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UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

NON PRESCRIPTION DRUGS ADVISORY COMMITTEE

DENTAL PLAQUE SUBCOMMITTEE

THURSDAY, 3 DECEMBER 1998

MEETING

The meeting took place in the Conference Room, FDA Building, 5630 Fishers Lane, Rockville, Maryland at 8:42 a.m., Robert J. Genco, DDS, Ph.D., Chair presiding.

MEMBERS PRESENT:

ROBERT J. GENCO, DDS, Ph.D, Chair
KATHLEEN REEDY. Executive Secretary
WILLIAM H. BOWEN, DDS, DSC
LEWIS CANCRO, Consultant
RALPH D'AGOSTINO, Ph.D.
MAX A. LISTGARTEN, DDS
EUGENE D. SAVITT, DMD
STANLEY R. SAXE, DMD, MSD
CHRISTINE D. WU, Ph.D.
FRED HYMAN, DDC, MPH, FDA
LINDA KATZ, MD, MPH, FDA
ROBERT SHERMAN, FDA

ALSO PRESENT:

DR. MICHAEL KENNEDY
PETER B. HUT
PATRICE WRIGHT, Ph.D.
MICHAEL L. BARNETT, DDS

A-G-E-N-D-A

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1 P-R-O-C-E-E-D-I-N-G-S

2 8:42 a.m.

3 CHAIR GENCO: Good morning to FDA staff
4 panel and the committed core from industry. You are
5 the ones who have been here all five years, all 16
6 meetings, all 31 days, and I appreciate your input.
7 Well, let's proceed then. First of all we
8 have call to order, introduction, and let's start with
9 Lew.
10 MR. CANCRO: Lew Cancro, Industry Liaison
11 Representative.
12 MR. SAVITT: Gene Savitt, Periodontist,
13 Wellesley, MA.
14 MS. WU: Christine Wu, University of
15 Illinois at Chicago, Periodontist.
16 MR. D'AGOSTINO: Ralph D'Agostino, Boston
17 University.
18 MR. SAXE: Stanley Saxe, University of
19 Kentucky.
20 CHAIR GENCO: Bob Genco, State University
21 of New York at Buffalo.
22 EXECUTIVE SECRETARY REEDY: Kathleen
23 Reedy, Food and Drug Administration.
24 MR. BOWEN: Bill Bowen, University of
25 Rochester.

1 MR. LISTGARTEN: Max Listgarten,
2 University of Pennsylvania.
3 DR. HYMAN: Fred Hyman, Dental Officer,
4 Division of Dermatological and Dental Drug Products,
5 FDA.
6 MR. SHERMAN: Bob Sherman, Senior Liaison,
7 Division of OTC Drugs, FDA.
8 DR. KATZ: Linda Katz, Deputy Director,
9 OTC.
10 CHAIR GENCO: Thank you.
11 I will ask Kathleen Reedy to read the
12 conflict of interest statement.
13 EXECUTIVE SECRETARY REEDY: The following
14 announcement addresses conflict of interest issues
15 associated with this meeting and is made a part of the
16 record to preclude even the appearance of a conflict.
17 The purpose of the subcommittee is to
18 review information on ingredients contained in
19 products bearing anti plaque and anti plaque related
20 claims to determine whether these products are safe
21 and effective and not misbranded for their labeled
22 use.
23 Since the issues to be discussed by the
24 subcommittee will not have a unique impact on any
25 particular firm or product, but rather may have

1 widespread implications with respect to an entire
2 class of products in accordance with 18 United States
3 Code 208B. Waivers have been granted to each member
4 and consultant participating in the subcommittee
5 meeting. A copy of these waiver statements may be
6 obtained by submitting a written request to the
7 Agency's Freedom of Information Office located in Room
8 12A30 of the Parklawn Building.
9 In the event that the discussions involve
10 any other products or firms not already on the agenda
11 for which an FDA participant has a financial interest,
12 the participants are aware of the need to exclude
13 themselves from such involvement, and their exclusion
14 will be noted for the record.
15 With respect to all other participants we
16 ask in the interest of fairness that they address any
17 current or previous involvement with any firm whose
18 product they may wish to comment upon.
19 CHAIR GENCO: Thank you.
20 Bob Sherman will make some announcements.
21 MR. SHERMAN: Yes, thank you, Bob.
22 I'd just like to acknowledge someone in
23 the vast audience this morning. Michael Kennedy who
24 is back here, Michael recently announced his
25 retirement from FDA after serving with the OTC

1 division since its inception. Michael was involved in
2 the development of the OTC review and in the planning
3 of the first meeting of the first OTC advisory panel,
4 that was the antacid panel, what, about seven, eight
5 years ago?
6 DR. KENNEDY: A few more than that.
7 MR. SHERMAN: No, that was in 1972
8 actually. He was the panel administrator for the
9 dental panel, and he's here just before retirement at
10 the last meeting of the last OTC advisory panel after
11 34 years, is that right?
12 DR. KENNEDY: Yes.
13 MR. SHERMAN: 34 years with FDA. We thank
14 you, Michael, and we wish you well.
15 DR. KENNEDY: Thank you.
16 CHAIR GENCO: Okay, thank you, and our
17 congratulations too for coming full swing on your
18 career.
19 DR. KENNEDY: We've ended up with a nicer
20 conference room than when we started out with.
21 CHAIR GENCO: Okay, let's now go to --
22 let's finish up the Warner-Lambert and then we'll go
23 to the NDMA report.
24 This morning we're presented with some
25 wording to be inserted on page 168 following the

1 second full paragraph, it's a single typed page that
2 I'll draw your attention to.
3 Peter, would you like to make some
4 comments?
5 MR. HUTT: This is exactly what was seen
6 yesterday with two changes. The first at the request
7 of Stan Saxe. We made clear that in the second
8 sentence data presented to the subcommittee
9 demonstrate that each of the four active ingredients
10 makes a contribution to the antibacterial activity of
11 the product, that was the first change.
12 The second was the beginning of the second
13 sentence, the word "experiment" was dropped, I
14 believe, Bob, at your suggestion, and it just says
15 "The sponsor has shown," rather than "Experiments have
16 shown." Otherwise it is the same, and it simply
17 adopts the wording straight from the draft report with
18 respect to the elements needed to show contribution
19 for each of the four active ingredients in the fixed
20 combination.
21 CHAIR GENCO: Thank you.
22 Again, where is the exact location of
23 that?
24 MR. HUTT: Okay, it's page 168 in our
25 version, the FDA version, following the second full

1 paragraph, the second full paragraph ends with the
2 sentence "For the reported plaque index score
3 reduction of 33 percent, the pooled eight studies
4 alteration was calculated as 10.5, confidence in it
5 was 7.06 to 15.7," then start "The subcommittee."
6 CHAIR GENCO: Okay, and then we're
7 inserting this paragraph into --
8 MR. HUTT: Right.
9 CHAIR GENCO: -- in its entirety.
10 MR. HUTT: That's the suggestion.
11 CHAIR GENCO: Comments?
12 Stan?
13 MR. SAXE: Yes. Thank you, Peter.
14 It's close, but I don't think this is
15 quite on target. I'm still concerned about the use
16 saying "Each is effective" in the paragraph here. You
17 took out the word "Makes a contribution to the
18 effectiveness of the product," but saying "each is
19 safe and effective," that to me, since the prime
20 concern is the anti gingivitis effect of the
21 combination, saying that each of the active, four
22 active ingredients is effective, this is something for
23 which we have no data in terms of its effectiveness as
24 an anti gingivitis, anti plaque agent. It certainly
25 is effective in making a contribution to the anti

1 bacterial activity, which we discussed yesterday. so
2 --
3 MR. HUTT: Would you feel better if we --
4 MR. SAXE: -- if we just said each is safe
5 and the combination does not decrease the effect of
6 any individual active ingredient would be fine.
7 MR. HUTT: That's absolutely fine.
8 CHAIR GENCO: Stan, your suggestion is
9 that we would simply delete three words in line one,
10 two, three, four, five, six, one, two, three, four,
11 five, six --
12 MR. SAXE: Actually two words.
13 CHAIR GENCO: -- beginning with "and
14 effective and?"
15 MR. SAXE: No, you need the "and." You
16 would need one of the "ands."
17 CHAIR GENCO: Okay, "and effective?"
18 MR. SAXE: Two words.
19 CHAIR GENCO: Correct, two words "and
20 effective," in the middle of the sixth line.
21 Okay, any other comments?
22 Bill?
23 MR. BOWEN: For completeness should
24 "ethanol" be after the listing of the four
25 ingredients?

1 MR. HUTT: I'm sorry, I didn't understand
2 that, Bill?
3 MR. BOWEN: It reads "The subcommittee
4 concludes that the fixed combination of the four
5 active ingredients" (i.e. thymol, etcetera,), and I'm
6 suggesting "dissolved in ethanol."
7 MR. HUTT: Fine. Well, no wait a minute,
8 because that would mean it would have to always be
9 used when dissolved, Bill, and that may or may not be
10 true in future formulations.
11 Please recall that the performance testing
12 is designed to make certain that in any future
13 formulation changes that it would remain equally
14 effective. So that the specific carrier would not be
15 of importance.
16 MR. BOWEN: I was under the impression
17 that the carrier was of importance in creating various
18 phases.
19 MR. HUTT: Well, it may well be that a
20 future carrier of a different type would be equally
21 effective. If it were not, then the performance test
22 could not be met, okay, that's the purpose of the
23 performance test.
24 MR. BOWEN: Okay.
25 CHAIR GENCO: Further comments?

1 Okay, the panel agrees then that we
2 should, as modified, insert this page 168. That's
3 clear? Okay, thank you.
4 Okay, let's proceed to the NDMA comments.
5 And I'd like to thank Patrice Wright and Betsy
6 Anderson who last night marked up the annotations for
7 the revisions, and I think everyone has these so you
8 can follow along with us. The (x) means that these
9 issues were dealt with, so we needn't go over them
10 again. And the page in brackets refers to the FDA
11 draft. And there's another annotation (x format)
12 means that the comment is a format issue, either has
13 been dealt with before or we could maybe consider a
14 format issue and not discuss at length, if
15 appropriate.
16 Let's proceed now. We have dealt with
17 page 56DWS41, bringing the two sections into harmony.
18 We spent quite a bit of time with that at the end of
19 the day. Bob and Lew and I are clear on that, I
20 think, as to what's to be done, so I think we can go
21 on with the next one, unless there is more comment
22 about that?
23 MR. CANCRO: Right. I think we can begin
24 this morning with comment 42 on page 59, and that is
25 being withdrawn by the industry. So as you have

1 created that section, it stands.

2 CHAIR GENCO: Okay.

3 MR. CANCRO: It's withdrawn.

4 CHAIR GENCO: Okay, thank you.

5 So let's drop down to page 62. It's our

6 FDA page 43.

7 MR. CANCRO: Bob, I wanted to say that

8 commencing with 61 and going on through 62 is what you

9 went through on testing. You may want to take a

10 minute just to look at it now in the sense that it's

11 laid out in the format that I think, you know, you've

12 agreed to, but at least you can get a picture of it in

13 terms of how the two testing are clearly distinguished

14 between each other.

15 CHAIR GENCO: Yes, I think we did go

16 through that and I think we had agreed that under item

17 F there should be a one and a two, and that that

18 clearly defines the dosage form as contracted to the

19 formulation.

20 Panel, are we clear on that, and that

21 there were specific bioequivalence and even clinical

22 tests for the formulations, and those are dealt with,

23 with each of the category one products. Or as the

24 dosage form required the randomized control of trial,

25 one six month trial, and the issue of how that's dealt

1 with, I'm assured by FDA staff will be worked out by
2 the FDA. In other words, if that is required to be
3 submitted, it's required to be reviewed, is simply
4 required to be done, and is necessary to be available,
5 if the FDA wants, and it's not something that we
6 should be concerned about.
7 MR. CANCRO: I would think that's correct,
8 Fred, that a change of dosage form, that material has
9 got to be reviewed by somebody at the agency.
10 CHAIR GENCO: So I'm left to understand
11 that the -- well the panel feels strongly that that
12 should be reviewed, and we could discuss that, but
13 that the agency will build the mechanism for that
14 compliance issue.
15 Does anybody on the panel want to express
16 an opinion on that? Okay.
17 MR. CANCRO: I want to draw your attention
18 to comment 49, which is in addition to that testing.
19 This is on line 14, page 62. It's page 44 of your
20 submission. It reads "However, during the rulemaking
21 process each sponsor should provide the criteria
22 appropriate for each test," and I think that's pretty
23 self-evident because as these individual ingredients
24 go from category three to category one there may be
25 some unique testing required, and hence I think that

1 addition is necessary.

2 CHAIR GENCO: Excuse me, you've jumped to

3 page 62, your comment 49?

4 MR. CANCRO: Yes.

5 CHAIR GENCO: Okay. That's on our page

6 44. Let me find it. I don't see it.

7 MR. CANCRO: The comment is in addition,

8 Bob. This is under the reformatted testing that we've

9 created on page 62. Remember originally on page 43

10 you just had the general caption "Testing of OTC anti

11 gingivitis, anti plaque drug products." Then we

12 recommended you break that up.

13 CHAIR GENCO: Okay. So it's at the top of

14 our page 44. The first two lines are the end of the

15 sentence saying "To the negative control is assessed

16 by reasonable statistical analysis" --

17 MR. CANCRO: Right.

18 CHAIR GENCO: -- and then you're

19 suggesting adding "However, during the rulemaking

20 process each sponsor should provide the criteria

21 appropriate for each test."

22 Ralph, I think that you were part of this

23 discussion. Are you comfortable with that?

24 MR. LISTGARTEN: Excuse me.

25 CHAIR GENCO: Yes?

1 MR. LISTGARTEN: I think that there was
2 another sentence that had been inserted here
3 yesterday.
4 CHAIR GENCO: I thought so.
5 MR. LISTGARTEN: Which reads "For
6 validation of the study, the standard must be
7 statistically superior to the negative control."
8 CHAIR GENCO: That was the third
9 comparison that Ralph pointed out, right?
10 MR. D'AGOSTINO: I'm no sure what is now
11 being asked, I mean just that the sponsor will clarify
12 what is going to be --
13 CHAIR GENCO: Well, let me read what
14 they're suggesting. Instead of that sentence that Max
15 noted and that you actually suggested, they would like
16 us to consider "However, during the rulemaking process
17 each sponsor should provide the criteria appropriate
18 for each test."
19 MR. D'AGOSTINO: I would think that that
20 validation statement test could still be in there, and
21 all I would interpret this is that what you mean by
22 achieving equivalency and so forth is going to be what
23 the sponsor is going to suggest.
24 CHAIR GENCO: So you would agree with
25 their suggestion rather than with our sentence?

1 MR. D'AGOSTINO: No, I'm saying I would
2 keep our sentence.
3 CHAIR GENCO: Keep our's and add this?
4 MR. D'AGOSTINO: We have the three things
5 that have to be done --
6 CHAIR GENCO: Right.
7 MR. D'AGOSTINO: -- you have to validate,
8 you have to show it's valid, you have to show you beat
9 out the new -- beats out the negative, and you have to
10 show equivalence. And I interpret this statement as
11 saying that the sponsor is now going to say what they
12 mean by equivalence --
13 CHAIR GENCO: Okay.
14 MR. D'AGOSTINO: -- and the types of tests
15 and so forth.
16 CHAIR GENCO: So add our sentence plus
17 this sentence?
18 MR. D'AGOSTINO: That's correct.
19 CHAIR GENCO: Okay.
20 Bob, is that clear?
21 MR. SHERMAN: Yes.
22 CHAIR GENCO: Okay, good.
23 MR. D'AGOSTINO: I think Dr. Bowen --
24 CHAIR GENCO: Oh, I'm sorry.
25 MR. CANCRO: The issue for the industry on

1 this inclusion is that, as new agents become category
2 one, they may have very different tests from those
3 being proposed for stannous fluoride or CPC or the
4 essential oils, and hence the burden is up to the
5 sponsor to say what those tests are. I meant that's
6 the intent.
7 CHAIR GENCO: Right. I think there's no
8 disagreement.
9 Bill?
10 MR. BOWEN: We've reviewed three category
11 one, and we've accepted the proposed tests and
12 suggested modifications. And, if I understand you
13 correctly, in future manufacturers can come in and
14 suggest their own or do their own tests and they're
15 not subject to any further review, is that correct?
16 MR. CANCRO: Well, I think the testing
17 proposed for a different ingredient, and I won't pick
18 one out, certainly wouldn't be the desquatention test,
19 nor would it be maybe something else because that
20 ingredient would necessarily fit those tests. So that
21 the test coming in should be a test which can be
22 validated, which adequately describes the performance
23 and can measure it against the performance standard.
24 Since it isn't created, it's hard to describe what it
25 should be. It's just the caveat that when these

1 things become category one, you're going to need some
2 sort of directions as the formulation changes.
3 MR. LISTGARTEN: I guess --
4 CHAIR GENCO: Max?
5 MR. LISTGARTEN: -- I guess what bothers
6 some of us is that the statement suggests that these
7 can be submitted by industry without any review by
8 anyone.
9 DR. WRIGHT: And they would eventually, in
10 the course of the rulemaking process, be ruled by FDA.
11 I think the intent is that you're not holding --
12 MR. LISTGARTEN: That's understood.
13 DR. WRIGHT: -- during the rulemaking
14 process we're not holding the other ingredients to the
15 tests that are already required for stannous, for CPC,
16 and for the essential oils.
17 MR. LISTGARTEN: But --
18 DR. WRIGHT: It has to be when the
19 proposed monograph is published, if information is
20 generated for other ingredients, then that issue would
21 be looked at by FDA and included in a TFM.
22 MR. LISTGARTEN: Okay.
23 CHAIR GENCO: So this allows for new tests
24 appropriate to new agents and the statistical design
25 of that study be up to the company to justify

1 essentially.

2 MR. D'AGOSTINO: Should it be specifically

3 said. I mean they're talking about category three to

4 category one, should something like that be said so

5 there isn't any confusion?

6 MR. CANCRO: Yes, I think Ralph's addition

7 covers broadly the statistical requirements, the

8 validation you've got to separate it from. So that

9 isn't affected here. We're not trying to say that

10 that's at issue. I think what Patrice said is you may

11 need different tests and the agency will have to look

12 at that before the rulemaking process is closed.

13 MR. SHERMAN: Right, it would leave open

14 the possibility of future tests that would have to be

15 reviewed in some way.

16 CHAIR GENCO: Okay, any further comments

17 on this? If not, then the top of page 44, that first

18 sentence would have two additions. One is the

19 sentence that Max read, and the other is PW49 from

20 NDMA. Okay, thank you.

21 Let's proceed now to the comment PW46,

22 which is page 62, FDA page 43.

23 I'm sorry, which comment do you want?

24 DR. WRIGHT: You just said 49 --

25 CHAIR GENCO: But we skipped two I think.

1 MR. CANCRO: What -- we're going to 50
2 now, right?
3 CHAIR GENCO: Excuse me. I have on my
4 list the PW46 and PW47 that neither had an (x), nor
5 did we cover, I don't think.
6 DR. WRIGHT: Right. But they are all sort
7 of the same issue --
8 CHAIR GENCO: We have covered those.
9 DR. WRIGHT: -- looking at the outline --
10 CHAIR GENCO: Okay.-
11 DR. WRIGHT: -- when you discussed that
12 earlier, you --
13 CHAIR GENCO: All right, so we've covered
14 PW46 and PW47, and now we're to page 62, PW50.
15 MR. CANCRO: Correct.
16 CHAIR GENCO: Okay. That's on FDA page
17 44.
18 MR. CANCRO: Now, that's the simple
19 addition of the necessity of testing for all of the
20 microorganisms as opposed to a selection of any one
21 you want. If you look on line 20, page 62, we have
22 inserted the word "must," making it a requirement that
23 your test include the microorganisms that you have
24 proposed.
25 CHAIR GENCO: So PW50, 51, they're

1 referring to the -- okay, it's page 44, 1, single
2 period that that implied, second sentence beginning
3 "Representative organisms," and then you want to add
4 "must," suggesting adding "must include, but are not
5 limited to type strains of," and then take out the
6 "ATCC" designations. "Type strains of actinomyces
7 viscous, fusobacterium nucleatum, porphyomas
8 Ginficitis, provotella," and in all instances take out
9 the strain designations.
10 Any comments about that? Okay.
11 So, Bob, are you clear on that?
12 MR. BOWEN:
13 CHAIR GENCO: Good.
14 All right, next is PW52, FDA page 44
15 again --
16 MR. CANCRO: It's removal of the --
17 CHAIR GENCO: -- yes, removing the
18 specific ATCC designations.
19 Is that clear, Bob? I don't see that.
20 MR. BOWEN: They're deleted.
21 CHAIR GENCO: Oh, they're deleted. So
22 that's a redundant comment.
23 MR. SAVITT: Bob, I have --
24 CHAIR GENCO: All right.
25 MR. SAVITT: -- I have a brief comment

1 about the, when we originally proposed the list of
2 organisms, the recommendation was for experiments to
3 be done on some of these organisms, but it was
4 originally not supposed to be a cast in stone list.
5 CHAIR GENCO: Right.
6 MR. SAVITT: This was just more of a
7 suggestion.
8 CHAIR GENCO: So you would --
9 MR. SAVITT: And by inserting the word
10 "must" --
11 CHAIR GENCO: "Must" yes.
12 MR. SAVITT: -- you end up with
13 requirement for all of these organisms and it becomes
14 much more fixed. And I'm hesitant to suggest this,
15 this particular list, as we know the types of bacteria
16 change over time as to which ones seem to be more
17 important.
18 CHAIR GENCO: That sounds reasonable.
19 Any other comments from the panel on that?
20 The idea is not to include the "must." We don't agree
21 with the "must." Say "Representative organisms
22 include, but not limited to that list."
23 MR. CANCRO: In terms of practical
24 application, Bob, what would someone do, select what
25 he wanted from the list, or I mean how do you handle

1 the actual implementation of that test?

2 CHAIR GENCO: Oh, yes, the language

3 "Representative organisms include, but are not limited

4 to" means they must be, doesn't it?

5 MR. CANCRO: Well, you tell me.

6 CHAIR GENCO: A list would include these

7 five, but not limited to these five, it could be

8 another five. So the "must" is redundant.

9 MR. CANCRO: Okay. Okay, that's a

10 different interpretation.

11 CHAIR GENCO: Okay. I mean, if you want

12 to include it, it just emphasizes it.

13 Bill?

14 MR. BOWEN: I'd like -- I see the point

15 about eliminating the type strain because it could be

16 lost and then you have a major problem. But I think

17 it would be desirable to insert where possible the

18 type strain should be used. I mean some of their

19 actinomyces I know are quite different from each other

20 and you would get a different response depending on

21 which strain you used. So I would like to leave some

22 flexibility, but the desire is to use a type strain.

23 If they're not available, obviously you can't use

24 them.

25 MR. LISTGARTEN: That's stated, that's

1 stated in the revision. It says "But are not limited
2 to type strains of."
3 CHAIR GENCO: That's their suggested
4 revision, "type strains of."
5 MR. BOWEN: They recommend deleting the
6 "type strains" --
7 CHAIR GENCO: No, no.
8 MR. BOWEN: -- altogether, that's my
9 interpretation of it.
10 CHAIR GENCO: Okay, their suggestion is
11 that sentence would read "Representative organisms
12 must include, but are not limited to type strains of,"
13 add "type strains of," "actionyces viccosus," and then
14 cross out the specific ATCC designation in case the
15 type strains change.
16 MR. LISTGARTEN: They do recommend type
17 strains, they just -- we just don't want to specify
18 which in case the strain is lost.
19 CHAIR GENCO: Those particular type
20 strains, right.
21 Does that cover it, Bill?
22 MR. BOWEN: Yes, okay.
23 CHAIR GENCO: Okay, so the panel then
24 suggest that the wording be "Representative organisms
25 include," not the "must," "but are not limited to type

1 strains of" the organisms listed there, minus,
2 scratch, or delete the ATCC designations. Okay, fine.
3 Okay, jumping to 53, we believe that that
4 is a selection of one test or the other. So, if you
5 look at line 23, page 63 of the industry submission,
6 and that relates to page 45 of your submission, the
7 issue here is the choice of a laboratory test.
8 MR. LISTGARTEN: We've already made that
9 correction before.
10 MR. CANCRO: This may have been caught
11 earlier, but I'm not sure.
12 MR. LISTGARTEN: Yes, we caught it
13 earlier.
14 MR. CANCRO: All right.
15 CHAIR GENCO: Okay, next is --
16 MR. CANCRO: 54 you've already handled.
17 CHAIR GENCO: Okay.
18 MR. CANCRO: 55 is formatting. This is
19 the industry's recommendation to move the inner -- I
20 mean the excipient ingredient alcohol to another
21 section.
22 CHAIR GENCO: So this begins the alcohol
23 discussion then.
24 MR. CANCRO: And we do recopy this in its
25 entirety at a later stage in the book. We simply

1 lifted it and copied it at another point in the book.

2 CHAIR GENCO: What's the panel's feeling

3 on that? I think there are two issues here. One is

4 the placement in the report, and the second is the

5 content of the alcohol description. Why don't we

6 discuss the placement first. Would it help to look at

7 industry's proposed table of contents?

8 Lew, could you -- it's where?

9 MR. CANCRO: The very back the handout,

10 the original handout.

11 CHAIR GENCO: Of the original handout. I

12 thought I had seen it.

13 Okay, so does everybody have the table of

14 contents? What NDMA is suggesting is that, and it's

15 page 21 of the original handout, that mouthwash and

16 oral cancer be -- oh, excuse me, that there be a

17 section on inactive ingredients, and essentially

18 that's all alcohol, isn't it? So that goes from page

19 311 to 322 of the proposed document. In other words

20 to take the material that is on page, where does that

21 begin in the FDA document?

22 MR. CANCRO: In the FDA document you start

23 on 46.

24 CHAIR GENCO: 46.

25 MR. CANCRO: And it goes on to --

1 CHAIR GENCO: And take it out of there and
2 put it to the end of the document. What's the feeling
3 of the panel on that? The logic is to separate the
4 inactive ingredients from the active for ease of
5 reading, consistency, format
6 MR. CANCRO: Your discussion of alcohol
7 is, in your book, 46 to 53, 46 to 53 --
8 CHAIR GENCO: And you're suggesting taking
9 that entire section, and we'll discuss the
10 modification of that later, but the placement of that
11 section as it may be revised, to the end of the
12 report?
13 MR. CANCRO: Right now you're going
14 through a series of ingredient reviews which are
15 active ingredients and suddenly you come upon an
16 incipient which you've devoted a lot of time to, but
17 nevertheless it just doesn't seem to fit where you're
18 discussing anti gingivitis, anti plaque active
19 ingredients.
20 CHAIR GENCO: Does anybody have any
21 feelings about that?
22 MR. SHERMAN: Bob?
23 CHAIR GENCO: Yes.
24 MR. SHERMAN: I think this was probably
25 lifted as a format structure from an older monograph,

1 and that's something that we'll consider.

2 CHAIR GENCO: Okay.

3 MR. SHERMAN: I mean I don't want to use

4 a lot of time on that here. We're more concerned with

5 the content.

6 CHAIR GENCO: The content of it, okay.

7 MR. CANCRO: We would like to hit the

8 content a little later on, Bob --

9 CHAIR GENCO: Good.

10 MR. CANCRO: -- so we can come back to

11 your pages.

12 CHAIR GENCO: Okay.

13 MR. CANCRO: In which case -- is that

14 okay, Max?

15 MR. LISTGARTEN: Just before we go to the

16 alcohol section, there was an insert from the Warner-

17 Lambert report. On page three there was a sentence

18 that had to be added at the end of page 45. At the

19 very end of page 45 there was an inserted comment from

20 Warner-Lambert --

21 MR. CANCRO: Are you talking about comment

22 53, is that the one, the testing?

23 MR. LISTGARTEN: It was a comment that

24 appears on the Warner-Lambert page three.

25 MR. CANCRO: Oh.

1 CHAIR GENCO: Did we decide to include it?

2 MR. LISTGARTEN: We agreed to insert it.

3 CHAIR GENCO: It's done, it's done.

4 MR. LISTGARTEN: That's done, okay. I

5 just wanted to be sure it's not missed.

6 CHAIR GENCO: Okay. Next?

7 MR. CANCRO: Okay, well moving beyond the

8 alcohol section now to page --

9 CHAIR GENCO: Are you up to page 95, the

10 FDA page 70, the insertion of the table? Okay, do you

11 see that? It's the -- on page seven of the NDMA,

12 third item from the bottom, which is now page 95 of

13 the NDMA, FDA page 70, and it represents the table.

14 So it doesn't occur on the FDA page 70, but --

15 MR. SHERMAN: Yes, that's something that

16 we'll put in.

17 CHAIR GENCO: -- we'll include, okay,

18 good.

19 MR. SHERMAN: Sure.

20 CHAIR GENCO: Any comments from the panel,

21 are you happy with that table? Okay, good. And of

22 course it will have to be updated with our vote

23 yesterday.

24 MR. LISTGARTEN: So which table are you

25 talking about now?

1 CHAIR GENCO: Okay, the table, actually it
2 doesn't occur -- it occurs on the NDMA 95, if you want
3 to see it. It's this table of the drugs. Do you see
4 it?
5 MR. LISTGARTEN: Yes.
6 CHAIR GENCO: And if there's no objection,
7 we'll simply insert that, update it. The vote
8 yesterday has to be included.
9 MR. LISTGARTEN: And has to be -- where is
10 that going to be inserted?
11 CHAIR GENCO: On page 70 "Classification
12 of active ingredients."
13 MR. SHERMAN: Actually it's already in
14 there because the report was in the draft.
15 CHAIR GENCO: Good. Okay, good.
16 So it will be some place where it makes
17 sense. Once you get into classification of active
18 ingredients, here is the table and then the text
19 describing each active ingredient deliberations.
20 Okay, the last item now is on page seven.
21 There's page 108, FDA page 79, it's the NDMA page 108,
22 FDA page 79. Is this the micelle formation? That's
23 been done? No. It's PW61, that we've dealt with,
24 okay.
25 So let's go on --

1 MR. CANCRO: 125.

2 CHAIR GENCO: 125, okay. NDMA page 125,

3 FDA page 92. Okay, it's PW62.

4 MR. CANCRO: Again the issue is

5 formatting. The recommendation is to put the labeling

6 sections up front.

7 CHAIR GENCO: Pardon?

8 DR. WRIGHT: Sorry, I missed crossing that

9 one out.

10 CHAIR GENCO: That we've done too?

11 MR. CANCRO: It's done too.

12 CHAIR GENCO: Okay. The next is the

13 format, okay, that's one. Then NDMA page 133, FDA

14 page 156, FDA 156.

15 MR. CANCRO: That's a correction that

16 eight studies were reviewed instead of seven. And you

17 have that on page 156.

18 CHAIR GENCO: Stan --

19 MR. CANCRO: It's at the top of the page,

20 do you see it?

21 CHAIR GENCO: Yes.

22 Chris, you reviewed those, is that all

23 right, it's a correction? It's on the -- okay, fine.

24 MR. SAXE: That seven is in there because

25 originally there were seven six month randomized

1 control trials. And following a call for more
2 analysis, there was the inclusion of the eighth. I
3 think eight is appropriate at this point.
4 CHAIR GENCO: Okay, so that comes at --
5 okay, on page 156, Bob, the first sentence reads
6 "Later published by reference 327 and is using five of
7 the seven," that becomes "five of eight," okay, good.
8 All right, next --
9 MR. CANCRO: 138.
10 CHAIR GENCO: -- it's page 138 NDMA, FDA
11 page 159.
12 MR. CANCRO: Just a typo.
13 CHAIR GENCO: Okay, any objection to that?
14 Do you see it, Bob?
15 MR. SHERMAN: On our 159?
16 CHAIR GENCO: It's page 159 "Analysis was
17 based on an index."
18 Where about on that page is it, Lew, do
19 you see it?
20 PARTICIPANT: Middle of page 159.
21 CHAIR GENCO: Middle of page "The study
22 was based on adjusted mean -- index scores," that
23 should be "The analysis," okay.
24 Bob, do you see that?
25 MR. SHERMAN: Yes.

1 CHAIR GENCO: Good.

2 Next is?

3 MR. CANCRO: Jump to page 150 of the NDMA
4 submission. And the corresponding page is at the FDA
5 165 and 166, and this we think is a general discussion
6 which, you know, applies really across all aspects of
7 testing, and hence we think it should be moved and
8 included in the safety and efficacy guidelines which
9 are created.

10 CHAIR GENCO: Which are where, which page
11 do you want it removed to and suggesting?

12 PARTICIPANT: 65 --

13 CHAIR GENCO: To page 65 of the original
14 FDA.

15 Does anybody on the panel have any
16 comments on that? It sounds like a formatting issue.

17 MR. SHERMAN: Okay, I think that was
18 included in Stan's original report --

19 CHAIR GENCO: Okay.

20 MR. SHERMAN: -- and if you feel that it
21 applies to all, we could move it and/or we can keep it
22 and just a slight look closely at some of the words
23 because, for example, if you look at the NDMA
24 revision, on their page 150, line 13, it says "Slight
25 differences exist in mean GI scores which are not

1 clinical obvious, cannot be easily discerned in a
2 subject," that was in direct reference to some of the
3 studies submitted by the sponsor here, but it is
4 basically kind of a generic statement and the wording
5 might be very slightly altered. For example the
6 wording may be "Slight differences may exist in mean
7 GI scores," etcetera. But I think it's, without
8 having to re-read it closely at the moment, once again
9 I think I would agree that it is kind of a generic
10 statement comment and can be reformatted.
11 CHAIR GENCO: Would you lose anything by
12 not having those specific references to your report in
13 with this report?
14 MR. SAXE: You have references that are in
15 there?
16 CHAIR GENCO: No, I mean the items
17 referred to. Do you think you'd lose anything from
18 your report by moving it to a more general section?
19 MR. SAXE: Well, if you look at page -- we
20 wouldn't move -- some of it, but not if you look at
21 the NDMA, it only goes down page 151, line 21 for
22 example. Beginning at line 22 it is specific to the
23 four essential oils review. Line 22 on page 151 which
24 begins "To quantify the findings (i.e. who and how
25 many in the study groups are affected and by how much)

1 and to present the findings with appropriate
2 indicators of measurement error or uncertainties such
3 a measurement error or uncertainties such as
4 confidence, you know, further analyses were
5 completed," that is specific for the four essential
6 oil reviews and should be left in place. And the
7 following on page 152 of the NDMA revision.
8 CHAIR GENCO: So it would require some
9 work to make it general, to be able to be moved.
10 MR. SAXE: Well, I'm saying the first like
11 about a page and a half --
12 MR. CANCRO: Clearly up to line 20 it
13 looks pretty generic --
14 CHAIR GENCO: Okay, that's the section
15 that you're suggesting we move?
16 MR. CANCRO: Yes.
17 CHAIR GENCO: Because you've got
18 underlined three or four pages here.
19 MR. CANCRO: Well, the underlining is
20 really to put it -- I mean to get it into the
21 Listerine area because then you're talking about the
22 Listerine studies as you go to page 152, and you
23 commence that somewhere in the middle of 151.
24 So we're talking about lines 1 through 20,
25 Stan, which look to us to be, you know, a very good

1 generic guidelines for the indices, etcetera.

2 CHAIR GENCO: Okay, so the suggestion is

3 to move lines --

4 MR. CANCRO: 1 through 20 .....

5 CHAIR GENCO: 1 through 20 which are on

6 your page 150, right?

7 MR. CANCRO: Yes.

8 CHAIR GENCO: And our page 165 which

9 begins with "Strength," yes. Okay, it's page 165,

10 last paragraph, "Strength of effect and concern about

11 statistically significant changes," that's the

12 paragraph which goes from the last paragraph, our 165

13 to the first paragraph at 166?

14 MR. SAXE: Yes.

15 CHAIR GENCO: Okay, so the last paragraph

16 on 165, first paragraph on page 166, to page 65.

17 Is that clear, Bob, that's what they're

18 suggesting?

19 And, Stan, you agree?

20 MR. SAXE: Yes.

21 MR. SHERMAN: Okay, where does it end on

22 166?

23 CHAIR GENCO: I'm sorry. It ends at the

24 end of the first paragraph. The second paragraph

25 beginning "General liabilities" is to stay there for

1 the time being. So there's two paragraphs to be
2 moved, the last paragraph on 165, the first paragraph
3 on 166, to page 65, okay.
4 All right, Lew, does that take care of
5 DSW66 then, the line 1 to 20?
6 MR. CANCRO: Yes.
7 CHAIR GENCO: We've moved those two
8 paragraphs out of this section to the more generic
9 page 65.
10 MR. CANCRO: Right.
11 CHAIR GENCO: Okay.
12 MR. CANCRO: And just to finish up with
13 the remaining section, which was underlined --
14 CHAIR GENCO: Okay.
15 MR. CANCRO: -- that is more appropriately
16 placed in interpretation of data, which I believe you
17 have on page 69 of the FDA.
18 CHAIR GENCO: All right. Now, we're
19 talking about our page 166 beginning with the second
20 paragraph and the third paragraph which is the
21 remainder of the page to where?
22 DR. WRIGHT: No, I think what we're asking
23 is that line 1 through 20 that we just talked about --
24 CHAIR GENCO: Right.
25 DR. WRIGHT: -- instead of on page 65,

1 it's more appropriate to put in the interpretation of
2 data under the safety and efficacy guidelines which is
3 on page 69.
4 CHAIR GENCO: Oh, page 69, not to page 65.
5 Bob, did you hear that? Okay. The same
6 two paragraphs, last paragraph 165, first paragraph
7 166 to page 69, not 651, okay.
8 MR. SHERMAN: Okay.
9 CHAIR GENCO: Good.
10 I'm sorry, the designated?
11 DR. WRIGHT: Under section three after
12 section --
13 CHAIR GENCO: Where on page 69?
14 MR. CANCRO: You have Roman Numeral V,
15 "Interpretation of data."
16 CHAIR GENCO: Right there at V, or after
17 the first paragraph, or what did you suggest? At the
18 end of that before Roman Numeral I? I guess, Bob, you
19 could fit that in linguistically --
20 MR. SHERMAN: Yes, we'll figure out how it
21 makes the most sense.
22 CHAIR GENCO: Great, all right.
23 Okay, we've dealt then with comment DSW66,
24 okay. Now, next I've got is, the next two are format.
25 MR. CANCRO: Yes.

1 CHAIR GENCO: We can deal with those, Bob?
2 Panel, any concerns? Did we discuss this
3 before about category three, there's no need to talk
4 about dosages, etcetera? Are we comfortable with both
5 suggestions, PW67, PW69?
6 Lew, is this more than format or is this
7 really content?
8 MR. CANCRO: Well, I don't think we've
9 changed the content at all in this.
10 CHAIR GENCO: But you said these sections
11 are not needed, that's what you're recommending,
12 that's what the -- sorry, what?
13 DR. WRIGHT: I thought we already adjusted
14 this.
15 MR. CANCRO: Okay, Patrice tells me we've
16 already adjusted this.
17 CHAIR GENCO: I think we've adjusted this.
18 MR. CANCRO: Sorry.
19 CHAIR GENCO: I thought it was still under
20 discussion. In other words, is it needed to talk
21 about the category three that may one day be category
22 one?
23 PARTICIPANT: Yes.
24 CHAIR GENCO: Is it useful to have that
25 discussion in there? I thought we discussed that

1 yesterday and not to leave it out.

2 DR. WRIGHT: I thought you concluded that

3 you were going to leave the labeling information in

4 there at the end of that sentence.

5 CHAIR GENCO: Okay.

6 Bob, are you clear on that?

7 MR. SHERMAN: No. Would you mind

8 repeating that?

9 CHAIR GENCO: Yes, essentially we're going

10 to leave it as is.

11 DR. WRIGHT: Ignore the comments.

12 CHAIR GENCO: Ignore the comments PW67 and

13 69.

14 MR. SHERMAN: That's easy enough.

15 CHAIR GENCO: Easy, and it makes Debbie

16 happy too I can see.

17 Okay, good. Page 61 general comment for

18 H202.

19 MR. CANCRO: 161.

20 CHAIR GENCO: I'm sorry, 161.

21 MR. LISTGARTEN: Where on 161?

22 MR. CANCRO: I'm sorry, we're talking

23 about the NDMA --

24 CHAIR GENCO: Yes.

25 MR. CANCRO: -- 161.

1 CHAIR GENCO: Where is that in the FDA?

2 DR. WRIGHT: 99.

3 CHAIR GENCO: It's FDA 99. Okay, it

4 begins on 99 and it goes through 105. You're talking

5 about the safety. Do you want re-revisions of that,

6 major revisions?

7 MR. SAVITT: I'm not opposed to many of

8 the revision that I've read through. There are some

9 various word changes and questions about exactly what

10 needs to get inserted. But the general philosophy

11 that we need to revise this from the original report

12 to include a lot of the discussion and extra

13 information that was gained over the three days I

14 think is perfectly appropriate.

15 CHAIR GENCO: Sounds like you've

16 volunteered to work with Bob on that?

17 MR. SAVITT: Yes.

18 CHAIR GENCO: Good. Okay, so the write-up

19 on pages 99 to 105 relative to the safety of H2O2 will

20 be deferred to after this meeting and Gene will take

21 the lead --

22 MR. SAVITT: That's fine.

23 CHAIR GENCO: -- to present suggestions to

24 Bob Sherman. This does not preclude interaction with

25 industry as appropriate. Okay, good.

1 Thank you, Gene.

2 DR. WRIGHT: So you can jump to page 13,

3 because all of those are hydrogen peroxide comments.

4 CHAIR GENCO: Oh, page 13 of your --

5 DR. WRIGHT: Of the handout from today.

6 CHAIR GENCO: Great.

7 MR. SHERMAN: And don't throw in another

8 set of pages.

9 CHAIR GENCO: No.

10 DR. WRIGHT: Number 13.

11 CHAIR GENCO: It's an unlucky number. All

12 right, so -

13 DR. WRIGHT: And start with the third one

14 from the top.

15 CHAIR GENCO: -- okay, we're talking about

16 -- now it's page 177 -- this is PW90, comment PW90,

17 okay, FDA page 110, and NDMA 177. So FDA page 110,

18 okay, this looks like sanguinaria extract. Let's see,

19 so this has to be made consistent with the designation

20 that it was safe.

21 Chris, did you have a chance to look at

22 these revisions? They're on page, suggested revisions

23 on page 177 of NDMA.

24 MS. WU: PW90 is okay.

25 CHAIR GENCO: Okay, PW90.

1 MR. CANCRO: And 91 is of a similar, the
2 same issue.
3 CHAIR GENCO: Oh, it's simply to take the
4 word "safety" out.
5 MR. CANCRO: Yes. I mean you've declared
6 it safe --
7 CHAIR GENCO: Right.
8 MR. CANCRO: -- and the sentence --
9 MR. SHERMAN: We'll correct that.
10 CHAIR GENCO: Okay, good.
11 MR. CANCRO: -- and similarly 91.
12 CHAIR GENCO: Okay. Okay, those are both
13 done then.
14 MR. CANCRO: Okay.
15 CHAIR GENCO: Format, the next two typo
16 errors --
17 MR. CANCRO: Well, let's just announce
18 that the pages were wrong. We're talking about
19 formatting changes on page 195 of the PA submission,
20 and it's page 123, and it's just a typo, and it's 92,
21 Bob. If you turn to 195.
22 CHAIR GENCO: Oh, the demonstrated?
23 MR. CANCRO: Yes.
24 CHAIR GENCO: Okay, good.
25 Now, PW93, which is FDA page 125, 126,

1 delete the proposed dosage and labeling from each
2 section. Those discussed --
3 DR. WRIGHT: Did that.
4 CHAIR GENCO: -- so this is a redundancy?
5 It looks like format --
6 MR. CANCRO: I think you've addressed --
7 CHAIR GENCO: -- okay.
8 MR. CANCRO: -- you've addressed that.
9 CHAIR GENCO: Okay. The next comment is
10 FDA page 126 at the top, it's PW94, NDMA page 198,
11 again --
12 MR. SHERMAN: The same issue.
13 CHAIR GENCO: -- safety issue here. PW94,
14 I don't see it.
15 MR. CANCRO: Page 198, 94 --
16 DR. WRIGHT: `97.
17 MR. CANCRO: -- 197, sorry.
18 CHAIR GENCO: Okay. Okay, it's 126, FDA
19 126.
20 MR. CANCRO: At the top of the page. No,
21 again simply -- that, you know, you have rules on the
22 safety.
23 CHAIR GENCO: Okay, any problems with
24 that?
25 MR. SHERMAN: Right.

1 CHAIR GENCO: Okay, good it's done.

2 MR. SHERMAN: We'll take care of it.

3 CHAIR GENCO: All right.

4 The next two are format. Do we need to

5 announce these or have we done this before? It sounds

6 like we have.

7 DR. WRIGHT: Yes.

8 CHAIR GENCO: Okay. Okay, now page 220 of

9 NDMA, which is FDA page 143, bottom, PW97.

10 MR. CANCRO: Again, the issue is that you

11 did declare it safe and we'd like that inserted.

12 CHAIR GENCO: Okay, it's under zinc

13 citrate. G "The subcommittee concludes that there is

14 sufficient evidence to support the effectiveness."

15 MR. CANCRO: To support the "safety."

16 CHAIR GENCO: Oh, it's "safety."

17 MR. SHERMAN: "Support the safety."

18 CHAIR GENCO: Okay. But not the

19 effectiveness?

20 MR. SHERMAN: Right.

21 MR. CANCRO: Right.

22 CHAIR GENCO: Okay, it's done.

23 The next two are formatting. The first

24 one --

25 MR. SAXE: There is a small typo here, or

1 not a typo actually but just a correction in grammar.
2 I believe with looking at zinc citrate and the FDA
3 page 143, the second paragraph under "zinc citrate,"
4 has a chemical name of, a chemical name, the word
5 "and" probably is better used on the following line
6 following the word "citric acid," so it would read
7 "The formula of zinc C6H5O7 taken twice is prepared
8 from zinc carbonate and citric acid and is described
9 as dihydrate, etcetera.
10 CHAIR GENCO: Okay, Bob?
11 MR. SHERMAN: I'm sorry, Stan, what page
12 is that on, on the FDA?
13 MR. SAXE: Page 143.
14 MR. SHERMAN: 143.
15 MR. SAXE: If one takes the -- I know
16 because I wrote this originally. If one takes the word
17 "and" following the formula for zinc citrate, deletes
18 the word "and" and inserts the word "and" on the
19 following line after "citric acid."
20 CHAIR GENCO: Read the sentence as it
21 should --
22 MR. SHERMAN: "Zinc citrate has a chemical
23 formula RZN3C6H5O7 taken twice is prepared from zinc
24 carbonate and citric acid and is described as
25 dihydrate or loose powder, so at least slightly

1 soluble in water," and then --

2 CHAIR GENCO: Thank you.

3 MR. SHERMAN: -- the reference.

4 CHAIR GENCO: Okay, the next two are

5 formatting we're told. So this is sections to suggest

6 it to be moved, so we'll take under consideration.

7 Bob, is that clear?

8 MR. SHERMAN: Yes.

9 CHAIR GENCO: Okay. Then let's go to page

10 278.

11 MR. CANCRO: 278 is where we come in

12 again, and it's PW100. It's page 184 of the FDA. And

13 the issue here is you have declared the combination of

14 sodium bicarbonate and hydrogen peroxide to be safe,

15 category one. The efficacy was three. And we believe

16 that should be, the combination, should be stated as

17 having been voted safe. So if you delete on page 277

18 of the proprietary association of the -- the NDMA

19 Association's manuscript --

20 CHAIR GENCO: We know how long you've been

21 with us.

22 MR. CANCRO: -- alas, line 22 -- I did

23 that for Mike's benefit. He remembers that. Line 22,

24 just delete "safety," and that would take care of it.

25 CHAIR GENCO: Bob, do you see that?

1 MR. SHERMAN: Yes.

2 CHAIR GENCO: Okay, good.

3 All right, next is PW101.

4 MR. CANCRO: Okay, I think the following

5 comments, if we look at 101 and 102 and 103, really we

6 believe, if you can read through the comments, that

7 that more fully reflects some of the additional work--

8 CHAIR GENCO: Okay, on your page 278 --

9 MR. CANCRO: Right.

10 CHAIR GENCO: -- it's not clear what

11 you're suggesting because nothing is underlined.

12 MR. CANCRO: Well, this is true. But

13 we've created text under each of the notes --

14 CHAIR GENCO: Okay.

15 MR. CANCRO: -- and what we're saying is

16 that some of that text, however you want to capture

17 it, should be incorporated --

18 DR. WRIGHT: Where is it?

19 CHAIR GENCO: -- it's on this sheet.

20 MR. CANCRO: It's on the sheet.

21 CHAIR GENCO: Is on this sheet. It's on

22 their handout sheet.

23 MR. CANCRO: It's on the sheet.

24 MR. SHERMAN: It's not on page 278.

25 That's the confusion.

1 MR. CANCRO: Right, it's a suggestion to
2 revise --
3 MR. CANCRO: Yes.
4 CHAIR GENCO: -- that section on your page
5 278 which would be --
6 MR. CANCRO: Right.
7 CHAIR GENCO: -- our page 184 beginning
8 "Although hydrogen peroxide," so that's the paragraph.
9 MR. CANCRO: And there are four comments
10 that we've made as examples of how you could capture
11 some of the work.
12 CHAIR GENCO: 101, 102, 103.
13 MR. CANCRO: 101, 102, 103 and 104.
14 MR. SAVITT: I feel that since this is --
15 it makes sense to go through the hydrogen peroxide
16 safety issue rewrite first, and then this is just a
17 matter of putting it together with that safety re-
18 write to include the combination.
19 CHAIR GENCO: Okay. So that in Gene's
20 analysis of the hydrogen peroxide, he will address
21 those suggestions 101 to 104, Bob.
22 MR. SHERMAN: Okay.
23 CHAIR GENCO: Good.
24 MR. CANCRO: The next series of comments
25 begin on 288, and they are 105, 106, 107, 108, and

1 they are all formatting or typo changes. So we can go
2 over those very quickly, if you'd like, commencing on
3 288.
4 CHAIR GENCO: Which is FDA page 192.
5 MR. CANCRO: Okay, it's simply again the
6 labeling issue 105.
7 CHAIR GENCO: So what you're suggesting is
8 on page 192 it says small Roman Numeral iii "Dosage
9 for labeling," to leave out IV, that sentence on
10 labeling, is that what you're suggesting?
11 MR. CANCRO: Well, this goes --
12 MR. SHERMAN: Yes, format again, and
13 you're suggest that it be thrown out.
14 CHAIR GENCO: You're saying to leave out
15 Roman Number IV, omit it from here, you're suggesting?
16 Just so we're clear on what the suggestion is.
17 Okay, so we take that in consideration?
18 MR. SHERMAN: Yes.
19 CHAIR GENCO: And the typo, that should be
20 easy to handle. Then the 107 labeling should reflect
21 it in the body of the report as discussed before,
22 again formatting?
23 MR. SHERMAN: It sounds like the same
24 thing.
25 CHAIR GENCO: Okay. And then 108

1 labeling, considered earlier, again formatting.

2 So, Bob, we'll make sure that that's

3 consistent?

4 MR. SHERMAN: Yes.

5 MR. CANCRO: And that takes you through

6 108, Bob.

7 CHAIR GENCO: Good.

8 MR. CANCRO: It's just, I can give you a

9 hand on that.

10 CHAIR GENCO: Just so that we're clear.

11 Okay, now DSW109, page 311, and the FDA

12 page 46 now. We're going back, right, 46?

13 MR. CANCRO: Now, are you going -- yes,

14 in your text you've got to go back to 46, and this is

15 the section on the inactive ingredient, alcohol.

16 Did we, or did we not indicate the

17 appropriateness of changing the position, the

18 formatting change, did we agree that it's more

19 appropriately removed from the -- sorry, you were

20 going to look that up I guess, Bob --

21 MR. SHERMAN: We'll consider that.

22 CHAIR GENCO: All right, that's fine,

23 okay.

24 MR. LISTGARTEN: Is this bold, small

25 capital writing on purpose or --

1 PARTICIPANT: No.

2 MR. LISTGARTEN: -- this isn't meant to be

3 like that? I'm just talking about the format to that

4 first paragraph on alcohol.

5 MR. CANCRO: Yes, yes. It wasn't

6 intended.

7 MR. CANCRO: Okay, I think we're ready for

8 the issue on alcohol. And I would say the general

9 statement that I think is appropriate here is that

10 you've had a workshop on alcohol which put into

11 perspective the epidemiological studies, you've heard

12 from a bunch of experts, Dr. Shapiro, Dr. Williams,

13 Dr. Philip Cole, some agency experts, and what they

14 said and how that all turned out is really entirely

15 missing from this section. It hasn't been created,

16 but that has to be captured in some way to support the

17 fact that you at this point realize that, you know,

18 that alcohol can be used in a mouthwash at the

19 concentrations, and that's what's missing here.

20 Additionally, there is some confusion

21 which may have been brought to your attention I think

22 in the Warner-Lambert submission of yesterday where

23 recommendations were discussed and not voted on, and

24 we never understood the status of that, and hence I

25 think the Warner-Lambert presenter recommended

1 deleting it. We as an industry group support that.
2 It wasn't voted on and, you know, it shouldn't appear
3 as a recommendation.
4 So this really necessitates additional
5 time to capture the deliberations of the workshop and
6 the logical progression of how you reached your
7 conclusions. Which you do state your conclusions are
8 stated, if I can find them --
9 CHAIR GENCO: Yes, Bill?
10 MR. CANCRO: -- page one.
11 MR. BOWEN: Did a document come out of the
12 workshop, Lew?
13 MR. CANCRO: Sorry, Bill?
14 MR. BOWEN: Did a document on the alcohol
15 workshop -- did a document come out of the alcohol
16 workshop? Is there an official of the workshop
17 available?
18 MR. CANCRO: I don't know.
19 MR. SHERMAN: I don't think so.
20 MR. HUTT: There was no written summary of
21 the results of the workshop. There was a vote at the
22 conclusion of the workshop.
23 MR. SHERMAN: That's something I think due
24 to time constraints was obviously somewhat overlooked,
25 and that's something that we will have to pull

1 together. We can go back to the original transcripts
2 and we should have all that information. But maybe we
3 could work with some of the subcommittee members on
4 that and we can --
5 CHAIR GENCO: Yes, I'd be glad to --
6 MR. SHERMAN: -- and we'll accept
7 industry's input --
8 CHAIR GENCO: -- offer with you on that.
9 I could work with you on that.
10 MR. SHERMAN: Okay.
11 CHAIR GENCO: And maybe Chris and --
12 MR. D'AGOSTINO: I actually was quite
13 vocal at some of those meetings. I'd be happy to --
14 CHAIR GENCO: Okay, fine.
15 So Ralph and I, and Chris, do you -- okay.
16 MR. SHERMAN: Is that agreeable?
17 CHAIR GENCO: Yes.
18 MR. CANCRO: I mean we can't create it
19 here --
20 CHAIR GENCO: No --
21 MR. CANCRO: -- this is something that
22 obviously because this was a draft, it is not
23 adequately dealt with, so we'll do that.
24 CHAIR GENCO: I don't know how important
25 it is, but I'll throw it up for your considerations.

1 We've now, I think, come to some agreements that says
2 that the document should reflect the totality of the
3 proceedings. And one of the things that strikes me as
4 missing, and again just for discussion purposes, is
5 some of the logic related to the request.
6 And the thing I have in mind, Bill, is the
7 thing that you brought in during your review of
8 peroxide where you had concerns with patients who in
9 effect had very little saliva flow, and those studies
10 were recommending you capture, but maybe some of the
11 rational as to why you wanted to capture those, and I
12 don't know if that's important, but it would make
13 better reading, better progression of why something
14 was done in response to something.
15 So I think that occurs in a number of
16 places, and I'm just throwing it up to this group by
17 way of whether or not you want to consider that.
18 CHAIR GENCO: Does anybody know if the
19 Wiggins paper has been published? That's the
20 University of Washington. The presentation was made
21 by the graduate student working on it. Nobody is
22 aware of that?
23 PARTICIPANT: No.
24 CHAIR GENCO: Is anybody aware of any
25 publication from the NIH? They were going to -- our

1 recommendation was for further studies. They did have
2 a study in progress in, I think it was Puerto Rico.
3 Has that been published or has that been presented as
4 a abstract even? Okay, so that was two years ago I
5 think, '96.
6 Well certainly, if anybody knows of any
7 more information than what we had, we would appreciate
8 hearing from you on that. Any sort of report, even an
9 abstract I think would be useful on those studies
10 which are obviously either in progress, near
11 completion or ongoing.
12 I think one of the issues there was the
13 one study from the Cancer Institute seemed to show an
14 effect. There were other smaller studies that didn't.
15 But then there were more studies in progress and I
16 think that those are going to be critical to helping
17 us resolve that issue. So I think that's really
18 important. Any new information could be quite
19 illuminating.
20 Yes, Bill?
21 MR. BOWEN: Are any of the manuscripts
22 from the workshop available? Presumably people did
23 prepare manuscripts.
24 CHAIR GENCO: Bill, I think they were more
25 oral presentations. As I recall, the Wiggins was a

1 graduate student or post doc who presented, and he had
2 slides.
3 MR. D'AGOSTINO: We should be able to get
4 a transcript of the slides.
5 CHAIR GENCO: The transcript of the slides
6 we'll have.
7 So, Bob, you're saying there wasn't really
8 time for the FDA to include all that material, and
9 that's one of the issues here. It's not an omission,
10 it's just --
11 MR. SHERMAN: It probably was somewhat
12 overlooked in preparing the draft. And we certainly
13 should have all that information available to us, and
14 we'll put it together.
15 CHAIR GENCO: Good. So we can go to
16 another draft and then maybe Ralph and I can look at
17 it.
18 MR. SHERMAN: That's right.
19 CHAIR GENCO: Any further information from
20 industry would be welcome at this point. The sooner
21 the better, and then --
22 DR. BARNETT: Yes, and -- I'm sorry.
23 CHAIR GENCO: -- go ahead, and then we'll
24 come to some final fair and complete discussion of
25 this item.

1 DR. BARNETT: Yes. And to answer Bill's
2 question, I do believe we have some of the, maybe not
3 formal transcripts, but material that some of the
4 presenters such as Dr. Cole used in our files.
5 CHAIR GENCO: Other than what was handed
6 out at the meeting?
7 DR. BARNETT: I'll have to check, I'm not
8 sure.
9 CHAIR GENCO: Okay, fine. Whatever,
10 whatever you would be willing to share --
11 DR. BARNETT: Yes, if we have it, of
12 course we'd be willing to share. Of course that was
13 one of the key analyses because it really looked at
14 that study that you referred to again and revealed
15 some of the questions that one could ask about the
16 conclusions. So we'll look into that and anything we
17 can provide, we'll send to you, Bob.
18 CHAIR GENCO: I think maybe through Bob
19 Sherman, yes.
20 DR. BARNETT: Bob Sherman, okay, sure.
21 CHAIR GENCO: Yes, send everything to Bob
22 Sherman so that we have an orderly conduit. You
23 haven't seen my desk lately.
24 MR. SHERMAN: You haven't seen my desk.
25 You can't see my desk.

1 CHAIR GENCO: We won't even look at Bob's.

2 MR. D'AGOSTINO: There might even be a

3 video on -- video back then and make it available.

4 PARTICIPANT: Do you know what page that's

5 on.

6 MR. D'AGOSTINO: 96.

7 CHAIR GENCO: And we could include body

8 language then, if we had a video.

9 MR. CANCRO: Bob Sherman --

10 MR. SHERMAN: Yes.

11 MR. CANCRO: -- we failed to see one

12 additional deletion of the term "safety" concerning

13 the review of sanguinaria, and you can find that on

14 page 191 of the NDMA manuscript, or page 120 of the

15 FDA manuscript. And again it's the same issue of

16 catching and deleting the appropriate word.

17 Bob?

18 CHAIR GENCO: Yes.

19 MR. CANCRO: If you think it appropriate,

20 the industry group certainly would be willing to put

21 together what we think would be a rather detailed

22 outline on that peroxide review and what the

23 contributions were from major speakers. That could be

24 sent to Ralph or you, or to Bob Sherman and, you know,

25 you could look it over as maybe a guideline as how you

1 want to recreate it.

2 CHAIR GENCO: I think that might be

3 helpful, Gene. In other words, if they sent it to

4 Bob, and you and Bob worked with that and other

5 materials. So, you know, as with anything else we

6 certainly welcome help --

7 MR. CANCRO: Right.

8 CHAIR GENCO: -- and throughout the five

9 years industry has been very helpful. It's got to be

10 our report --

11 MR. CANCRO: I don't know what --

12 CHAIR GENCO: -- obviously --

13 MR. CANCRO: -- yes.

14 CHAIR GENCO: -- I mean that's the intent.

15 And our report is going to be advisory to the FDA, so

16 we understand the process.

17 MR. CANCRO: I think, I don't know whether

18 I indicated the peroxide or alcohol, but on both of

19 those things we could make a contribution.

20 CHAIR GENCO: Good.

21 MR. CANCRO: Bob could get it and I think

22 you could look it over.

23 CHAIR GENCO: Excellent. That would seem

24 to be helpful.

25 Again, time is important here. Not to

1 hurry it, but Bob our schedule from now to when we
2 want to make the final report is what, months?
3 MR. SHERMAN: Oh, in the next two to three
4 months --
5 CHAIR GENCO: Two to three months.
6 MR. SHERMAN: -- or so, just roughly. We
7 don't have an absolute deadline at this point.
8 CHAIR GENCO: But it's not six months or
9 a year?
10 MR. SHERMAN: No, no, we wouldn't want it
11 to go that long, no.
12 CHAIR GENCO: So your time table there
13 could be adjusted accordingly.
14 MR. SHERMAN: Does that give you
15 sufficient time?
16 MR. CANCRO: Yes, I think that would be
17 adequate and, you know, hopefully that could speed the
18 process along.
19 CHAIR GENCO: Excellent.
20 MR. SHERMAN: All right.
21 CHAIR GENCO: So the process would be
22 whatever you submit, information about manuscripts,
23 information handed out a meetings that we may not have
24 shared, submit to Bob, or your considered outlines or
25 even drafts to Bob, then Bob will share them with the

1 panel member or members assigned to that particular
2 area, come to final conclusion, and then we will
3 communicate as a panel with Bob, to come to a final
4 consensus on whatever is changed so that this will be
5 truly our report. Good.
6 Now, were there other items?
7 MR. SHERMAN: Does that about take care of
8 the comments, do you know?
9 CHAIR GENCO: I don't think so.
10 PARTICIPANT: Yes.
11 CHAIR GENCO: Oh, is that it?
12 MR. SHERMAN: Do you want to take a quick
13 break or a not so quick break and then we'll come back
14 and wrap it up.
15 CHAIR GENCO: Okay.
16 MR. SHERMAN: Peter, did you want to say
17 something? I mean we can do that after break. I'm
18 just asking.
19 CHAIR GENCO: Yes, let's take a break. I
20 think we're all getting dry mouth. Xerostomia is
21 setting in. Okay, can we come back at 10:15?
22 (Whereupon, at 10:01 a.m., a recess until
23 10:27 a.m.)
24 CHAIR GENCO: I'd like to call this group
25 to order, which will be the last time we'll do this,

1 and I'm sure everybody is happy about that.

2 We have finished most of our official

3 business. We would now like to have some comments

4 from various individuals on the panel and its process,

5 and we'll start with Peter Hutt.

6 MR. HUTT: Thank you, Bob, for the

7 opportunity to make just a few concluding remarks.

8 I'm particularly pleased that Michael

9 Kennedy is here today. Not only did he and I attend

10 the first meeting of the first panel, but we are

11 probably two of a very rare and vanishing group who

12 have attended at least one meeting of every over the

13 counter drug review panel that has ever been convened.

14 This process began, as you all know,

15 actually in the fall of 1971. It was planned at that

16 time, and it began in full swing in early 1972. I

17 remember very distinctly being given the task of

18 calling Dr. Franz Ingelfinger to ask him to chair the

19 first panel, the antacid panel. I said, Dr.

20 Ingelfinger, where is what I can offer you, we are

21 asking you to come on Saturday and Sunday mornings to

22 un-air conditioned room in the basement of the

23 building next door, at the Parklawn Building, to work

24 all day long for $137.50, which was the honorarium at

25 that time, and to craft a report for the country. And

1 he established a tradition that frankly all of you
2 have followed. He immediately said yes, this is worth
3 doing, this is something that any physician, dentist,
4 scientist in the country should welcome the
5 opportunity to do.
6 He established my version of the
7 Ingelfinger Rule, and that is the rule of public
8 service. Because what all of you have done, and here
9 I speak not on behalf of one company, but all of the
10 companies who have participated and people who are not
11 here today, but what each member of this panel has
12 done, what our two Chairs, Bill Bowen and Bob, what
13 you have done, is to achieve the ultimate in public
14 service. To give up many more opportunities of far
15 more lucrative ventures to spend your time in these
16 rooms, going over these details. You have been the
17 ultimate also of a democratic process. There isn't a
18 single person who has appeared before you who hasn't
19 been heard and heard in full with enormous opportunity
20 to participate.
21 I would commend the liaison members. We
22 have had more than one on both the industry and the
23 consumer side who also did a tremendous job, and
24 lastly the FDA staff. So this is really your legacy.
25 It isn't the words on the paper, and it isn't what's

1 just going to be published in the Federal Register,
2 but it is the legacy of public service that I admire
3 so greatly. And so on behalf of all of us, I thank
4 you.
5 CHAIR GENCO: Thank you, Peter. And,
6 Peter, it's clear, and I speak for the panel and I'm
7 sure that they would agree, that you have been
8 extremely helpful and very fair, and we appreciate all
9 of your good advice through the years. Thank you.
10 We'd now like to ask Bob Sherman for his
11 comments.
12 MR. SHERMAN: Thanks. I just have a brief
13 statement that I'd like to read.
14 EXECUTIVE SECRETARY REEDY: Can I say
15 something first for just one moment?
16 MR. SHERMAN: Sure.
17 EXECUTIVE SECRETARY REEDY: What year was
18 that, that you invited Dr. Ingelfinger.
19 MR. HUTT: 1972.
20 EXECUTIVE SECRETARY REEDY: 1972. And
21 that's 45 years, what 49, 50?
22 MR. HUTT: 26 years.
23 EXECUTIVE SECRETARY REEDY: 26 years,
24 okay. Math is not my -- in 26 years the compensation
25 has only increased $12.50, so these people are truly

1 giving their time and effort to their country.

2 MR. SHERMAN: Thanks.

3 To the members of the subcommittee, on
4 behalf of the Food and Drug Administration, the
5 Division of Over The Counter Drug Products would like
6 to acknowledge your expertise as a consultant to the
7 Non Prescription Drugs Advisory Committee and a member
8 of the Dental Plaque Subcommittee, and to express our
9 appreciation for your participation in the OTC Drug
10 Review.

11 The achievements of the subcommittee
12 reinforces our conviction that responsible regulation
13 of consumer drug products depends greatly upon the
14 participation and advice of the non governmental
15 health community.

16 We thank you for your valuable time and
17 effort in developing the subcommittee's report. The
18 report will become the basis for FDA's final monograph
19 for OTC drug products for the reduction or prevention
20 of dental plaque and gingivitis, that will help make
21 safe and effective drug products available to
22 consumers.

23 In recognition of your distinguished
24 service to the Food and Drug Administration, we are
25 pleased to present to you this, and normally here we

1 would say letter or certificate, but I think it's
2 appropriate that this time it's a plaque and we have
3 one of these for each of you. Thank you, we
4 appreciate it.
5 CHAIR GENCO: Well, thank you, Bob. I
6 guess we could advise on plaque control, but we really
7 can't control plaques, can we. Thank you very much.
8 (PLAQUES PRESENTED)
9 CHAIR GENCO: I'd like to say a few words.
10 First, I don't think we can be accused of making snap
11 judgments. In the USA Today Ralph pointed out an
12 article on the staff of the FDA that's a little
13 concerned about decisions on fast track. Well, we
14 certainly can't be accused of doing that after five
15 years, 31 days of meeting, and 16 different meetings.
16 However, I think that really says
17 something about the process, which I have to admit
18 that initially being a rather impatient person in
19 general, I never thought it was a reasonable process,
20 but now I'm very much convinced that it is a good
21 process. And Peter Hutt has had that perspective, and
22 I'm sure Dr. Kennedy, through the years, that this is
23 a deliberative process and reiterative process and I'd
24 like to thank all who are here and those who have
25 helped over the last five years to make it a very

1 thoughtful, deliberative process.

2 I guess as human endeavors go, it's

3 probably prone to the least error possible as a human

4 endeavor, and I hope that our document reflects that

5 and that we won't have any major surprises in the

6 future. Science always has its unexpected happening.

7 Some agents that we thought were safe may show some

8 side effects, that's for sure that may happen.

9 However, I think on December 3rd 1998, this is our

10 best judgment as to safety and efficacy, and the

11 process is a good process and I'm very pleased and

12 honored to have been a part of it.

13 I'd like to thank the FDA staff beginning

14 with Linda for her perspectives and her guidance

15 through the years.

16 Bob Sherman for his untiring efforts,

17 particularly in the last few months, but all through

18 the time he's been with us.

19 And Stephanie, who has been with us the

20 entire time, for her wonderful efforts. And it's hard

21 to imagine the amount of work that goes into preparing

22 those mountains of materials that we all have received

23 which are very important.

24 Sandy Titus who substituted this morning

25 for Kathleen, and Kathleen Reedy, our Exec Secretary,

1 we thank for taking care of all the important details
2 of our meetings.
3 Debbie Lumpkins who has been here almost
4 every meeting, maybe every, and although quiet did
5 make her messages known by a smile or a frown. And my
6 peripheral vision is good and very much aware of her
7 view on things.
8 And Fred Hyman who let us in on the NDA
9 perspective, which many times was very important, and
10 gave us the vision or goal of looking at OTC
11 differently. We knew what the NDA process was, and
12 Fred kept us reminded that this was not an NDA
13 process, this was an OTC process. So by contrast it
14 was very important that you were here and made your
15 comments known.
16 The panel has evolved over the years to I
17 think a very smooth working panel of like mind.
18 Certainly not agreeable, agreeing on all concepts, but
19 agreeable. It's an agreeable panel, and I think we
20 got a lot done even though it took time.
21 I thank Bill Bowen for providing being a
22 mentor for the chairmanship. He certainly ran a tight
23 committee and I hope I've come to his standards in the
24 last couple of years.
25 Also, I'd like to thank the committed core

1 of industry who are here today. Your faces are all
2 very familiar here. You're even sitting in the same
3 seats. It's like High School 101 Biology Class here.
4 You've been of great help. And I in particular like
5 the interaction, it's been very constructive.
6 Obviously you have a viewpoint, we have a viewpoint,
7 we each have our own constituencies to deal with, but
8 I think it's been done in a very productive manner.
9 So in all, I'd like to thank you. It's
10 been a wonderful five years. I'm glad to see it end,
11 as all of these things should end, and we're on to
12 other things, all of us. So thank you very much, and
13 if anybody else has any other comments, this is the
14 time to make them, otherwise we will convene this
15 panel.
16 Okay, the panel deliberation is complete.
17 Thank you all very much.
18 (Whereupon, the meeting was adjourned at
19 10:38 a.m.)
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25

C E R T I F I C A T E

This is to certify that the foregoing transcript in the matter of: MEETING

Before: DENTAL PLAQUE SUBCOMMITTEE

Date: DECEMBER 3, 1998

Place: ROCKVILLE, MD

represents the full and complete proceedings of the aforementioned matter, as reported and reduced to typewriting.

Irene Gray