 that the whole process is flawed because you
21 picked one, more or less, incidental element of
22 something that was discussed there is just an
23 inappropriate characterization of the decision-making
24 process.

25 And I think it's the sort of thing that Lynn

1 got into on this notice of rule making and getting
2 tripped up because you didn't appropriately respond
3 to some insignificant detail along the way. We're
4 clearly looking at the important scientific signal on
5 the problem at hand, the full body of evidence that
6 relates to that. And if the background document
7 doesn't handle something properly or is
8 insignificant, then we can generally deal with that.

9 I'd like to come back to one thing. Susan
10 Nathanson and William Kennedy brought up some
11 points with regard to pharmaceutical agents that
12 particularly focused on Tamoxifen. What I'd like to
13 say, and is this is something that was discussed by
14 the board at the time we discussed Tamoxifen, is
15 it's clearly a problematic area. It was discussed as
16 a problematic area.

17 There are a variety of pharmaceutical
18 agents, immunosuppressive agents, that sort of
19 thing, that are very important, very useful. Some
20 of these can induce secondary cancers, and if
21 they're placed before us, we have to respond to
22 that issue.

23 I think there's a legitimate question on
24 whether we should be evaluating those materials,
25 and if we evaluate those materials and respond to a

1 scientific signal with regard to carcinogenic risk,
2 then how that information should be communicated
3 to the public.

4 And I think we all have some concerns in
5 that particular area because this is an advisory
6 document, and I would certainly urge Ken Olden and
7 NTP staff, even as we did in the discussion on
8 Tamoxifen, to try to find the way to appropriately
9 communicate this information to the public because
10 we want to do the right thing. It's not to just
11 follow some written process and have some
12 negative consequence.

13 I think that's -- those are all my comments.

14 **DR. GOLDSTEIN:** Okay. Thank
15 you.

16 I'm going to suggest, to start with, that we
17 focus on what Lynn has brought us into. That's
18 sort of an underlying issue. Should the general
19 approach be changed into more of a regulatory, if
20 you will, approach, for want of a better term? If
21 that were to happen, then the whole discussion that
22 Clay just had about the background document would
23 inevitably change. So this would be central to us
24 of the issues.

25 There's a number of the people who have

1 presented a number of the documents which point
2 out that the NTP listing has implications as strong
3 to their particular products as does a regulatory
4 agency's action. There are others who have been
5 here who pointed out -- who, basically, strongly
6 said that, no, this should be kept as a scientific
7 approach by the National Toxicology Program's
8 group of scientists and only have this relatively
9 minimal, compared to IARC or EPA, review of the
10 Board of Scientific Counselors. So that seems to
11 be a generic issue. Anybody want to comment on
12 that, speak to that?

13 Sara, please give us your name.

14 **MS. SCHOTLAND:** Sara Schotland.
15 I am Counsel to CMA's Ethylene Oxide Industry
16 Council. I do want to respond to Dr. Goldman's
17 points.

18 Let's not set up a false dichotomy
19 between process and science. Process need not be
20 the enemy of science. On the contrary: Good
21 process leads to good science.

22 If, referring to something that Clay
23 Frederick alluded to earlier, the decision is made to
24 take mechanistic data into account in considering
25 whether to upgrade or downgrade a chemical, there

1 may be a question as to whether (inaudible) market
2 data justifies upgrade or whether it doesn't. It may
3 be questionable to the extent to which human
4 genetic studies versus animals genetic studies are
5 relevant. These are scientific issues and (inaudible)
6 should be encouraged.

7 Now, I understand Dr. Goldman has a
8 concern and NTP must surely have a concern not to
9 be dragged into the kind of lengthy process that
10 has made it so difficult and so burdensome for EPA
11 and OSHA to issue standard-setting rules.

12 Again, let's not make a false dichotomy
13 between the current status quo of virtually no
14 meaningful process and going into a 400-page
15 regulatory justification needed for an OSHA
16 standard. That's not the necessary conclusion.

17 EPA's SAB and EPA's (inaudible) Committee
18 give a better opportunity for all different sectors
19 to present their comments. They respond on
20 numerous occasions. There's more of an iterative
21 opportunity. They consider maybe four substances
22 in a day rather than eighteen.

23 This is the kind of compromise model
24 which would provide better process, giving greater
25 acceptance to the decisions, and I think actually

1 reducing your legal burden because it would reduce
2 the vulnerability on judicial review.

3 Let's not forget that, in fact, the minute
4 NTP makes a classification decision, it has the
5 impact of a rule because it is absolutely mandatory,
6 mandatory on our clients to change the OSHA
7 hazard communication and to change EPA community
8 right-to-know.

9 This isn't some voluntary little thing that
10 we do because we think it may or may not be
11 appropriate. We are required. It has a regulatory
12 impact, and if you click on the NTP website, NTP is
13 proud of the use to which its classifications of
14 carcinogens are put and recognized. So it's used
15 for OSHA and community right-to-know purposes.

16 I want to also make a comment, again, on
17 SAB. It provides an instructive model about the
18 role of industry science. I cannot emphasize
19 enough how inappropriate I find disparaging
20 attacks on industry science. It is just as
21 inappropriate as it would be to disparage the
22 contribution of the scientists from the
23 environmental movement or to denigrate the
24 government scientists, any one of whom can have
25 problems with their credibility, can appear to have

1 their own axe to grind, but that applies to lawyers,
2 scientist, doctors from all different sectors.

3 The EPA Science Advisory Board invites the
4 participation of qualified scientists. The scientists
5 it's been my privilege to be associated with in
6 industry, when they serve on these kinds of panels
7 and present to these kinds of panels are terribly
8 important to -- terribly conscious of the need to be
9 credible. In many instances, they are the authors
10 of peer-reviewed published literature. I know with
11 ethylene oxide, the scientists my client presented
12 were leaders in the field on that subject, including
13 one who's now at EPA.

14 So I absolutely reject disparagement of the
15 contribution of industry scientists, and I really think
16 that we have to move beyond the black hat/white
17 hat and say that there ought to be, instead, a
18 balanced sector representation both on the Board of
19 Scientific Counselors and that we should welcome
20 stakeholder efforts to improve the process and
21 stakeholder involvements to provide comments, as
22 the OMAN (phonetic) Commission on Risk
23 Assessment has recommended.

24 Thank you.

25 **DR. GOLDSTEIN:** Are there other

1 comments on the subject of the extent of
2 stakeholder involvement and the process?

3 **MR. AUERBACH:** My name is
4 Martin Auerbach (phonetic). I represent the makers
5 of Sweet-N-Low from time to time, but I'm also a
6 father. I'm also a consumer, and I live in America.

7 And, first, I'd like to thank all of the
8 people from NTP for taking the time to have this
9 kind of forum, and I know that this forum was
10 expanded from its original one day to two days,
11 and I think that's reflective of what I think the best
12 of all the comments I've heard here today were
13 about.

14 I think there's actually a surprisingly large
15 degree of common ground between industry and
16 between those who appropriately believe that they
17 are representing the public of America, and that is
18 how the process of analysis and review becomes an
19 open and fully credible process so that the very
20 significant impacts that a listing or delisting
21 decision by the NTP has, whether they are technical
22 or simply practical or fully the result of a balanced
23 process.

24 And, you know, for us as an industry
25 member, we were quite pleased that RD1 and RD2

1 and the Executive Committee all voted in favor of
2 delisting, and we were dismayed that the BSC
3 process seemed to be a rushed process. It seemed
4 to be a process in which although we had made a
5 submission a year in advance, most of the people
6 who were called upon to deliberate were only given
7 the briefest period of time to review the material,
8 and the actual discussion session was so
9 compressed and so abbreviated that the kind of
10 dialogue that has existed here today on the process
11 didn't exist on complicated scientific issues that go
12 on and have gone on for over a century.

13 Now, we take great comfort in the fact that
14 there is a final review process and that all of the
15 other input within the organization will be
16 ultimately reviewed by variable scientists, but I do
17 think that everybody benefits from having a process
18 that everybody can unequivocally acknowledge is
19 one that takes a due amount of time -- and here
20 it's two days instead of one day to hear the
21 comments.

22 If we're talking about two weeks or a
23 month before a BSC hearing or meeting takes place
24 so that people really have an opportunity to reflect
25 so that we never hear, as we've heard today, that

1 on some issues, members of the panel were
2 ultimately called upon to vote and do vote say that
3 they haven't really had time to review and
4 understand the issues.

5 So I think there's actually a lot more
6 common ground here than would ordinarily is
7 perceived by the people who come from either the
8 environmental side or come from the industry side.
9 We are actually all living, breathing human beings
10 in this society, and we really do have a lot of
11 common ground, and I welcome this opportunity to
12 share that thought.

13 **DR. MIRER:** Frank Mirer again.
14 Just a couple of points brought up by the
15 discussion on the process issues.

16 First, Mr. Coogan and I had a long
17 discussion of a misquote from the IARC document
18 on silica, and the fact is that when we review these
19 things, we have the IARC document in front of us,
20 and I reviewed the IARC document on silica, which
21 has been an interest of mine since '75, when I first
22 walked through a (inaudible) representative
23 boundary. And I think we're hearing exactly what
24 the problem is with excessive concern for the
25 process, like a little quote being used to try and

1 discredit the effort of the whole review committee.

2 I don't think anybody on the committee
3 who does these reviews would object to getting the
4 review material earlier, having more time to work
5 on it, but there has to be -- I think there's a
6 rhythm on which these things work.

7 And the fact is, again, the background
8 document is a layering on top -- usually, on top of
9 IARC, which is a pretty complete review, which has
10 been available to people for quite a long time
11 before.

12 With regard to the saccharin issue, which
13 was just raised and we shouldn't be talking about,
14 let's talk about the impact of the process. I was
15 prepared to vote for the listing of saccharin until I
16 read the review materials and saw that the picture
17 of the epidemiologists was substantially different
18 than you think it is when you haven't read the
19 individual papers and had the analysis done in the
20 committee.

21 And those of us who recall that, there was
22 an extensive -- I think we're not talking about a
23 five-minute presentation by Dr. Cohen. He went on
24 for quite a long time presenting his life's work -- or
25 not his life's work but a major piece of work as a

1 major advocate of saccharin not posing a risk to
2 people.

3 So I think that what we're getting here is a
4 very consistent negative, incorrect picture of the
5 degree to which the Advisory Group gets the
6 information, works on the information. And the fact
7 is, remember, we are, like, the third step in a
8 six-step process. We are advisory to NTP. We
9 give what I view as peer-review comments on the
10 background document, peer-review comments on the
11 level of evidence, and we do, in writing, justify our
12 positive -- certainly, if it's a negative vote, we are
13 required to submit that in writing, and there's a
14 record of it.

15 So there's plenty there for anybody to
16 review who wants to review it, and there is a
17 transcript because I see myself quoted in some of the
18 comments that are here. So there is a
19 transcript of it. It's a very well-documented
20 process.

21 **DR. GOLDSTEIN:** Other comments?

22 **MR. FINKEL:** Adam Finkel from
23 OSHA and OSHA's rep on the Executive Committee.
24 There hasn't been much talk about that group's role
25 towards the end of the process, and I just -- and I

1 apologize for having to leave almost as soon as I
2 finish this little minute or so to catch a plane, but
3 there are times when I have felt hurried as a rep
4 on the Executive Committee, but I think hurried has
5 to be thought of in a context that, you know, there
6 are times when I would like, as an academic with
7 academic aspirations, to understand more about an
8 issue, but as Clay said there, very often times
9 issues come before us where we know enough to
10 know that -- for the purposes of the classification
11 decision, that there are already enough unanswered
12 questions raised by the provocative information that
13 further discussion of how interesting it would be to
14 know more than we know would be helpful but not
15 germane to making the decision.

16 So I think, you know, to say just how many
17 days did somebody get to read some piece of
18 material wasn't enough given the thickness of the
19 document is not really the question. You know, the
20 question is: Is there an issue that is really
21 dispositive to decisions that are being made?

22 At OSHA, when we did one of our rules a
23 couple of years ago, we spent almost a year on a
24 set of scientific papers because we had to make a
25 quantitative determination about adjusting potency

1 estimates based on the possibility of the inner-
2 species differences.

3 If I had gotten those same papers to make
4 a determination on the Executive Committee, it
5 would not have taken a half hour to begin to ask
6 myself enough questions about holes in the
7 argument to know that it was not going to be, in
8 my view, enough to change a classification.

9 And I just wanted to pick up on something
10 Bill Kelly said earlier in the day, which I think has
11 been a subtheme running through the whole day so
12 far about the appropriate scope of the BRC. And,
13 certainly, I agree that there are other ways to
14 present information to make it more consumer-
15 friendly, if that was, in fact, part of the original
16 Congressional intent, but, again, from a personal
17 perspective, I always have to put aside my intense
18 interest in potency in special circumstances of
19 signals of carcinogenicity being not universally
20 applicable, the issue, as Clay pointed out, of
21 ancillary benefits of pharmaceuticals, a very
22 important issue that I think NTP ought to talk about
23 real seriously before new categories are carved out
24 because of the slippery-slope aspect of this.

25 There are ancillary benefits to all kinds of

1 other categories of agents, but, really, ultimately, a
2 consumer-friendly document would have a lot more
3 information about substitutes, about industrial
4 processes, about costs of control, about the
5 profitability of the firms making the substance,
6 things which consumers might have a lot of intense
7 interest in but would clearly not be the province of
8 NTP. There's a role for a document that talks about
9 qualitative signals of carcinogenicity, and
10 there are roles for other kinds of documents that
11 other agencies or federal bodies or public private
12 bodies could engage in.

13 **DR. GOLDSTEIN:** Don't go yet. I,
14 basically, think you've answered this question. This
15 is some of the -- these are some of the issues that
16 I, again, thought I heard, and one is the issue of
17 hazard versus risk, risk being, obviously, exposure
18 plus hazard, and to specify the circumstances is,
19 really, a subset of that. And, of course, the issue
20 of exposure criteria, is it just simply for inclusion
21 in the NTP selection process or, again, is it part of
22 the process, part of the dose?

23 What I think I heard you say, Adam, is that
24 from the point of a regulator at an agency which is
25 part of the group that takes the information from

1 NTP and guides NTP in its lecturing process -- did I
2 hear right, you saying that to specify the
3 circumstances and inclusion of exposure is really
4 your job, not their job?

5 MR. FINKEL: Well, I don't want to
6 be dogmatic about it. Certainly, if there is
7 information that a particular agent exists in a bunch
8 of forms and that there's affirmative information
9 that one or more of those forms is qualitatively
10 different from the main form, then that becomes a
11 qualitative, very key ingredient in the classification.

12 But, you know, part of my remarks about
13 being hurried versus having enough time related to
14 that. If I have enough time to realize that people
15 are calling into question that there are multiple
16 forms, but there's no affirmative information to
17 suggest, you know, compelling evidence of
18 noncarcinogenicity for those forms, then I think that
19 that would be deferred to the regulatory agency
20 that would have to be making decisions about
21 whether all those forms would, in fact, be subject
22 to controls. Same goes, I think, with high dose/low
23 dose issues.

24 I'm somewhat persuaded by the discussion
25 on beverage alcohol. I gather that that was made

1 part of the record, that there may be a qualitative
2 difference caused by some biological phenomenon
3 that can be distinguished at high or low doses, but
4 when you get into, again, as Clay said earlier,
5 these issues about: Is it several hundred or
6 several thousand people being exposed? Is it parts
7 per million or thousand or hundred? where there
8 may be non-linearities, I think all of that is the
9 province of the regulatory agencies and not this
10 particular exercise in classification.

11 **DR. GOLDSTEIN:** Okay. Comments
12 on this issue of exposure or the extent to which
13 specific circumstances might be cited?

14 **DR. OLLER:** I guess as a member
15 of the (inaudible), I think I am very interested in
16 finding out what compounds -- what substances
17 around me are carcinogenic and try to avoid them.
18 And if the NTP document and listing is going to be
19 used for the public to make those kind of decisions,
20 I think it is important to consider that we do need to
21 put more information into that document, and I
22 would just illustrate for the case of nickel.

23 I looked into the 9th Report, and I see
24 nickel and nickel compounds are (inaudible) known
25 carcinogens, and I may ask them, "Well, what

1 should I do about my stainless steel sink in my
2 kitchen? Should I get rid of it? What about the
3 pitcher where I keep my water? Should I get a
4 filter so that if there is any nickel in the water, I
5 can decrease it? What about the multivitamins I'm
6 giving to my child that have nickel in them? Should I
7 worry about all of those things?" And
8 perhaps we do need to consider that the route of
9 exposure and the circumstances should be part of
10 the narrative on that document.

11 **MR. KENNEDY:** Bill Kennedy,
12 AstraZeneca. I'd like to respond to the comment
13 made about let's be careful about going down a
14 slippery-slope on pharmaceuticals.

15 I think with NTP having in their mandate
16 information on risk management and public health,
17 you have to take into consideration the information
18 in the public health aspects of it and the risk that
19 is generating a lot of fear in the minds of people
20 who are currently taking medications.

21 And I can only share with you an
22 experience that we had when the IARC information
23 -- IARC classification was being used to push
24 Proposition 65 in California. After it was all over,
25 we saw a decrease in the use of Tamoxifen on a

1 nationwide basis. It coincided with the discussion
2 that was going on on Proposition 65.

3 We checked further and found out there
4 was an inordinate decrease in the western states. It
5 calculated out to be a reduction of 30,000 women
6 had stopped taking Nolvadex, and it coincided with
7 Proposition 65 discussion. If you consider Nolvadex
8 having a 35 to 50 percent positive response in
9 treating breast cancer, we're putting 10- to 15,000
10 women at risk of not having appropriate therapy.

11 We took this one step further and followed
12 up with physicians who were treating breast cancer
13 patients in California, and they did confirm that at
14 the time of the Proposition 65 discussion, there
15 were women who stopped taking their Nolvadex
16 without discussing it with their physician.

17 So we do think that there is an appropriate
18 use of a pharmaceutical category. We shared this
19 information, just for information, with the FDA
20 about 18 months ago, and they have used it in a
21 document that the Deputy Commissioner exchanged
22 with the State Department in supporting a
23 pharmaceutical category on a worldwide basis, not
24 just in the NTP classification.

25 **DR. GOLDSTEIN:** Thank you.

1 We've got about four or five minutes.

2 Anyone --

3 **MS. WIND:** Marilyn Wind from the
4 Consumer Product Safety Commission.

5 I have to agree with Adam Finkel that it is
6 within the realm of the regulatory agencies to deal
7 with risk analysis, and I think that it would be a
8 huge mistake to extend what the Report on
9 Carcinogens does beyond hazard assessment.

10 For any given chemical, there may be three
11 or four of the regulatory agencies that deal with
12 various aspects of that chemical use, and each one
13 of us has a different act under which we regulate,
14 and there are different criteria that we need to
15 fulfill. And, believe me, the NTP does not want to
16 get involved in this.

17 **DR. GOLDMAN:** Yes. Just a point
18 of information. We're sitting here chatting, but on
19 the nickel issue -- I thought it was interesting that
20 you put your five cents in on it -- that, actually in
21 that listing, that the alloys -- the metal forms are not
22 included.

23 **DR. FREDERICK:** That's right.

24 **DR. GOLDMAN:** That's my
25 understanding. So there is already some

1 consideration of exposure and that forms where -
2 like nickel alloys, nickel metal, it's supposed to be
3 clear, at least, in a listing that that's not where the
4 cancer assessment was, and I would assume that's
5 because of the lack of exposure.

6 So I'm not sure that the question is really
7 whether there should be any consideration at all
8 because I think from that it's obvious there is
9 already some consideration, but whether that's
10 going far enough or, you know, there needs to be
11 more information than that --

12 **MS. NUNLEY:** Carolyn Nunley from
13 Consumers Union.

14 This question about exposure, I just want
15 to remind everybody that chemicals are not limited
16 in how they're used. Just because a chemical is
17 used for a pharmaceutical product today doesn't
18 mean it's not going to be used for something else
19 tomorrow. We don't approve chemicals solely by
20 their use or limit their use once they're on the
21 market.

22 So, you know, my concern, I guess, with
23 taking an exposure-based approach to this listing is
24 that, you know, what's going to happen tomorrow
25 when somebody decides to use Chemical A that was

1 delisted because it's only used in these uses that
2 don't cause a lot of exposure today, you know,
3 down the road tomorrow when somebody puts it in
4 something else that is much more
5 exposure-intensive?

6 **DR. GOLDMAN:** That's actually
7 right. There are some pesticides that -- fungicides
8 that are also anti-fungals as pharmaceuticals. So
9 it's not clear-cut. It's not absolutely simple, but if
10 people are aware of that, it might be a way of
11 dealing with it, too.

12 **DR. GOLDSTEIN:** Let me ask if
13 there's any further comments.

14 (No response.)

15 Good. Why don't we go into our next
16 group of presentations. Joseph Shapiro, I'm told,
17 is here from the Unimin Corporation and Crystalline
18 Silica Panel.

19 **MR. SHAPIRO:** My name is Joe
20 Shapiro, and I'm here to talk about the NTP process
21 concerning crystalline silica. Crystalline silica, in
22 its most common form, is quartz. It's the second
23 most abundant substance on the landmass of the
24 earth, and I brought a sample with me.

25 This is sand like you find on a beach or in

1 a sandbox. I brought it in a little sandbox toy cup,
2 and I guess I'll give it to the Chairman, Dr.
3 Goldstein. I was on the beach in New Jersey just
4 last month, and I missed my opportunity to retain a
5 sample of the sand. That actually is from
6 Minnesota, I must say.

7 Now, the sand, of course, is predominantly
8 crystalline silica, and, of course, it includes in it
9 some respirable crystalline silica. And lest anyone
10 have any fears about it, this is the same stuff that
11 hundreds of millions of Americans are exposed to
12 every day because it's in the air we breathe, and
13 it's those Americans who will be asking about your
14 decision-making process: How did you decide that
15 crystalline silica ought to be classified as a known
16 human carcinogen?

17 I'm here to talk about silica, or sand,
18 because of the 9th Report on Carcinogens because
19 NTP is on the verge of classifying silica as known
20 to cause human cancer without having meaningfully
21 looked at the data.

22 Our government's pronouncements about the
23 carcinogenicity of the second most abundant
24 substance on the crust of our planet deserves to be
25 based on a process which looks closely at the

1 available information and at public input.

2 At my company, we try to keep our
3 employees up to date on the science and on the
4 government's pronouncements and on the health
5 issues concerning silica. The U.S. Department of
6 Labor chose my company's CEO to make the
7 industry plenary session presentation at the
8 government's conference two years ago on how to
9 eliminate silicosis. That's a disease well known to
10 be caused by silica.

11 With regard to cancer, what can we tell
12 our employees and the people who live near our
13 plants about how NTP reached its conclusion in the
14 9th Report on Carcinogens? What can we tell the
15 millions upon millions of people who breathe sand
16 dust in the air every day in the natural
17 environment?

18 Do we tell them that the U.S. government
19 agency charged with evaluating published studies
20 didn't think the second most abundant substance on
21 the landmass of the earth was important enough to
22 read about before making a decision or that their
23 health wasn't important enough to merit a serious
24 look at the health science or that their health was
25 not important enough to allow meaningful public

1 input?

2 I came here today to talk about the NTP
3 process and silica not just as an executive of
4 Unimin Corporation. I'm also the Chairman of the
5 Crystalline Silica Panel housed at the Chemical
6 Manufacturers Association, the CMA.

7 Now, let me turn to some recent history.
8 Silica was nominated for the recent NTP process
9 because of IARC. At IARC, a Working Group
10 meeting in late 1996 issued a -- the issue was very
11 hotly debated at that meeting. There was a sharply
12 divided vote of the committee experts. Of the 19
13 experts in the IARC Working Group, 10 supported the
14 reclassification of crystalline silica; seven noted
15 against; one abstained; one was not present.

16 Silica's reclassification, though, was
17 carefully circumscribed, an issue that I think has
18 been raised, and that's quite unusual for IARC. The
19 reclassification was based on an evaluation that
20 found, quote, "sufficient evidence in humans for the
21 carcinogenicity of inhaled crystalline silica in the
22 forms of quartz or cristobalite from occupational
23 sources," closed quote. Whether non-occupational
24 exposures may present a comparable risk was not
25 addressed. The Working Group further limited its

1 conclusion by noting, quote:

2 "In making the overall evaluation, the
3 Working group Noted that carcinogenicity was not
4 detected in all industrial circumstances studied,"
5 closed quote.

6 Now, despite the obvious need, as shown
7 by the IARC deliberations, for NTP to conduct its
8 own careful assessment of this difficult-to-interpret
9 evidence, we have seen no indication that such a
10 review ever occurred at NTP.

11 Now, it has long been clear that respiration
12 of excessive silica dust can cause this form of
13 pneumoconiosis called silicosis. However, assessing
14 whether crystalline silica should be determined to
15 be a known human carcinogen is a complex
16 scientific issue.

17 Numerous epidemiology studies have been
18 connected in different occupational settings, and
19 they focus on two different questions. One is
20 whether silica exposure increases the risk of lung
21 cancer and whether silicosis, the disease, increases
22 the risk of lung cancer. Each of these studies has
23 to be carefully examined.

24 Accordingly, following the IARC meeting,
25 the CMA Crystalline Silica Panel asked a

1 distinguished epidemiologist who attended the IARC
2 Working Group meeting, Dr. John Gamble of Exxon
3 Biomedical Sciences, to review the silica
4 epidemiological studies and prepare a report to
5 assist NTP in determining whether silica should be
6 classified as known to cause human cancer. We
7 submitted his lengthy, well-documented, and
8 carefully considered report to NTP in November of
9 last year.

10 The record in this matter, though, contains
11 no indication that NTP ever wrestled with the
12 principal scientific issues concerning silica, the
13 issues on which Dr. Gamble focused in his report.
14 As far as we can tell, NTP participants may have
15 never read, let alone assessed, the Dr. Gamble
16 report.

17 We obviously do not know what occurred in
18 the RG1 and RG2 meetings since they were closed
19 to the public, but we have seen the background
20 document that forms the basis of the RG1 and RG2
21 recommendations. And as you know, we are told
22 that the background document presents the
23 scientific information and arguments upon which the
24 opinion of the BSC Subcommittee is based.

25 Well, the background document on silica

1 does not discuss in any detail all the available
2 studies; nor does it assess which of those studies
3 provide the most relevant data for assessing a
4 potential causal relationship between silica exposure
5 and human carcinogenicity.

6 Nowhere in the background document is
7 there a careful review of potential biases in the
8 various studies, most significantly whether
9 confounding exposures, most importantly, cigarette
10 smoking, a powerful known carcinogen, precludes
11 reaching a valid conclusion regarding the potential
12 carcinogenicity of silica. Nor does the background
13 document provide a careful assessment of whether
14 the studies demonstrate a dose-response
15 relationship, although that's the central criterion for
16 assessing human cancer causation.

17 In his report, the Dr. Gamble report
18 submitted to the NTP, Dr. Gamble meticulously
19 looked at all these issues. We don't know why RG1
20 and RG2 rejected this.

21 We do know what happened at the NTP
22 Board of Scientific Counselors Subcommittee
23 meeting. In his five-minute presentation -- he had
24 only five minutes available to him -- Bob Glenn
25 attempted to summarize Dr. Gamble's 72-page

1 report, an impossible task. He did point out that in
2 the studies of silicotics, there was no consistent
3 increase in lung cancer risk found when risks are
4 evaluated by comparing silicotics with nonsilicotics,
5 persons with high severity of silicosis with those
6 with low severity of silicosis, silicotics with high
7 silica exposure versus those with relatively low
8 silica exposure.

9 And he did observe that classifying an
10 agent as a human carcinogen in the absence of an
11 increasing risk by gradient of exposure or disease
12 severity is counter to long-standing scientific
13 criteria, yet there was virtually no discussion of
14 these points following Mr. Glenn's presentation. We
15 don't find any discussion in the record that we see.

16 Now, if the NTP Report on Carcinogens is
17 meant to be only a rubber stamp of IARC, which, in
18 fact, it wasn't because it didn't even have IARC's
19 limitations, even an IARC decision with a closely
20 divided vote, as happened in this case, then the
21 report doesn't serve a useful purpose to the
22 American people. On the other hand, if the Report
23 on Carcinogens should be meaningful, then a much
24 more complete, independent assessment of the data
25 must occur than has occurred with respect to

1 crystalline silica.

2 The decision now facing NTP and DHHS is
3 this: The arm of the U.S. government charged with
4 advising the American public on the carcinogenicity
5 of substances is making a decision about the
6 cancer-causing effects of the second most abundant
7 substance on the landmass of this planet.

8 There is crystalline silica dust, sand dust,
9 in all the outdoor air we breathe, presumably in the
10 indoor air as well, but according to a 1996 EPA
11 report, about 95 percent of the respirable
12 crystalline silica that Americans find in their
13 ordinary outdoor air does not come from
14 manufacturing or mining. We are talking about
15 exposure to sand dust that neither the government
16 nor private industry can control.

17 We must remember that when we are
18 talking about crystalline silica, it's a major
19 component of our farm soils, of the surface of
20 paved roads and unpaved roads. It's used in all
21 construction projects. It's the major component, of
22 course, of beach sand and play sand, yet when the
23 American people ask NTP why they classify this
24 pervasive substance as a known carcinogen, all NTP
25 will honestly be able to reply is, We basically

1 rubber-stamped an IARC decision made in
2 (inaudible) 1996.

3 **DR. GOLDSTEIN:** Mr. Shapiro, you
4 have one minute.

5 **MR. SHAPIRO:** Thank you.

6 Now, I firmly believe that before NTP and
7 DHHS advise the American people that respirable
8 crystalline silica, the most commonly found form of
9 sand dust, is a known human carcinogen, the
10 agency owes it to the American people to study the
11 issue seriously. Accordingly, we request that no
12 report on crystalline silica should be published in
13 the 9th Report on carcinogens. NTP should
14 implement a new, improved process and then give
15 the science concerning this ubiquitous substance
16 the attention it deserves.

17 Thank you very much.

18 **DR. FREDERICK:** Clarification
19 point, Bernie.

20 You said there's a 72-page paper report. I
21 don't remember exactly what all the documentation
22 package was we had on the table for silica. We
23 were working with a ton of stuff there. Was that
24 paper submitted well ahead of time before the
25 meeting?

1 **MR. SHAPIRO:** It was.

2 **DR. FREDERICK:** Okay. Then it
3 was reviewed. The five-minute summary was a
4 recapitulation of material that was already
5 submitted and should not be considered to be the
6 whole --

7 **MR. SHAPIRO:** My comment was
8 we saw no evidence that any of the studies --

9 **DR. GOLDSTEIN:** Basically, let's
10 get to the process issues.

11 The next speaker is Ralph Gingell from the
12 Shell Chemical Company representing the Ethylene
13 Oxide Industry.

14 **DR. GINGELL:** Good afternoon.
15 I'm Ralph Gingell, and I'm speaking as Chairman of
16 the Ethylene Oxide Industry Council's Toxicology
17 Group, otherwise known as the EOIC. The EOIC is
18 a trade group of ethylene oxide manufacturers
19 operating within the Chemical Manufacturers
20 Association.

21 I want you to rest assured, Mr. Chairman, I
22 haven't brought any free samples of ethylene oxide
23 with me today.

24 The Ethylene Oxide Industry Council
25 understands that EO, ethylene oxide, is being

1 proposed to be upgraded from the reasonably
2 anticipated to the known to be a human carcinogen
3 classification in the 9th NTP Report on Carcinogens.

4 I want to address one specific procedural
5 problem that was experienced at the Board of
6 Scientific Counselors public hearing on ethylene
7 oxide in October of last year, which led to, I
8 believe, the erroneous recommendation for
9 upgrading to known human carcinogen.

10 The EOIC does not argue with the current
11 classification of reasonably anticipated to be a
12 human carcinogen. However, there is a distinction
13 between reasonably anticipated and known human
14 carcinogen which can have significant regulatory
15 and legal repercussions for which I believe conveys
16 very little to the general public.

17 The criterion for known human carcinogen
18 simply states, and I quote: There is sufficient
19 evidence from carcinogenicity studies in humans
20 which indicate a causal relationship between
21 exposure to the agent, substance, or mixture and
22 human cancer.

23 If (inaudible) epidemiological cancer data
24 was the sole information considered, then ethylene
25 oxide, I believe, would not be upgraded to known

1 human carcinogen. There's a rich database which
2 includes 12 independent studies, over 33,000
3 workers, and the conclusions are that there was no
4 increase in cancer overall or in muscle or organ
5 sites of interest and only weak or inconclusive
6 evidence of data for leukemia and lymphomas.

7 And, overall, there is limited evidence of
8 human carcinogenicity which does not support
9 upgrade to the known category, and all this data
10 has been recently submitted and accepted for
11 publication in the journal, as noted at the bottom
12 here.

13 However, recent clarification by the NTP of
14 the criteria for the known human carcinogen
15 includes, and you can see the direct quote here:
16 Data derived from the studies of tissues from
17 humans exposed to the substance in question and
18 useful for evaluating whether a relevant cancer
19 mechanism is operating in people.

20 For ethylene oxide, this relevant data was
21 cytogenetic changes in the peripheral lymphocytes
22 of workers, manufacturing workers predominantly,
23 exposed to high levels of ethylene oxide.

24 I won't try to recapitulate here all of the
25 discussion at the public hearing, but there was

1 considerable disagreement among the members of
2 the Board of Scientific Counselors on whether these
3 effects did, in fact, indicate a relevant mechanism
4 for human cancer.

5 At this board meeting, Dr. Julian Preston,
6 who was (inaudible) EPA, stated that these human
7 cytogenetic studies were small, subject to
8 confounding, and of questionable validity for
9 various technical reasons. He also went on to
10 state, and I quote from his journal article which
11 has been published, at the bottom: Chromosomal
12 changes in peripheral lymphocytes are markers only
13 of recent ethylene oxide exposure, not predictors of
14 carcinogenicity. These assays are typically
15 conducted and not appropriate for chronic
16 exposures because they assess nontransmittable
17 alterations.

18 As I mentioned earlier, and as the
19 transcript of that October meeting shows, the NTP
20 reviewers differed in their recommendations. The
21 primary reviewer, Dr. Balinski (phonetic), (inaudible)
22 reasonably anticipated classification for ethylene
23 oxide. The second reviewer, Dr. Yamasaki
24 (phonetic), proposed upgrading to known based on
25 these questionable cytogenetic monitoring studies.

1 After much discussion, and it was a
2 protracted discussion, the board was still divided,
3 and several members had difficulty forming an
4 opinion on this complex issue in the time available.
5 The disagreement is exemplified by the split vote of
6 the board, six votes for to five against to
7 recommend upgrading to the known human
8 carcinogen category.

9 In summary, the EOIC have a few
10 recommendations, and we believe that when a
11 consensus of the board or at least no convincing
12 majority can be obtained, then no classification
13 should be made. Especially for the known
14 classification, the chemical should be deferred for
15 further consideration in a future report, emphasizing
16 those issues on which agreement could not be
17 reached or at least a consensus or a majority
18 decision could not be reached.

19 As this pertains specifically to ethylene
20 oxide, we believe that because of the split vote, EO
21 should not be upgraded to the known human
22 carcinogen at this time, and we believe continued
23 classification as reasonably anticipated adequately
24 protects the public.

25 I think you've heard lots of issues raised

1 here, that the NTP process certainly could be
2 improved, and we would recommend that the 9th
3 Report not be published at this time until many of
4 the issues raised here could be addressed and
5 corrected.

6 I understand you have a Congressional
7 mandate to put out a report, so if you feel that the
8 9th Report must be issued at this time, I suggest
9 that it go forward at least excluding those
10 chemicals for which we're showing a contention
11 here today, one of which is ethylene oxide.

12 Thank you.

13 **DR. GOLDSTEIN:** Thank you,
14 Dr. Gingell.

15 Our next speaker is Sara Schotland of
16 Cleary, Gottlieb, Steen and Hamilton and the
17 Ethylene Oxide Industry Council.

18 **MS. SCHOTLAND:** Good afternoon.
19 NTP, thank you, thank you for holding this hearing.
20 This particular day and tomorrow are an example of
21 good process.

22 Skip to the second slide. That's of no
23 interest to anyone but my mother.

24 You have sought comments on the criteria
25 for listing as well as on review procedures, so I'd

1 like to focus in on three different issues, that
2 known criteria should be reserved for chemicals –
3 the known category should be reserved for
4 chemicals where there is direct evidence of
5 carcinogenicity. I'd like to address, as Counsel, the
6 point that the criteria constituted agency rule, and
7 then talk a little bit more about the process issues.

8 EO is illustrative of a chemical which could
9 not possibly be upgraded to known carcinogen on
10 the basis of the epidemiologic data. Everybody
11 agrees that it's limited. The question is whether
12 cytogenetic studies provide data indicative of
13 carcinogenic risk. As Dr. Gingell mentioned, the
14 two NTP reviewers and the BSC were directly split
15 on this question down the middle.

16 We think that the cytogenetic data is
17 terribly problematic, small-scale population
18 monitoring data on one hand or SCE bio market
19 (phonetic) data on the other. We think that under
20 these circumstances there is a criteria problem. We
21 are not adequately communicating to the public that
22 a chemical is a known carcinogen if we're using
23 such data to make that determination when there is
24 a rich epidemiologic database with one follow-up,
25 exceptionally long follow-up and exceptionally large

1 size, that does not indicate that ethylene oxide
2 presents human cancer risk.

3 Being a known carcinogen is serious
4 business. There's a branding of the chemical.
5 Workers are unduly alarmed. Most seriously, the
6 point that was raised earlier about nickel, possible
7 misleading of the public. And there should be no
8 doubt but that there is a mandatory regulatory
9 impact in terms of OSHA has a communication and
10 EPA right-to-know.

11 I don't want to reiterate or belabor the
12 deficiencies in the peer-review process that we saw
13 with respect to EO. I do want to mention the first
14 point. We felt that the first pages of the process,
15 because they were internal to NTP, did not really
16 provide for an independent peer review.

17 When there was a peer review, it was
18 before the BSC, and although we appreciate that the
19 time was a little extended on EO, we really did
20 have a situation there, as the transcript will reflect,
21 where there were comments from the members of
22 the Board of Scientific Counselors asking Dr. Lucier
23 for clarification on the criteria, where people
24 wanted to ask more questions, Chairman Brown
25 gaveling them down. It was a circus. It was not

1 adequate opportunity to present scientific
2 information.

3 I emphasize we had people like Jane Peda
4 (phonetic) and Julian Preston, the leaders in the
5 field on epidemiology and genetic toxicology, that
6 there was informed debate. Members of the BSC
7 included some very distinguished people, including
8 some here today. There were questions asked.
9 There wasn't enough time.

10 And we are concerned that NTP has not
11 indicated whether it has responded to our
12 comments, appreciated our comments. Again, I
13 would focus on the most significant comment.
14 Nobody is suggesting NTP needs to respond to
15 every little nit.

16 As a lawyer, it is my opinion that the NTP
17 decisions constitute agency rules. They are
18 statements of general applicability. The annual
19 report indicates the secretary's judgment as to
20 carcinogenicity. It is used by a broad range of
21 regulatory agencies. In particular, it is
22 automatically used in OSHA hazard communication,
23 and it is automatically used in EPA community
24 right-to-know.

25 Yes, there's a case which said: We agree,

1 in the particular instance, that NTP was right in the
2 way it treated mechanistic data in the chemical
3 listing decision under challenge, but the decision is
4 very clear that what NTP is doing is agency action
5 by rule.

6 I don't really think that there's reasonable
7 level doubt about it, and as I indicated earlier, the
8 fact that the agency is engaged in a rule-making-
9 type activity, putting out a classification criteria as
10 a rule, does not mean that it needs to go through
11 the same extended process that is used by EPA in a
12 TSCA rule or used by EPA in some other decision
13 or by OSHA (inaudible), but it's got to get more
14 process than it is now.

15 And this is not just a matter of a legal
16 defense. I think the OMAN Commission was a
17 wonderful report. Dr. Goldstein, I don't recall.
18 Were you part of that commission?

19 **DR. GOLDSTEIN:** Yes, I was.

20 **MS. SCHOTLAND:** Indeed. And I
21 think David Rall was part of that report, too, and I
22 congratulate the people who were part of that
23 report.

24 Let me just read that quote, and I -- the
25 word risk management is used in a quote. If

1 anyone has any doubt when you read the report, it
2 includes risk assessment in its context: Experience
3 increasingly shows that risk management decisions
4 that are made in collaboration with stakeholders
5 are more effective and more durable. Stakeholders
6 bring to the table important information, knowledge,
7 expertise, and insights for crafting workable
8 solutions. Stakeholders are more likely to accept
9 and implement a risk management decision they
10 have participated in shaping.

11 Of course, of course.

12 The Commission acknowledges concerns,
13 costs, and additional time needed to involve
14 stakeholders can be considerable. However, risk
15 management by government agencies has been
16 costly anyway, and investment in stakeholder
17 involvement can bring long-term savings and reduce
18 litigation.

19 Again, we have successful models, and I
20 ask NTP to consider in the form of EPA-SAB, EPA
21 Eagle (phonetic), IARC, with respect to a more
22 reasonable process.

23 Dr. Olden, I would volunteer to work with
24 you and your staff regardless of the decision made
25 on ethylene oxide, regardless of whether I have a

1 client, to donate my time to the process on this
2 matter. I think it's so important, and I think it is
3 possible to find a process that is a compromise
4 between giving people of all sectors a fair shake
5 and avoiding an excessive burden to NTP is critical.

6 Is that it? Well, then I'll sit down. Thank
7 you very much.

8 **DR. GOLDSTEIN:** Thank you.

9 In the interest of fair disclosure, the
10 author of that is probably sitting in the room here,
11 Gail Charnley, who is the Executive Director of the
12 Risk Assessment Management Commission.

13 I'm not sure -- is George Alexeeff here? He
14 came in from California for the last one?

15 **DR. GOLDMAN:** He may be here
16 tomorrow.

17 **DR. GOLDSTEIN:** He may be here
18 tomorrow. Okay.

19 Our next speaker, then, is Rudolph
20 Valentine of DuPont Dow Elastomers.

21 **MR. VALENTINE:** Thank you,
22 Mr. Chairman, ladies and gentlemen. My name is
23 Rudy Valentine. I'm an employee of the DuPont
24 Company. However, I'm here at the request of
25 Mr. Michael Lynch of DuPont Dow Elastomers to

1 express our learning, specifically, with regard to
2 the RoC process (inaudible).

3 I've heard a lot of discussion today, and I
4 must say that our interest in this material was
5 tweaked roughly three years ago when the draft
6 report on chloroprene was issued. It was a
7 contentious issue for us from the standpoint that it
8 had contradicted a number of toxicology studies
9 that had been done, and our subsequent
10 involvement with the NTP was geared to understand
11 the science behind the decision.

12 What I'd like to do, based on those
13 learnings, is suggest some things that the NTP may
14 wish to consider, some improvements that may be
15 indicated in the pre-study planning phases,
16 including compound nomination and selection,
17 during the course of the actual animal testing for
18 study conduct and results communication, and,
19 finally, after the data is all collected and it's time
20 to look at it and interpret what it means, review of
21 that data, and, finally, the RoC classification itself.

22 In terms of compound nomination and
23 selection, it may be presumptive on our part, but
24 we think the objective of the NTP ought to obtain
25 the best available information that justifies testing

1 on a particular material. We're aware that the NTP
2 has certain exposure criteria, including poundage as
3 well as a number of people potentially exposed.

4 And what we encountered in our review of
5 the information was that the NTP categorization of
6 worker exposure was grossly exaggerated based on
7 the quality of the National Occupational Exposure
8 Survey. We didn't fully understand the impact of
9 the NOES survey until we began to ask questions
10 about how many people were actually exposed, and
11 we found considerable error in there.

12 The same applies for air-monitoring data.
13 Some of the air-monitoring data recorded was not
14 exactly consistent with our own experience. We
15 provided the NTP information regarding what our
16 experience has been in air monitoring.

17 Additionally, certain constraints on other
18 sorts of data was an issue for us. We understand
19 the NTP prefers using only peer-reviewed data.
20 However, as many of you will attest, there is
21 probably a great deal of information available from
22 various manufacturers that could impact NTP
23 interpretation at issue. To that end, DuPont Dow
24 Elastomers had a considerable body of information
25 as it related to epidemiology, toxicity, and exposure

1 assessment information, which would have been
2 gladly provided to you.

3 In terms of study conduct and results
4 communication, again, if I may be so presumptive
5 to suggest why we might want information, it would
6 be to conduct studies in a manner consistent with
7 chemical use and to communicate study findings in
8 a timely way.

9 With regard to our experience, particularly
10 with chloroprene, we think it's important that the
11 testing group fully understand how the material is
12 used and processed so that whatever regimen is
13 used in the animal testing represents actual use
14 conditions the way that people might be exposed. I
15 may point out that many of the comments I'm
16 making are discussed in much more detail in the
17 written comments which have been submitted, also.

18 An item, again, of interest for our
19 company was communication of the results. We
20 understand that the studies were going for several
21 years, particularly in the animal bioassay, and what
22 we don't fully understand is if significant results
23 were observed in the conduct of that study, why
24 they weren't expressed sooner in the process rather
25 than at the time they were.

1 It is well known that if industry were to
2 generate such toxicologic information, that we are
3 required by law, in addition to adherence to
4 responsible care commitments, to communicate
5 within a very rapid time frame the significance of
6 that information, particularly if it constitutes an
7 adverse health effect. What we don't understand is
8 why that information wasn't communicated sooner.

9 Should the NTP decide that information
10 should not be presented in a timely way, something
11 we'd like to encourage, obviously, and points that
12 have already been brought up numerous times
13 before, we think there should be ample time in
14 advance of the dissemination of that information for
15 review by appropriate folks.

16 Okay. What we think an objective ought to
17 be for data review and interpretation is to ensure
18 that the process is open to stakeholders, the
19 people on both sides of the fence here, that it
20 should be equitable and that procedural checks are
21 followed when the review is taking place.

22 If the data that is derived by the NTP is
23 contentious -- and from what I've heard today, much
24 of it is -- there should be lots of opportunities
25 where the NTP should openly seek -- solicit

1 contribution in terms of what might be a
2 responsible next step to take as well as comment
3 upon the data that was generated.

4 In our case, specifically, we are very
5 interested in understanding the mechanistic basis
6 behind the results that were observed, and, to that
7 extent, we are taking appropriate steps by
8 developing additional epidemiological data as well
9 as mechanistic studies, which we are openly sharing
10 with NTP and EPA and anybody else who is
11 interested in listening. Again, as it's already been
12 described earlier, there should be ample opportunity
13 to comment. There should be some acknowledgment
14 of those comments.

15 An issue that came up last year after the
16 RG1 and RG2 met was that certain critical pieces of
17 information were developed in relatively rapid
18 succession, including the data and IARC review of
19 betachlorophren (phonetic), and we are uncertain
20 whether this information was communicated within
21 the Board of Scientific Counselors and if, indeed, it
22 was considered. We are somewhat out of the loop
23 on that, and I don't know if they were considered.

24 This is an item for consideration. We
25 think that perhaps there may be some discussion

1 around whether the NTP could harmonize the cancer
2 classifications with other regulatory agencies and
3 that by not harmonizing, by not considering the
4 other classification schemes, that perhaps we
5 compromise our ability to fully understand the
6 human health impact of those decisions.

7 I'd also like to suggest something perhaps
8 rather heretical, based upon some earlier
9 discussions, was that the delayed classification
10 pending would be with supplemental information.
11 Again, our interest is making sure that the right
12 scientific information is there to make a coherent,
13 cogent estimation of the hazard that a chemical may
14 present, and if this means developing sufficient
15 epidemiological or mechanistic data in a timely way --
16 and I must underscore that it must be timely --
17 especially if there is no indication of significant
18 exposure to people, that that might be an item
19 worthy of further consideration.

20 I suggested several things that the NTP
21 might want to consider, but two of them hinge upon
22 actively involving representatives from industry in
23 the process. We believe that that participation will
24 assist in the reform of the process by a key
25 stakeholder.

1 We think that by sharing exposure toxicity
2 information that studies can be designed better
3 (inaudible). We can expand participation and
4 perspectives in scientific overviews, and, most
5 importantly, we can communicate in a timely way
6 the hazards and risks posed by chemicals to the
7 regulators and the public.

8 And lastly and most importantly, we
9 certainly embrace the idea of developing research
10 partnerships with the NTP to understand the hazards
11 of these materials presented.

12 Thank you.

13 **DR. GOLDSTEIN:** Thank you.

14 Our next speaker is Michael Gipko from the
15 J&L Specialty Steel, Incorporated. He's representing
16 the Specialty Steel Industry of North America.

17 **MR. GIPKO:** Thank you.

18 I guess the first question is: Why is the
19 stainless steel industry here? And the reason, we
20 are a consumer of chemicals, primarily metals. And
21 our concerns are that the NTP process has not
22 adequately paid attention to the scientific data
23 presented to them by one of our suppliers, which is
24 the nickel industry and, in addition, has not
25 adequately paid attention to the requirements of the

1 public because the public, as we see it, is confused
2 what nickel data means because they don't
3 understand what alloys mean.

4 With that, I will begin. My name is Mike
5 Gipko, and on behalf of the Specialty Steel Industry
6 of North America, I am pleased to have the
7 opportunity to comment on the procedures used by
8 NTP in the preparation of the Report on
9 Carcinogens.

10 SSINA is a national trade association
11 comprised of 15 producers of specialty steels and
12 products which account for over 90 percent of the
13 specialty steel manufactured in the United States,
14 including stainless and other alloy steels that
15 contain nickel and chromium, substances that
16 recently have been the subject of NTP's attention.

17 The Specialty Steel Industry globally
18 consumes 90 percent of the ferrochromium and 65
19 percent of the nickel produced annually worldwide.
20 And if you look at the alloy industry, the stainless
21 and alloy industry combined consumes about 80
22 some -- 84, I think, percent of the nickel production
23 globally.

24 Stainless steel itself is 100 percent
25 recyclable. 85 percent of the raw materials used

1 by the stainless steel industry are recyclable,
2 making the stainless steel industry one of the
3 largest recyclers in the world.

4 SSINA, which is one organization, has been
5 concerned with the listing process employed by
6 NTP, particularly with respect to the potential
7 listing of nickel compounds currently under
8 consideration. The current recommendation to list
9 nickel compounds as known human carcinogens was
10 plagued by numerous procedural and substantive
11 errors that raise serious questions about the
12 reasonableness and legal and scientific adequacy of
13 the recommendations. These concerns have already
14 been detailed at length by other presenters and are
15 addressed in the written comments presented by
16 SSINA.

17 Instead, today I would like to touch on a
18 particular concern of SSINA's as a user of nickel
19 and other substances subject to NTP's review
20 process. That is, the significant downstream
21 regulatory and economic impacts of what we believe
22 to be the NTP's flawed decision-making process.

23 NTP's decisions are very important because
24 while the agency maintains that it is not a formal
25 regulatory agency, in fact, NTP's decisions are the

1 first step in the regulatory process. For example,
2 NTP's website catalogs some of the formal
3 regulatory actions taken by EPA, OSHA, and the
4 FDA on the basis of NTP classifications.

5 California has identified NTP as one of five
6 authoritative bodies under Proposition 65 for
7 identifying carcinogens. NTP's actions also
8 influence classification decisions made by regulatory
9 agencies and scientific bodies in Europe and other
10 regions of the world.

11 Beyond federal and state regulations,
12 identification as a carcinogen has widespread social
13 and economic impacts. For example, carcinogen
14 listings may spur toxic tort litigation and consumer
15 product deselection and impact material purchasing
16 decisions by manufacturers and other users of
17 chemicals.

18 Let me say that again. Carcinogen listings
19 may spur toxic tort litigation and consumer
20 product deselection and impact material purchasing
21 decisions by manufacturers and other users of these
22 chemicals. In some cases, however, these
23 elements, such as nickel and chromium, provide
24 great public health benefits through the properties
25 they bring to the products into which they are

1 incorporated. Substitutes for these elements either
2 may not be as effective or may themselves present
3 other risks to human health and the environment.

4 Stainless steel provides a good example of
5 what I'm talking about. Nickel and chromium impart
6 to stainless steel properties -- such as exceptional
7 hardness, strength, resistance to heat, corrosion,
8 chemicals, and abrasion -- that make it essential in
9 a number of applications related to the protection
10 of public health.

11 The medical industry is particularly reliant
12 on stainless steel instruments, equipment, and
13 implants for their hygienic qualities. Stainless steel
14 is similarly essential for food preparation and
15 chemical processing equipment and in the aerospace
16 and defense industries, which are crucial to the
17 U.S. economy and national defense.

18 In alloy forms, such as stainless steel,
19 nickel and chromium are essentially benign, as the
20 nickel and chromium are essentially bound within
21 the alloy and unavailable for exposure.

22 Despite the benign nature of stainless
23 steel, were nickel and chromium to be identified as
24 carcinogens, whether in alloy form or not, the use
25 of stainless steel could be adversely affected.

1 Consumers would be less likely to purchase
2 stainless steel products, particularly with
3 Proposition 65 and similar labels attached.

4 Manufacturers would be pressured to limit
5 uses of materials containing nickel or chromium for
6 public relations reasons and out of fear of toxic
7 tort lawsuits. Let me say that one more time.

8 Manufacturers would be pressured to limit uses of
9 materials containing nickel or chromium for public
10 relations reasons and out of fear of toxic tort
11 lawsuits. Did you hear any safety there at all? No.
12 No, you didn't. European stainless steel producers
13 already are experiencing such product deselection
14 as a result of inappropriate, non-scientific-based
15 regulatory treatment of nickel.

16 In place of stainless steel, substitutes
17 would be utilized that are not likely to be as
18 efficient and combine all the characteristics of
19 stainless steel, such as corrosion resistance,
20 strength, health protectiveness, and environmental
21 friendliness. Product quality would suffer, but even
22 more importantly, these substances are likely to
23 generate their own risks to the public.

24 This could happen in many ways. One
25 example would be if a substitute is less corrosion

1 resistant than stainless steel, then it could expose
2 the public to health risks resulting from less
3 hygienic conditions. Likewise, an increased risk of
4 physical injury could result from the use of less
5 strong substitutes for those that corrode more
6 easily and compromise product integrity.

7 In addition, who is to say that substitutes
8 would not be inherently more risky than stainless
9 steel due to their chemical makeup? While nickel
10 and chromium alloys are essentially risk-free, this
11 may not be the case with substitutes containing
12 other substances.

13 NTP's listing decisions have especially
14 significant downstream impacts due to the agency's
15 historic refusal to recognize inherent toxicological
16 differences among various metal species, including
17 those of nickel and chromium. As a result, NTP
18 promotes an inaccurate notion that all compounds
19 of a metal may be linked to cancer in humans,
20 resulting in the serious economic and public
21 relations problems I just discussed.

22 Recently, SSINA has been encouraged by
23 NTP's decision after publication of the 8th Report to
24 list only hexavalent chromium compounds rather
25 than all chromium compounds and the similar recent

1 decision to consider nickel compounds separately
2 from nickel metal and nickel alloys.

3 While a step in the right direction, SSINA
4 remains concerned by NTP's failure to list specific
5 metal compounds as they do for individual organic
6 compounds. SSINA would be very happy to discuss
7 this issue further with NTP.

8 In conclusion, SSINA understands that it is
9 not the province of a strictly scientific body to
10 consider policy issues, but by acting as part of the
11 regulatory process, NTP should be wary of the
12 impacts of its listing decisions, including those on
13 downstream users and on consumers of the
14 substances NTP addresses, such as the specialty
15 steel industry.

16 Because of these impacts, NTP has a legal
17 duty to ensure that its decisions are based on
18 sound science and the product of reasoned decision
19 making before stigmatizing a substance as a
20 carcinogen. NTP should address technical issues
21 such as speciation, and NTP should address
22 property changes associated with alloys.

23 Thank you again for the opportunity to
24 speak, and my organization would be happy to work
25 with NTP in the future to address these issues more

1 thoroughly. Thank you.

2 **DR. GOLDSTEIN:** Thank you,
3 Mr. Gipko.

4 Our next speaker and, actually, our last
5 speaker today, because I understand Sylvia Kieding
6 is not here, will be Gail Charnley of Health Risk
7 Strategies, here representing the Chlorine Chemistry
8 Council.

9 **MS. CHARNLEY:** Last and possibly
10 least, I am Gail Charnley. I am President of the
11 International Society for Risk Analysis, and I have
12 private practice involving environmental (inaudible)
13 policy matters. I am speaking today on behalf of
14 the Chlorine Chemistry Council, but my views, as
15 always, are my own.

16 I would like to start by thanking Dr. Olden
17 and NTP staff, the Executive Committee, and the
18 Board of Scientific Counselors for this opportunity
19 to express my views on the carcinogen listing
20 process.

21 I know you all work hard to honor the
22 right of the public to know what chemical exposures
23 might cause harm. The process you have employed
24 to do so is not perceived to be in the same spirit
25 of right-to-know, however. There is clearly, as

1 we've all seen today, a perception that the process
2 used to evaluate carcinogens is ancillary and
3 exclusive. We've debated that point all day, and all
4 I can really add at this point is that whether the
5 process is open and fair or ancillary and exclusive,
6 as long as there is such a strong perception that
7 the latter is the case, I think that you have a
8 problem that needs to be addressed. It is
9 instructed to compare the carcinogen listing process
10 and the process used by the new NTP Center for
11 the Evaluation of Risks to Human Reproduction.

12 At the August 1999 meeting of the expert
13 panel charged with evaluating the reproductive and
14 environmental hazards of phthalates, for example.
15 Three half-hour formal scientific presentations to
16 the panel were made by independent groups of
17 stakeholders of all stripes (phonetic). An additional
18 half-hour was made available for unscheduled
19 stakeholder comments.

20 Presenters were invited to remain
21 throughout the three-day meeting to serve as
22 scientific resources for the expert panel. And, in
23 fact, they weren't just invited to remain. They
24 were strongly encouraged.

25 By contrast, we've heard a lot today about

1 the perception that stakeholder input is not taken
2 seriously by the Board of Scientific Counselors
3 Report on Carcinogens Subcommittee, and, in fact,
4 it is not really taken at all. As the world famous
5 Commission on Risk Assessment and Risk
6 Management pointed out -- by the way, Dr.
7 Goldstein is far too modest in terms of his
8 (inaudible). I thought the only person who called it
9 the Oman Commission was Oman.

10 As the Risk Commission pointed out --

11 **DR. GOLDMAN:** It was the Oman-
12 Goldstein Commission.

13 **MS. CHARNLEY:** -- a good risk
14 management decision emerges from a decision-
15 making process that elicits the views of those
16 affected by the decision so that differing technical
17 assessments, public values, knowledge, and
18 perceptions are considered.

19 While you may argue that carcinogen
20 listing is not the same as risk management
21 decision-making, it does trigger risk management.
22 The NTP carcinogen listing program should
23 acknowledge the increasingly valuable role that
24 stakeholders are playing in risk management efforts,
25 as NTP did when it created the Reproductive Hazard

1 Evaluation Program.

2 The latter program is a good model for
3 assuring that valuable scientific expertise is
4 available to the expert panel and that panel
5 decisions are made after a careful evaluation of all
6 the available scientific evidence.

7 My recommendation, then, is that the
8 process used by the NTP to evaluate carcinogens
9 should be reevaluated in view of the perception
10 that a more open process that fosters dialogue
11 among scientists and that values and encourages
12 diverse scientific input is needed. The NTP's own
13 Reproductive Hazard Evaluation Program for process
14 is a good model.

15 Secondly, identifying carcinogenic hazards
16 absent the evaluations of human health risk adds
17 little value to risk management and public health
18 protection. The NTP Report on Carcinogens does
19 not provide information that is useful for public
20 communication regarding carcinogenic risks to
21 health.

22 As we have discussed, the goal of the NTP
23 carcinogen listing procedure is just that, listing. It's
24 a hazard identification procedure. And the problem
25 with identifying hazards absent the risk context is

1 that doing so is sometimes not very useful.
2 Everything, as (inaudible) told us, is a hazard, and
3 whether everything poses a risk, of course, is
4 another matter.

5 Devoting emotional and other resources to
6 worrying about a hazard when it is not a risk
7 reinforces fear and misunderstanding of risks and
8 leads to misallocation of risk management
9 resources. As the Risk Commission once again put
10 it in its final report, risk assessment integrates
11 information about toxicity or intrinsic hazard and
12 information about exposure in the specific context
13 of a particular receptor to produce a risk
14 characterization.

15 The purpose of a risk characterization is to
16 provide qualitative and scientific information about
17 the nature, severity, and likelihood of a particular
18 risk in a form that is useful for risk management
19 decision makers. If the purpose of the NTP's
20 carcinogen listing process is not to provide
21 information that is useful to risk management
22 decision makers, then what is the point?

23 It is useful, I think, to compare the
24 authorizing language for the NTP carcinogen listing
25 process and NTP's announcement of the

1 developmental and reproductive toxicant evaluation
2 process.

3 Bill Kelly did his homework much better
4 than I did and actually went back to the actual
5 report language, but I just looked at the legislative
6 language.

7 With regard to carcinogens, as we all
8 know, Congress requires a list of substances known
9 or likely to be human carcinogens and information
10 concerning the nature of such exposure and the
11 number of persons exposed. Congress does not
12 require information on how much exposure occurs.

13 Taking the proposed entry for TCDD from
14 the 9th Report on Carcinogens as an example of
15 NTP's interpretation of Congress's intent, we see
16 that there are exactly two sentences devoted to
17 exposure analysis, neither of which is particularly
18 useful for helping to judge TCDD's potential risks.

19 By contrast, the Federal Register
20 announcement of the Center for the Evaluation of
21 Risks to Human Reproduction states clearly that the
22 reports produced by the center, quote, will provide
23 a timely, scientifically sound source of information
24 to the public and the scientific communities on the
25 reproductive risks of environmental agents.

1 Similarly, we can compare the preamble
2 found in the 8th Report on Carcinogens to the
3 charge to the expert panels convened by the Center
4 for Evaluation of Risks to Human Reproduction. As
5 Bill Kelly noted earlier, the preamble states the
6 listing of a substance in the report is descriptive
7 and qualitative in nature and represents an initial
8 step in hazard identification, which is generally
9 considered the first step in the analytical process
10 known as risk assessment.

11 It is necessary to conduct a risk
12 assessment in order to estimate the potential for
13 any substance to harm human health. The listing of
14 a substance in the report, therefore, does not
15 establish that any such substance presents a risk to
16 persons in their daily lives.

17 By comparison, the charge of the expert
18 panels evaluating reproductive and developmental
19 toxicants states: Integrate information about
20 toxicity and exposure using a weight of evidence
21 approach. Determine how human, animal, and other
22 data can reasonably be used to predict reproductive
23 or developmental defects in humans under particular
24 exposure conditions. Provide judgments that an
25 agent presents a potential risk to human

1 reproduction and/or development.

2 What is clear from these comparisons is
3 that we have an institutionalized risk versus hazard
4 problem. The risk versus hazard problem probably
5 results from the real difference between the NTP
6 approach to carcinogens and to developmental and
7 reproductive toxicants, which is 22 years.

8 Back in 1978, we didn't have a National
9 Academy of Sciences Red Book or Science &
10 Judgment or the Risk Commission Report. We
11 didn't have members of Congress actively promoting
12 the use of risk assessment. We didn't have a
13 president who read *Against the Gods - A*
14 *Remarkable Story of Risk* on his summer vacation.

15 Back in 1978, Congress's intentions were
16 honorable, and NTP carries out those intentions as
17 best they can, but times have changed, and there
18 needs to be a way for the NTP program to change
19 with them, which, of course, is why we're all here.

20 Congress did not prohibit NTP from
21 including evaluations of risk in its Report on
22 Carcinogens, and I see no reason why it cannot.
23 Absent evaluation of risk, I believe that the
24 Report on Carcinogens does not add as much value
25 as it could to our efforts to manage risks and

1 assure public health protection.

2 In the case of reproductive and
3 developmental toxicants, NTP saw an empty niche
4 and filled it. By comparison, listing carcinogens is
5 a potentially overworked and misplaced niche.
6 Now, I'm not saying that NTP should venture into
7 the regulatory realm. Regulation should be left to
8 the regulators, but risk assessment should not be
9 confused with regulation.

10 My recommendation, then, is that the NTP
11 should broaden its mission beyond one of simply
12 listing potential human carcinogens to one that
13 evaluates whether public health is at risk as a
14 result of exposure to such carcinogens.

15 Alternatively, NTP could consider pointing
16 out to Congress that EPA, FDA, OSHA, ATSDR,
17 (inaudible) IARC, and others already identify human
18 carcinogens and evaluate human cancer risks from
19 chemical exposures and that perhaps the public's
20 right to know about such potential risks is being
21 adequately served by others.

22 Instead, redirecting NTP resources towards
23 strengthening its efforts to make better connections
24 between environmental exposures and public health
25 outcomes would make a very valuable contribution

1 towards improving public health.

2 Those are my thoughts. Thank you for
3 listening.

4 **DR. GOLDMAN:** I have just a
5 point of clarification. I was both a consultant on
6 the board when it looked at the Center, and I also
7 attended the Phthalate Panel meeting, and that
8 effort does look at exposures in the sense of trying
9 to understand what the relevant exposure scenarios
10 might look like. It does not quantitate exposure. It
11 does not do a risk assessment. It does not, for
12 example, compute reference doses or, you know,
13 the cancer equivalent. If it were doing cancer, it
14 would not be doing the modeling and developing
15 risk numbers for different scenarios.

16 So what she said is accurate in terms of
17 that the panel does put the toxicity information into
18 kind of a context in terms of possible exposure
19 scenarios. It does not actually do a risk
20 assessment. I don't think it would be accurate to
21 say that.

22 I don't know if you want to add to that,
23 but --

24 **DR. LUCIER:** I think that's a good
25 depiction of it, Lynn, but the bottom line is that

1 the Reproductive Tox Center, which is in the
2 process of evaluating reproductive risk of phthalates
3 now is not doing a quantitative risk assessment.
4 It's not deriving specific uncertainty factors. It's
5 meant to establish the science base, however, on
6 which a risk assessment could be made and where
7 the scientific underpinnings for such a risk
8 assessment have gone through a rigorous scientific
9 peer review so their credibility would be enhanced.

10 **MS. CHARNLEY:** But does it not
11 draw an ultimate conclusion with regard to
12 (inaudible)?

13 **DR. LUCIER:** It's hard to say
14 because we haven't seen the first report yet. You'll
15 have to wait until sometime in '00, but it's our
16 intent not to do a quantitative risk assessment to
17 describe, certainly under some exposure
18 circumstances, when a risk might exist, however.

19 **DR. GOLDSTEIN:** I think we can
20 agree that it does go a little beyond where NTP
21 currently is right now.

22 Let me just -- we're about 15 minutes early
23 in terms of the discussion, which is scheduled to
24 go to 6:00. I'll stay as long as anybody else
25 wants, but I guess the real end of time is when our

1 expert transcriber will leave. I don't know that
2 we'll need all that time, but, basically, I know I'm
3 here and the NTP folks are here. We're completely
4 open for discussion of any kind.

5 Let me again start with the NTP to ask if
6 there's any other clarifications you want of anything
7 that's come up during this period of time, anything
8 you'd like to speak to. Great. And then turn it
9 over to Lynn and to Clay in terms of any specific
10 themes they think might be useful at this time.

11 **DR. FREDERICK:** I did want a
12 couple of clarifying comments. Mr. Gipko, nickel
13 metal and nickel alloys are explicitly not included
14 in the discussion of the nickel compounds that were
15 evaluated in the last listing, and I think it is
16 important to emphasize that, but I think the text of
17 the listing does do so.

18 Coming back, actually, to David Guston's
19 comments with regard to industrial participation in
20 the process and I'll say me sitting on the board,
21 those of us who are involved in the industry do
22 understand that there are economic ramifications of
23 these listings.

24 And I would say to the extent that we
25 understand that, we may evaluate the data more

1 carefully, possibly, to be sure that the decision is
2 right than somebody who may not be as mindful of
3 the economic consequences of the decisions. I
4 don't necessarily put that in the category of bias.
5 I'd say you'd put it into the category of being
6 aware of all of the ramifications of the decision
7 making of the process. In my experience, and I
8 don't think there's any difference in the way the
9 votes go because the essence is definitely the
10 scientific evaluation, but that's what it is.

11 One thing -- Rudy Valentine's comments I
12 thought were very good in the sense of offering the
13 partnership of NTP scientists on scientific
14 investigation relative to these listings. In my
15 experience, NTP scientists are very open to
16 scientific evaluations of the issues at hand, and I
17 think that the meat of this -- can't really decide
18 that. The meat of this is the scientific information.
19 We can never forget that.

20 And if further research, additional data,
21 on the table suggests that the wrong decision was
22 made, for whatever reason, I think the NTP
23 scientists have demonstrated that they would be
24 willing to support a delisting petition if that is the
25 appropriate thing to do based upon the appropriate

1 scientific body of information. And that, to me, is
2 the right answer.

3 I mean, at one point in time, the
4 appropriate -- the body of information may suggest
5 one answer. As more data is put on the table, it
6 may indicate that a different conclusion should be
7 reached. And the appropriate thing is to have this
8 process (inaudible) and provide the appropriate
9 advice for the public. I think those are all my
10 comments.

11 **DR. GOLDSTEIN:** Let me point out
12 a follow-up on Clay's comments. We've heard two
13 different opinions as to, if you will, what the
14 default assumption is, the discussion of a six-to-
15 five vote and that's not really a consensus, and we
16 really should have a consensus before we move
17 something to the full classification from the
18 reasonably anticipated classification. Basically, it
19 has implicit in it a default assumption that says
20 that until we're reasonably certain, we don't go to
21 a full approach.

22 On the other hand, we've also heard from
23 people who say that the default assumption is for
24 protection of public health. And my goodness. If
25 you've got even a one-person majority that says

1 that this is a known carcinogen, that the direction
2 ought to be going absolutely, certainly, in the
3 direction of that should be treated as a full
4 carcinogen.

5 We've heard these two different views as
6 to, if you will, a default. I'm not going to put
7 words in George's mouth or ask him to respond.
8 I'm sure if George or Ken responded there, their
9 answer would be, "Well, our default is good
10 science, and we're going to good science," but, in
11 essence, we've heard these others. Does anyone
12 want to comment further on those two?

13 Dr. Bingham, please identify yourself. We
14 all know who you are, but there's a transcriber
15 here.

16 **DR. BINGHAM:** Eula Bingham. I
17 have thought about that. You know, it works --
18 something is proposed to be raised, let's say, to a
19 known human carcinogen from the reasonably
20 anticipated, and the vote is six to five against
21 doing that, so there had to be five people who
22 thought it should be done, but six people thought
23 it shouldn't be.

24 It's the same situation that you've
25 described, and I'm wondering whether or not in the

1 NTP report one ought to consider putting in there,
2 in those situations -- and I don't know what the
3 numbers are, unanimous or ten to two or -- let's
4 say a six to five. You actually describe what the
5 committee came up with.

6 It would say, for example, Dr. Olden having
7 to say, "Well, I agree with this one. It was six to
8 five," or, "I agree with" -- or, "I don't agree." It's a
9 very tough burden, I think, but if you put down in
10 writing the way the vote went, it would provide
11 workers, for example, with information. They'd say,
12 "Well, they didn't really put it all the way up into
13 that category, but some people were nervous," or
14 some of the workers would say, "Well, it only was
15 put up there by one vote."

16 I think it gives a little information, more
17 information than we have now. I don't know.
18 Maybe it's a bad idea, but it does get at the issue you
19 brought out.

20 **DR. FREDERICK:** Eula, let me just
21 chip in on that. I think it's a bad idea to put the
22 text in, but that's okay. I actually think the vote
23 on EO, and I don't care about EO, the fact that it
24 was a mixed vote, six-five, it was exactly the right
25 vote, and it doesn't make any difference if it was

1 six-five either way.

2 The point I'd like to make is I think you
3 got it right that there's a mixed scientific opinion
4 on this type of body of information. This is an
5 advisory group. The advice to Dr. Olden is that
6 looking at this body of information, there's a mixed
7 scientific opinion here.

8 **DR. BINGHAM:** Then put it in the
9 report.

10 **DR. FREDERICK:** Well, we could
11 do that or not. I mean, that would be his choice,
12 but the main thing is I think the recommendation to
13 him was exactly right on the money. Some people
14 might get hung up on the fact that it was 6-5 one
15 way or the other. That wasn't the point. The point
16 is it's a mixed vote.

17 **DR. GOLDMAN:** I just want to add
18 to that, Bernie, because this is the area that,
19 actually, I thought might be interesting for more
20 discussion but broader in that it seems to me, from
21 a lot of the comments that we've heard over the
22 course of the day, that there is a greater richness
23 of information, whether it's about the vote or
24 whether it is about the database or whether it's
25 about, you know, issues such as the nickel issue,

1 about the difference between different forms of the
2 substance that people would like to see more fully
3 reflected in the report.

4 And whether -- and a couple of people said
5 things like, "Well, you know, actually, the
6 conclusions of the NTP, the listing could be longer.
7 Instead of a couple, you know, it could be longer.
8 It could be two or three times longer." A couple of
9 people have said that. And it just seems to me
10 that's another area where we could get more input,
11 in general, not just on this issue about votes, but
12 also on other issues like the exposure issues.

13 **DR. MIRER:** Frank Mirer. I hope
14 that sentiment on a split vote for ethylene oxide
15 would also be reflected in the split vote on
16 saccharin and the action to be taken there. And,
17 actually, in the saccharin debate, we had one
18 scientist who had done the epidemiology and, Clay,
19 had been unsuccessful in producing tumors in mice,
20 I believe, and that colored his opinion. So the
21 split votes are really at issue.

22 Let me make a couple of points from the
23 discussion. First, I served on the Red Book
24 Committee my first two or three with Ken Olden,
25 and at that point we separated risk assessment from

1 risk management. And, to me, the taking quotes
2 about risk management being something that's a
3 consensus process of bringing all the stakeholders,
4 that -- you know, it does not translate into risk
5 assessment being the same kind of thing or hazard
6 identification being the same kind of thing. We
7 make the effort there, and you can't just jump over
8 that. So I think that those remarks are actually
9 inappropriate to make.

10 The other issue has to do with how this
11 data is treated. We represent a lot of foundry
12 workers. Foundry workers suffer excess mortality
13 from lung cancer almost uniformly. Most of that
14 comes from silica exposure. That's a real thing.
15 This argument about whether it's carcinogenic or
16 not has real public health impacts.

17 I read through Dr. Gamble's summary. We
18 read through all that material. There is a vast
19 body of information on silica and carcinogenesis,
20 and to stand here and joke around about beach
21 sand and all that stuff and to try and denigrate the
22 findings or delay the findings, this is a very
23 important material the workers are exposed to every
24 day, and if you don't think known human carcinogen
25 makes a difference in whether management takes

1 precautions or not, I agree with our industry
2 colleagues. It makes a big difference. Reasonably
3 anticipated to be a human carcinogen means they
4 don't have to control the exposure, and they apply
5 that every day.

6 Similarly, the first mortality study we did
7 ourselves in the UAW had to do with a nickel and
8 chrome plating in an automotive hardware plant.
9 Those employees suffered excess mortality from
10 lung cancer. In trying to devise a control strategy,
11 it makes a difference which -- whether you look at
12 the dye-cast smoke, the chromium gas mist, or the
13 nickel plating mist. It's an important issue.

14 And, again, as we raise the distinction
15 between nickel metal and nickel compounds, people
16 take a nickel rod. People weld a cast-iron casting
17 with a nickel rod. They weld on stainless steel. It
18 may be steel when it's sitting there, but it's nickel
19 compound when they breathe it in. And steel
20 welders suffer excess mortality from cancer.

21 So this hazard identification step is the
22 first entry into risk assessment, and we can't, like,
23 play around with all of the, "It will scare people,"
24 because that's what we have the rest of the
25 regulatory process to deal with.

1 And then the final point, and this goes
2 more to the pharmaceutical issues which were
3 raised, and it came up at the time we heard the
4 Tamoxifen issue in the meeting, the scientific
5 purpose of this determination of what's a human
6 carcinogen and what's an animal carcinogen and so
7 forth, we're constantly reevaluating the predicted
8 value of the bioassay in the face of epidemiology
9 and epidemiology in the face of a bioassay.

10 And if we allow nonscientific
11 considerations such as, "Oh, somebody might get" --
12 we recognize people might not take their
13 medication, but if you allow those extra scientific
14 considerations, you distort the body of evidence
15 that we have to work with and you cause real
16 problems down the line with the next chemical.
17 And so I would not want to see that change of the
18 classifications, then. Thanks.

19 **DR. GOLDSTEIN:** There's a
20 comment in the back.

21 **MR. GIPKO:** Mike Gipko from the
22 Specialty Steel Industry. And I thank you, Dr.
23 Frederick, for your explanation. I just wanted to be
24 clear what this means in the real world. Okay?

25 We understand how the listings of nickel

1 and nickel compounds. I mean, we can read, but
2 the problem is some of our mom-and-pop customers
3 can't. We get questions from Ford Motor. We get
4 questions from Mercedes. We get questions from
5 some of the big boys, and I said mom-and-pop to
6 be funny. The big boys are calling our membership
7 and saying -- and have implemented (inaudible)
8 queries, asking whether nickel is present in our
9 stainless steel. Well, of course it is. And they are
10 considering deselection processes because of
11 potential NTP ramifications.

12 So these are real. And, you know, we may
13 say, "Well, you know, alloys aren't included." In
14 the real world, that's what's going on, and I just
15 wanted everyone here to be aware of that. Thank
16 you.

17 **DR. GOLDSTEIN:** Okay. We have
18 two folks over there, then Dr. Guston.

19 **MR. TORSON:** Mark Torson
20 (phonetic) from NIOSH. I'm on the RG2, and when
21 we finish voting -- or deliberating on a chemical,
22 we always ask: What happened at RG1? What was
23 the vote and why? We're most interested in the
24 dissenting vote or the minority vote, and I think
25 that there's always a minority opinion with our

1 group and I see it with the BSC (inaudible).

2 It shows up in the discussions and it often
3 shows up in the presentations at the BSC where
4 people give arguments as to why it should be listed
5 and why it should not be listed. And this "why
6 not" seems to be lost later on in the documents,
7 and it might be helpful that the minority opinion be
8 included in the discussion of why something is
9 listed.

10 **MS. WARREN:** My name is
11 Jackie Warren. I've been a career public interest
12 advocate for environmental groups. I just wanted
13 to respond to some of the statements that have
14 been made here. This statute was passed in 1978,
15 and I agree it's been 22 years, almost, but Congress
16 did not change the agency's mandate when it
17 revisited the statute in 1993.

18 And it's not appropriate for the agency to
19 go off on a frolic of its own to do something that
20 it might think is more timely now. I think it
21 doesn't actually have the authority to deviate from
22 the mandate that Congress gave it, and that is to
23 produce -- first of all, to do toxicology studies, but
24 to base the Report of Carcinogens on scientific
25 conclusions, that they're not colored by conflicts of

1 interest or by the (inaudible) interest in the
2 outcome of an evaluation but to just come out with
3 the best scientific judgment they can make, which
4 is, at bottom, going to be protective of public
5 health.

6 And it's not going to be a majority, but if
7 you took the majority vote of the people in this
8 room to decide whether NTP should go one way or
9 the other, it's clear to me that they would be
10 going to some sort of formal ruling, you know,
11 regulatory agency mode. I don't think that the
12 agency really has the discretion to make that kind
13 of change without a clear signal from Congress,
14 which it definitely has not gotten in the past.

15 I think that the report's purpose is to come
16 out with a list of substances which also includes
17 how adequately they are presently being regulated
18 or whether they are being regulated at all, and it's
19 an alert. Look at these next. It isn't really the
20 regulation itself, and it isn't risk assessment. The
21 risk assessment stage comes later.

22 That's the thing with respect to the
23 Tamoxifen example. I think that the downside of
24 taking Tamoxifen is a factor that a woman needs to
25 be considering when making the decision of whether

1 to take it in the first place. I don't think that that
2 is served by keeping that information from people,
3 and one would think and hope and expect that a
4 woman's doctor would inform her of what the
5 downside and the contraindications may be along
6 with the very great benefits that would come from
7 it, but I think that to, effectively, shoot the
8 messenger of bad tidings so that people don't hear
9 it and don't trouble their little pretty heads about it
10 is not an appropriate response.

11 So I think, in general, the agency, as I
12 said earlier, should not move to transform itself
13 into a regulatory agency holding formal rule
14 makings. I mean, there's plenty of opportunity for
15 public input already, as this shows, but if every
16 inch that's given results in a demand for another
17 foot, you will be in a regulatory agency mode
18 before you know it. I think you're halfway there
19 already.

20 **DR. GUSTON:** David Guston,
21 Rutgers University.

22 Two points, one on the Chairman's question
23 about the default assumption. That seems, to me,
24 to be something that's more properly pushed up the
25 chain. We've, I think, had a somewhat unfortunate

1 focus simply on the Report on Carcinogens
2 Subcommittee to the exclusion of the rest of the
3 process of decision making, as was described at the
4 beginning of the meeting, that there is an RG1, that
5 there is an RG2, and there are several layers of
6 political administrative review on top of this
7 advisory process.

8 The decision about whether something, you
9 know, to put it crudely, should be innocent until
10 proven -- whether a substance should be innocent
11 until proven guilty or guilty until proven innocent
12 strikes me as exactly that kind of decision that we
13 want to put in the hands of a responsible political
14 decision maker who is subject to direct political
15 controls. That's the first point.

16 Second point, I want to highlight something
17 that Dr. Frederick said about this being an iterative
18 process, and I want to highlight by way of a
19 question that most of the presenters this afternoon
20 who have spoken about the process with respect to
21 individual substances have called for a delay for
22 the 9th Report until all these procedural flaws, in
23 their eyes, should be fixed. And I guess the
24 question I have in that respect is: Well, what's
25 wrong with the 10th Report or the 11th Report or

1 the 12th Report?

2 And the answer to that question -- you
3 know, why is the option not move for delisting in
4 the 10th Report rather than delay the 9th Report?
5 And I don't think the answer to that question can
6 be: Because it will confuse the public. Because I
7 think the public, since the filming -- the screening
8 of Woody Allen's *Sleeper*, is perfectly comfortable
9 with the idea that science is a moving target, and,
10 you know, what may be carcinogenic one day may
11 not be carcinogenic the next day.

12 So I think that that's an important question
13 for people whose initial impulse right now is to
14 delay the 9th Report. Why not petition for
15 delisting or a change in status in subsequent
16 reports?

17 **MR. KENNEDY:** Bill Kennedy,
18 AstraZeneca. I have to comment that in no way, I
19 think, should our comments be taken as shooting
20 the messenger. The issue of listing Tamoxifen we
21 didn't address. We were talking about -- using
22 Tamoxifen as an example for a (inaudible), and
23 that's the inclusion of a pharmaceutical category.

24 I do recognize that there's a precedent, but
25 I also recognize that the precedent has already

1 been accomplished by the FDA having made an
2 evaluation of this compound as well as other
3 compounds 25 years ago when the initial approvals
4 were granted.

5 Coming back to the -- I think what the
6 initial mandate of what Congressional intent was on
7 the mandate, and that was to provide information to
8 the public so that they would be aware, and I think
9 the balance of the benefit and risk is terribly
10 important in fulfilling that mandate. When a
11 physician and patient are making that decision, they
12 should have the information. I've already cited the
13 example we've had on 30,000 patients leaving.

14 But an important piece that I like to keep
15 in mind is that we're talking about compounds. If
16 we're talking about a compound, there are
17 restrictions that are placed upon unqualified
18 statements of efficacy. There has to be a fair
19 balance when the pharmaceutical industry is talking
20 about efficacy. The agency requires -- the law
21 requires us to provide evidence of comments on the
22 safety.

23 I think when you're talking about a
24 compound, the same should happen if you're talking
25 about safety. There should be fair balance on the

1 efficacy side. Thank you.

2 **DR. FREDERICK:** Could I say one
3 thing about the 30,000 patients leaving? That really
4 troubled me when you said that, and the reason
5 why it troubled me was, one, was the process in
6 California wrong or whatever it could be or does
7 this represent 30,000 cases of poor doctor-patient
8 communication and inappropriate briefing of people
9 with regard to the issues at hand relative to the
10 benefits of the medication?

11 I don't think we can necessarily resolve
12 that question here today, but I think there's more
13 to that observation than might be -- you can say
14 something about it if you wish, but I'm not sure in
15 this particular case -- I think with regard to what's
16 going on here, that -- this whole issue of
17 communication -- appropriate communication of
18 information like this is, basically, more complex
19 than a superficial analysis might indicate.

20 **MR. KENNEDY:** Well, I think that
21 the 30,000 number is very close to real. These
22 were patients who were on five years of therapy.
23 They're in contact with their physician. An initial
24 meeting with their physician could have taken place
25 a year ago, two years ago, three years ago. That

1 placed over a background of sensationalism as
2 Proposition 65 is being argued in California, there
3 was a significant impact.

4 If I could provide one anecdote on this -

5 **DR. GOLDMAN:** When did
6 Tamoxifen come on the market for cancer
7 chemotherapy?

8 **MR. KENNEDY:** Twenty years ago.
9 In the United States, twenty years ago.

10 **DR. GOLDMAN:** So that was well
11 prior to Prop 65. I mean, I'm confused by the
12 timing. The history, as I remember it, is different
13 than this, so -- you know, in terms of timing.

14 **MR. KENNEDY:** If you're confused,
15 imagine what it's like for a woman out there who
16 has, perhaps, a mother who has been treated for
17 breast cancer with Tamoxifen, a sister who's had
18 Agiden (phonetic) therapy and just finds out that
19 she is at highrisk and goes on Tamoxifen as a way
20 to reduce her risk and then reads that this drug
21 that is being used to treat and reduce the risk of
22 cancer is identified as a carcinogen. She's going
23 to be very, very confused.

24 **DR. GOLDMAN:** I was there then
25 and I just didn't see that media. I mean, I just --

1 that's the thing. I mean, I was in the middle of it
2 and not personally involved, but I worked for the
3 State then, and I -- you know, so the history just
4 doesn't mesh with, you know, what I remember
5 hearing and seeing, but that's okay. It's just -- you
6 know, I'm finding the example -- I think the point is
7 a good one, that there could be a separate listing
8 for therapeutic drugs that are regulated by the FDA,
9 but the anecdote, you know, we're having trouble
10 understanding. I think both of us are.

11 **DR. GOLDSTEIN:** You've greed to
12 the point. Let's --

13 **MR. KENNEDY:** Okay. So you're
14 not going to shoot this messenger?

15 **DR. GOLDMAN:** Not at all.

16 **MR. KELLY:** Bill Kelly with
17 Federal Focus.

18 A couple of times now I've heard
19 references to Congress revisiting the Report on
20 Carcinogens in 1993, and it sounds like the
21 inference to be drawn there is that Congress really
22 deliberated on this subject and had decided that the
23 way that the report is being prepared is just fine
24 and it was going to leave everything unchanged.

25 And my recollection in trying to look into

1 this (inaudible) history materials is that what
2 happened in 1993 is they changed it from an annual
3 to a biennial report, and that was done in one
4 sentence in miscellaneous provisions at the end of
5 an extremely long bill that wouldn't even have the
6 strength of something like an appropriations
7 (inaudible), for example.

8 And I think it's a very weak argument to
9 try to argue Congressional acquiescence on
10 something like this unless there is some evidence,
11 which we haven't seen, that Congress really did
12 deliberate on this some time recently, and if that
13 does exist, I'd love to see it brought forward. As
14 I've said before, I haven't seen it so far. And if all
15 they did was change it from one year to two years
16 and stick it one sentence at the end of a bill, I
17 doubt very seriously that Congress has really
18 focused on this issue since 1978.

19 **DR. GOLDSTEIN:** Jackie Warren is
20 up to make a comment. Sara Schotland would like
21 to make a comment. And then I'm going to call
22 this subject closed.

23 **MS. WARREN:** I want to make a
24 quick response. What he said, it's very true about
25 what Congress says with every statute that comes

1 before it. It doesn't reopen the statutes very often,
2 and when it does, it has the opportunity to make
3 any changes that it thinks should be made. The
4 fact that it didn't make any changes says what it
5 says.

6 **DR. GOLDSTEIN:** I thinks that the
7 NTP folks will take a look at this more than they
8 might have before, and I appreciate the fact that
9 people have brought it up. It's something that I'm
10 sure they will look at the issue.

11 Are there comments?

12 **MR. LEBER:** Phil Leber from
13 Good Year.

14 I just wanted to get back to a point that
15 Dr. Valentine made, and I think it may have been
16 part of your slide, Dr. Goldstein, at the end of the
17 last session with regard to the criteria for
18 exposure, the importance of that as far as listing.

19 This morning I made the comments that
20 there was some question about the exposure criteria
21 for listing in an isoprene example. Dr. Valentine
22 brought it up again. I understood from Clay
23 Frederick saying any exposure is significant
24 exposure. Is that an NTP position? It says clearly
25 in the act that a significant number of people have

1 to be exposed before a chemical is listed. Is that
2 being discarded? Is that not an issue any longer?
3 Because it will save me time next time the
4 (inaudible).

5 **DR. GOLDSTEIN:** That's a good
6 question. Yours was about the only comment we
7 had on this and Gail Charnley's comment, which is,
8 you know, clearly NTP shouldn't do this unless it
9 has some risk management input. Obviously, maybe
10 that first step is the step in which, basically, the
11 hurdle is: Does it have risk management input?

12 Let me ask the NTP folks to sort of
13 describe what happens. How does a chemical get
14 on the list to be evaluated?

15 **DR. LUCIER:** I'll backtrack and
16 come back to the exposure issue, but there are a
17 number of entries one could get into consideration
18 for the Report on Carcinogens. The bottom line is
19 anyone in the world can nominate something to us,
20 and we do get nominations from all around the
21 world. That doesn't mean we take all those
22 nominations through this very lengthy process that
23 we described today.

24 The charge we have from Congress is to
25 list substances as known or reasonably anticipated

1 to be human carcinogens to which a significant
2 number of people in the U.S. are exposed. How
3 one defines that significant number of people,
4 obviously, is difficult to do, but some people may
5 consider 100 people a significant number. Some
6 people may consider it more. Some people may
7 consider it less. Obviously, if you're the one
8 person who is exposed to a high level of a
9 carcinogenic substance, it's of concern to you, but,
10 obviously, that issue is debatable.

11 Often, the exposure information they're
12 working from, I think the point has been made, is
13 based on some outdated exposure information that
14 may exist from the NOES Survey or something, and
15 whenever those surveys are updated and we have
16 information available, they, of course, are
17 considered by us. We can only go on the
18 information that we have at hand.

19 **DR. GOLDSTEIN:** Of all the
20 chemicals that get nominated, can you give us some
21 numbers as to how many make it through the
22 process? Are we talking about most of them, a few
23 of them?

24 **DR. JAMESON:** We currently have
25 a list of chemicals or exposure circumstances or

1 mixtures that we're looking at, and I think the
2 number on that particular list is about 198 that
3 there is scientific literature available that we want
4 to look at to see if it meets the criteria.

5 As far as outside nominations or
6 nominations that come in from reviews from people
7 other than an NTP review of the literature, every
8 one of those goes through at least review by the RG1.
9 And I would say probably, in my experience
10 with the report, which is for the 7th, 8th, and 9th
11 and now the 10th, probably at least 90 percent of
12 those go all the way through -- have gone all the
13 way through the review process. In other words
14 90 percent have enough information available to us
15 that we feel we need --

16 **DR. GUSTON:** What percent?

17 **DR. JAMESON:** 90 percent.

18 **DR. GOLDMAN:** Where do they
19 come from? Who nominates them.

20 **DR. JAMESON:** Where do they
21 come from? We get nominations from other
22 government agencies, from OSHA, NIOSH. EPA has
23 nominated materials. We get nominations from
24 some environmental state organizations, and we also
25 have gotten nominations from private citizens and

1 industry. Nominations -- let me qualify. Most of
2 the nominations we get from industry are for
3 delisting.

4 **DR. LUCIER:** There are a number
5 of things that will stimulate the priority for
6 something. One is, obviously, if we have just
7 completed an NTP study that's undergone rigorous
8 peer review in terms of the chronic bioassay and
9 that's given a strong carcinogenic response, that's
10 something that we want to consider very soon for
11 the Report on Carcinogens, and we need to do that
12 for public health reasons.

13 The other triggers would be priorities of
14 various kinds of regulatory agencies that might
15 nominate things to us. If something has recently
16 been upgraded or established as a known human
17 carcinogen by IARC, that might be another trigger
18 for us.

19 **DR. GOLDSTEIN:** Another comment
20 there?

21 **MR. TORSON:** Mark Torson from
22 NIOSH. I hate to take a step back, but just for the
23 record, I want to let people know that the patient
24 is not the only concern with exposure to the
25 pharmaceutical. We have people involved in the

1 manufacturing, especially the healthcare workers
2 that are exposed to these chemicals and affected by
3 them.

4 **DR. WADDELL:** Bill Waddell,
5 University of Louisville.

6 It's bothering me a little bit about
7 relegating hazard identification to lack of
8 consideration of the conditions of use, namely dose.
9 It's my contention that we must have some
10 consideration of dose to identify it as a hazard.

11 Water, sugar, and salt ingested in
12 sufficient quantities will kill so that they are a
13 potential hazard. They're not a risk under ordinary
14 conditions of use at an ordinary dose. So the
15 notion that dose must only be considered in risk
16 assessment is not correct. You have to consider
17 dose in a broad quantitative sense, at least, to
18 identify something as a hazard.

19 And I think a lot of the discussion we've
20 heard today saying, "It's not risk assessment. It's
21 hazard identification," does not recognize that in
22 order to identify a hazard, we must consider the
23 conditions.

24 There are many things that we use
25 ordinarily, and a lot of the problems would be

1 resolved if we're simply admitting that we have to
2 consider dose, at least in a broad sense, to identify
3 a hazard such that there are many things in low
4 dose that you've identified as a carcinogen that are
5 not carcinogens (inaudible) the only carcinogens are
6 hazardous. So if you recognize this distinction in
7 hazard identification, then it all resolves itself.

8 **DR. GOLDSTEIN:** Dr. Waddell,
9 would you continue with that? Because Gail
10 Charnley raised the same issue, and I guess just to
11 follow up on it, the issue, I guess, would be -- as I
12 understand what NTP is trying to do is first agree
13 that everything is a hazard but that not all things
14 are carcinogenic hazards and that their goal is
15 really to narrow down which chemicals intrinsically
16 can act as carcinogens.

17 **DR. WADDELL:** The problem is
18 that many things are carcinogenic in high doses,
19 and those same substances are not carcinogenic in
20 low doses. And the problem that NTP is shackling
21 itself with is saying, "Well, if it's carcinogenic at
22 any dose, then we have to classify it as a
23 carcinogen," and I don't think they have to be
24 shackled with that.

25 I think that they can say it is a carcinogen

1 at the high dose, recognize that and say that,
2 instead of saying it's a carcinogen and implying
3 that it's a carcinogen at any dose, and that's
4 somebody else's job. It's not.

5 **DR. GOLDSTEIN:** So you would
6 support, basically, some degree of explanation or --

7 **DR. WADDELL:** Absolutely.

8 **DR. LUCIER:** Let me just make
9 one quick comment. This issue was addressed in
10 significant detail when we went through the two-
11 year review for the criteria by which we would
12 determine which substances should be listed or not
13 listed in the report, and it's really addressed in the
14 criteria itself in the last paragraph in which the
15 Board of Scientific Counselors as well as the other
16 review groups and the NTP Executive Committee
17 operate under.

18 It says conclusions regarding
19 carcinogenicity in humans or experimental animals
20 are based on scientific judgment with consideration
21 given to all relevant information. Relevant
22 information includes -- it does not limit it to --
23 dose response, route of exposure, chemical
24 structure, metabolism, pharmacokinetics, sensitive
25 subpopulations, and so forth.

1 So that's sort of the Bible which the
2 various review groups use in determining which
3 substances should be listed.

4 **DR. WADDELL:** I understand that,
5 and I have read that, too, but what I'm saying is
6 you're not using that. If you consider dose and
7 you have named dose as part of the consideration,
8 you're saying that only at high dose something is a
9 carcinogen, and you ignore the facts that at low
10 dose it may actually be essential.

11 So what I'm saying is, you point to that,
12 and I read that in the document, but my contention
13 is you're not using that as far as your decision if
14 only at the high dose drives your decision.

15 **MR. JANKE:** My name is Ron
16 Janke, and I'm with Jones, Day, Reavis & Pogue.
17 My comments are purely personal.

18 It strikes me as only logical that if NTP
19 has information that there are special circumstances
20 that special populations are going to misinterpret
21 what NTP says in the normal way, that NTP should
22 speak differently on that subject.

23 I'll use Tamoxifen as an example. My wife
24 began taking that drug about five months ago, and
25 she now reads all reports about breast cancer and

1 breast cancer treatments far different than she did
2 ten months ago. And if it's brought to NTP's
3 attention that women may make ill-advised medical
4 choices because of a classification, it would do my
5 wife and a lot of women a great service if you
6 said, "We've classified this drug as a carcinogen.
7 We recognize it's FDA approved for certain
8 treatment, and we make no statement one way or
9 another whether FDA should do anything different
10 as a result of what we're doing today."

11 **DR. GOLDSTEIN:** Thank you.

12 **MS. MILLER:** Karen Miller. I just
13 want to make a comment that it is about the
14 process, but it's about how you communicate what
15 you do, and that's really what's at stake in terms of
16 communicating to the public. I've dealt with the
17 media for six years and all these issues around
18 Tamoxifen and the sensationalism any time there's a
19 story about endometrial cancer. So I just urge you
20 to think about how you communicate the listing, not
21 that you communicate it.

22 To the man's comment about whose wife
23 has breast cancer, it's really not what you say but
24 how you say it. And it's very complex to talk
25 about these issues and listings, and the press

1 frequently gets it wrong. So please be as clear as
2 possible in how you communicate the listings
3 because that's what women will take away from the
4 press is the misinterpretation, not necessarily what
5 you say.

6 **DR. GOLDSTEIN:** Thank you.

7 Okay. Other comments on any subject?

8 My goodness. There's still about 30 or 40
9 people here. It's amazing. Let me thank you all.
10 (WHEREUPON the Public Meeting was adjourned at
11 5:45 p.m., to be reconvened on October 22, 1999 at
12 9:00 a.m.)

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C A P T I O N

The Public Meeting in the matter, on the date, and at the time and place set out on the title page hereof.

It was requested that the Meeting be taken by the reporter and that same be reduced to typewritten form.

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