

1 get a higher concentration of macrophages. You
2 ultimately activate more and more the acute
3 inflammation reaction.

4 But of course, if they phagocytize the
5 material, which is resorbable in the user zones, it
6 will disappear. But if it is an impure material,
7 hydroxyapatite, it will not be resorbable. So on the
8 market now it's the tendency, you know, no particles
9 for a bone regeneration material, and these particles,
10 of course, are phagocytized by the macrophages, but
11 there is no chance, because these particles is
12 hydroxyapatite.

13 DR. SUZUKI: Jon Suzuki again. Just a
14 follow-up question. Sir, the macrophage is then when
15 they begin the phagocytosis of the particles that are
16 10 microns or less. They are impeded in their
17 "regulation." Is that what you are implying?

18 DR. UHR: Yes.

19 DR. SUZUKI: Or if you're not familiar
20 with the macrophage, they are sometimes considered the
21 field generals or the sponsor or the host.

22 DR. UHR: Yes, yes.

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1 DR. SUZUKI: And sometimes referred to as
2 the quarterback.

3 DR. UHR: Yes.

4 DR. SUZUKI: And where they came from.

5 DR. UHR: Okay, right.

6 DR. SUZUKI: So this is impeding?

7 DR. UHR: Yes.

8 DR. ARROWSMITH-LOWE: And in addition to
9 that, you are having a loss of material as well, and
10 so instead of the material being able to do its
11 initial function, if the particle size is too small,
12 then it is not able to do its intended use, because
13 the particles are phagocytized by the macrophages and
14 you are actually losing some of the material that
15 would have been maintained as a part of the graft for
16 the reparative process. And so there's the downside
17 of it not being able to actually meet its intended
18 use, because the particle size being somewhat say
19 below 8 microns actually.

20 DR. UHR: And the other point is you
21 extend the phase of low pH.

22 DR. ARROWSMITH-LOWE: Right.

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1 DR. UHR: And we know Beta Tricalcium
2 Phosphate dissolved very quickly in a low pH in an
3 acid environment.

4 DR. SUZUKI: Jon Suzuki. And you also
5 indicated that some of these particles are seen
6 histopathologically in sites in the lymphoid tissue of
7 lymph glands.

8 DR. UHR: Yes.

9 DR. SUZUKI: It's not the macrophages that
10 have carried this product, but it is rather the
11 lymphoid cells. Is that my understanding?

12 DR. UHR: No, no, the macrophages runs
13 part of it.

14 DR. SUZUKI: And what are the lymphoid
15 cells doing there?

16 DR. UHR: The T lymphocytes, for example,
17 they stimulate the fever of the fiber, and the fever
18 is the temperature, yes, and they release
19 interleukines, for example, you know, to attract the
20 interleukines. Probably they are transported to the
21 liver, yes. You know, they induce release of factors.
22 You know it, certainly, there is an interconnection

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1 between the T lymphocytes and the macrophage.

2 DR. SUZUKI: One last question, Madam
3 Chair. The T lymphocytes that you just mentioned are
4 frequently associated with a delayed hypersensitivity
5 or allergic type or rejection reactions. Are you
6 suggesting that that might be a parameter, too, that
7 we need to consider?

8 DR. UHR: I think so, so that's in the
9 histological figure. At 11 weeks, we see a reaction
10 to this small particles distributed in still
11 connective tissue. It's not a bone formation there,
12 yes, and at this time, the women have a bone
13 regeneration. That's the point.

14 CHAIR REKOW: Daniel?

15 MR. SCHECHTER: Dan Schechter. Taking for
16 argument's sake that all of the biological information
17 you have given is true and that these various factors
18 are important to the product and to the safety and
19 effectiveness of the product, these parameters could
20 be spelled out in special controls in a Class II
21 product, and my question is are you saying that the
22 parameters are not known in the literature, and the

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1 only way that an application could be properly
2 reviewed would be with data, since there is nothing to
3 compare it to, as I suppose your company has done, or
4 is it that it just needs to be spelled out, because
5 it's known? The purity is known. The particle size
6 that is needed is known in the literature that we, as
7 a Panel, could recommend it be put into special
8 controls, because then you are not just comparing to
9 another product, you're comparing to a standard, but
10 that can be done with a reclassification?

11 DR. ARROWSMITH-LOWE: No, that's exactly
12 right. It could be done with a reclassification, and
13 so what -- that's why the final slide was there, that
14 if the reclassification occurs, you know, we feel that
15 it's absolutely essential that those parameters be
16 assessed as a part of a determination of substantial
17 equivalents. There is a good bit that is known, at
18 least a good bit based on work that has been done
19 either in Curasan AG or by independent researches that
20 Curasan AG has been collaborating with to make a
21 determination about what is an acceptable level of
22 purity.

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1 And, you know, I have to say that the
2 acceptable level of purity that Curasan supports is a
3 higher acceptable level of purity than the ASTM
4 standard, for instance, on this, and that really is
5 based upon the clinical performance of the product,
6 the fact that you can actually see histologically that
7 you have a better healing process when you have far
8 fewer impurities, and the same holds true for the
9 other aspects that we're talking about, as well. For
10 particle shape, that you can see actual clinical
11 negative occurrences that can happen from particle
12 shape.

13 In addition, particle shape may prevent
14 having intragranular spaces that really are sufficient
15 for blood vessel introduction, you know, from a
16 standpoint of porosity, that the healing process is
17 going to proceed more appropriately, because the
18 porosity provides the opportunity for adequate fiber
19 and attachment, and then that's a pathway that is
20 subsequently used through the healing process and,
21 ultimately, to the point of creation of new bone
22 there.

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1 And so each of these actually does have
2 what we feel is some fairly high significance and yes,
3 one of the ways of approaching that would be to use a
4 special control to develop a mandatory standard and
5 just say that, you know, adherence to this mandatory
6 standard is going to be something that would be
7 required of any product that is regulated, the Beta
8 TCP product, if it were regulated as a Class II.

9 CHAIR REKOW: Just as a point of
10 clarification, Dianne Rekow again, I would like a
11 simple yes or no if it's possible. Is --

12 DR. ARROWSMITH-LOWE: I worked at FDA too
13 long.

14 CHAIR REKOW: Yes.

15 DR. ARROWSMITH-LOWE: So there is never a
16 simple yes or no.

17 CHAIR REKOW: Is it your belief that there
18 is scientific data to support upper and lower
19 thresholds for each of those four parameters that you
20 specified, the purity, the particle size, the particle
21 shape and --

22 DR. ARROWSMITH-LOWE: Yes, particle shape

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1 and porosity.

2 CHAIR REKOW: Porosity, yes, I'm sorry.

3 DR. ARROWSMITH-LOWE: Yes.

4 CHAIR REKOW: Okay. Thank you.

5 DR. ARROWSMITH-LOWE: That was an easy
6 one.

7 CHAIR REKOW: Susan, did you have --

8 DR. PATTERS: But is that data available?

9 CHAIR REKOW: Yes, is that in the open
10 literature? Is that within the company study?

11 DR. ARROWSMITH-LOWE: Well, some of it is
12 within the company. Some of it is published European
13 literature. All of that we would be able to make
14 available.

15 CHAIR REKOW: Okay. Susan?

16 DR. RUNNER: But my question for that is
17 is that, those limits, the standard of care, is that
18 accepted in the clinical community or is that
19 something that is proprietary to Curasan and you would
20 be making the standard yourself, as opposed to out in
21 the broad literature? Is it something that FDA or the
22 Panel could recommend or is this just your opinion

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1 based on your product and the clinical data you have?

2 DR. ARROWSMITH-LOWE: It's the latter.

3 CHAIR REKOW: I have one other question,
4 if I may, David, before -- I have heard each of you
5 refer to the fact that historical material was
6 withdrawn from the marketplace. I don't need to know
7 all the details. I am just curious if it was removed
8 because of market pressures or if it was removed from
9 requirements from any of the regulatory agencies.

10 DR. ARROWSMITH-LOWE: It was based on
11 market pressures. It essentially was a response to
12 the fact that the product was not performing
13 effectively. Clinically, it was not performing.

14 CHAIR REKOW: Clinicians were not happy,
15 so the market --

16 DR. ARROWSMITH-LOWE: The clinicians were
17 not happy and so it ceased to be purchased, and was
18 ultimately removed from the market.

19 CHAIR REKOW: Okay. That's an important
20 point, I think. Dr. Cochran?

21 DR. COCHRAN: David Cochran. I guess my
22 question is a little bit of follow-up the same way. I

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1 mean, with any parameters for a product, there is
2 going to be a range, and clearly it's in the interest
3 of any company to produce the best product they can,
4 and I think, you know, the Panel needs to consider
5 that as a Panel making a recommendation when we think
6 of controls, certainly we're going to probably make
7 recommendations or when we do, that it's some sort of
8 range, but we don't think ever an intention is that a
9 company is going to come out with a product that's not
10 something that's going to be effective. Otherwise,
11 it's a little silly.

12 CHAIR REKOW: Dr. Burton?

13 DR. BURTON: Richard Burton. Just to
14 carry on to that, was the product that was removed
15 from the market the license that you now own?

16 DR. ARROWSMITH-LOWE: No.

17 DR. BURTON: So it was a different product
18 than the one that you have purchased the license to?

19 DR. ARROWSMITH-LOWE: Yes, that's correct.

20 DR. UHR: We have, may I say, some
21 additional information to that. Curasan was the first
22 on the market in Europe with a pure Beta Tricalcium

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1 Phosphate, and then other companies recognized this as
2 a very successful material, so they tried to imitate
3 it, and they go with the material on the market as a
4 CE certificated product, and then it disappears and
5 you can wait two, three or probably yes, one year, and
6 they have the result. And, you know, one dentist to
7 try a material and he has a bad result, he will not
8 use this material anymore, and so we have no negative
9 publication or a publication about negative results.
10 It's a problem. That material comes on the market.
11 It is tested and the human being is the model, and
12 then it disappears. This is the way.

13 CHAIR REKOW: Yes.

14 DR. ARROWSMITH-LOWE: And I think a part
15 of what we're saying, if I may follow-up on that, is
16 that in the European situation, the competing company
17 is able to introduce a less pure product given the
18 regulatory situation that exists there in Europe, and
19 what then subsequently happens is the performance --

20 CHAIR REKOW: Right.

21 DR. ARROWSMITH-LOWE: The effectiveness of
22 that product is not up to the standard that has been

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1 set by Curasan's product, and so the product ceases to
2 be purchased and to be implanted and to be used, and
3 it eventually leaves the market.

4 CHAIR REKOW: Good five-year market share.
5 That way, they will gain. I'm teasing.

6 DR. GLOWACKI: This is Julie Glowacki. I
7 want to ask the question, Dr. Arrowsmith, in just a
8 slightly different way, but I think it will be a yes
9 or no answer. To any degree, has your opinion been
10 informed by an analysis of the guidance document that
11 was generated out of the orthopedic proposal to
12 reclassify it to Class II?

13 DR. ARROWSMITH-LOWE: Yes. Actually, I
14 have read the document. I have had discussions with
15 people in that branch and they let me know when the
16 document was forthcoming, because again, Curasan has a
17 product that was cleared from market through the
18 510(k) process for orthopedic use, so we have been
19 interacting also with the Orthopedic Branch, and so we
20 were made aware of this previously, yes.

21 DR. GLOWACKI: So you're saying that these
22 four terms should really just be highlighted in that,

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1 being to a greater degree than it is? I haven't
2 reread it since your presentation.

3 DR. ARROWSMITH-LOWE: Yes.

4 DR. GLOWACKI: But to be sure that those
5 four parameters as far as --

6 DR. ARROWSMITH-LOWE: Exactly, and we
7 really do support the idea of the central nature of
8 assessing those four parameters and, you know, as Mr.
9 Schechter pointed out, that can be done in several
10 ways. We think probably the most appropriate way is
11 through establishing the safety and effectiveness, but
12 if there were a reclassification, then the use of a
13 special control and mandatory standard would be
14 another way of trying to achieve that, as well.

15 DR. GLOWACKI: Thank you very much.

16 CHAIR REKOW: Dr. Cochran?

17 DR. COCHRAN: I'm a little naive about the
18 European products over there, but I understand that
19 Ceros is another product. Is that a product that you
20 would say is the current type TCP standard or the old
21 type standard?

22 DR. UHR: No, sorry. I know the Ceros.

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1 We also studied this product, and this material has no
2 inter-connective porosity.

3 DR. COCHRAN: Which means what?

4 DR. UHR: Which means you put this
5 material into the defect, and there is only from the
6 surface the solvent, but there is no ingrowth into a
7 granule. It's not possible. It just bubbles, yes,
8 which make the porosity, but it's not inter-
9 connective, but we need an inter-connective porosity
10 that is lodged, invades into the granule, and
11 afterwards --

12 DR. COCHRAN: What is the purity of that?

13 DR. UHR: It's not larger than 99. It's
14 smaller, and there is an impure phase in it.

15 DR. ARROWSMITH-LOWE: If I may just
16 follow-up on that. The role of the micro-porosity is
17 really for fibrin attachment, and it forms a pathway
18 that ultimately, fibroblast can follow the pathway and
19 there can be an establishment of connective tissue,
20 and it helps maintain the integrity of the implant
21 itself. Whereas, if you have something without
22 adequate micro-porosity, you're going to have a

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1 decreased opportunity for fibrin attachment.

2 DR. COCHRAN: The reason I raise that
3 question is that we were provided documentation from a
4 published manuscript that indicated that that product
5 was used, and there didn't seem to be any outstanding
6 problems with that material.

7 DR. ARROWSMITH-LOWE: Well, some of that
8 may have to do with the method of assessment of how
9 they made a determination of problems or
10 effectiveness. I think we would think it appropriate
11 to be looking at healing time, to be looking at any
12 possible other negative things that might occur from
13 differences in the product. And, again, to me that
14 sort of argues for the whole option of doing some
15 clinical evaluation, rather than just strictly making
16 a determination on what are more physical factors.

17 CHAIR REKOW: We have a published schedule
18 for the open hearing, and we're getting close to the
19 end of that time. Perhaps I could ask if there are
20 any other groups in the audience that would like to
21 make a public presentation.

22 DR. UHR: Thank you.

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1 CHAIR REKOW: And then I would like to
2 have options for questions to be asked to any of the
3 people. Are there any other groups that would like to
4 say anything? Okay. Failing to hear that, does the
5 Panel have any questions for any of the people that
6 have presented or any of the experts that you know are
7 in the audience? Mark?

8 DR. PATTERS: Mark Patters. I would like
9 to give the petitioners just a couple of minutes to
10 respond to Curasan's presentation, if that's
11 appropriate, Madam Chair.

12 CHAIR REKOW: I think it is. Thank you.

13 DR. MORGAN: Having heard their
14 presentation, the logic escapes me. The history is
15 the following. Thomas Driskell is the person who
16 developed the product under a U.S. Department of
17 Defense grant, and was the owner of the Miter that
18 initially sold this product. May I discuss the issue,
19 the PMA? May I?

20 CHAIR REKOW: Go ahead.

21 DR. MORGAN: The PMA that they so state
22 that they have, and that the FDA recognizes that they

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1 have, is not, in fact, reality. The history, and
2 Thomas Driskell could give it to us, is the following,
3 that he initiated a PMA.

4 CHAIR REKOW: Can I interrupt for one
5 second? It will be fascinating, I'm sure, to hear
6 that, but unless it addresses some important
7 scientific issues --

8 DR. MORGAN: Okay.

9 CHAIR REKOW: I think that unless the FDA
10 is anxious to have it in the public record, I'm not
11 sure that it helps us with our decision.

12 DR. MORGAN: Okay. Then I can bypass
13 that.

14 CHAIR REKOW: Thank you.

15 DR. MORGAN: Then if what they are saying,
16 they purchased the Miter PMA, that it was marketed in
17 the United States for over 20 years without a single
18 dental device report, which is true, so this product
19 has been continuously marketed until they purchased
20 it, I believe, last year. Why would they purchase it?

21 It is already on the market in the United States.
22 Now, they are bringing it back to Germany and claiming

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1 that that product, which they claim the FDA recognizes
2 as a PMA, is going to be modified to their standards.

3 No American company has the opportunity of conforming
4 to their standards without a PMA. Am I making sense?

5 CHAIR REKOW: So the point that you're
6 making is that, from a scientific perspective, if I
7 may, and, please, correct me if I'm wrong, is that a
8 less than a 100 percent pure Beta TCP has been
9 successfully used in dental products in the United
10 States for over 20 years?

11 DR. MORGAN: Over 20 years.

12 CHAIR REKOW: Without an adverse --

13 DR. MORGAN: Without a single adverse
14 report.

15 CHAIR REKOW: Without a single adverse
16 report.

17 DR. MORGAN: And personally, I have used
18 it.

19 CHAIR REKOW: Right. And so yours becomes
20 a counter argument to the need for higher purity. Is
21 that --

22 DR. MORGAN: Well, I'm not adverse to

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1 higher purity.

2 CHAIR REKOW: No.

3 DR. MORGAN: And I don't --

4 CHAIR REKOW: But you're arguing that the
5 lower purity has been able to perform successfully in
6 the market?

7 DR. MORGAN: No, because I don't think you
8 or I know --

9 CHAIR REKOW: Okay.

10 DR. MORGAN: -- the exact purity of Miter
11 or their claim.

12 CHAIR REKOW: Fair point.

13 DR. MORGAN: So we don't know what the
14 purity is. I could state Miter is 100 percent pure.

15 CHAIR REKOW: Yes.

16 DR. MORGAN: I could state the product is
17 going to -- you know, we don't know.

18 CHAIR REKOW: Okay.

19 DR. MORGAN: So I think there was a lot of
20 smoke and mirrors, but logic escapes me.

21 CHAIR REKOW: Well, I think that there is
22 a lot of business issues that are critical for each of

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1 your companies to succeed, but I don't think that this
2 is the forum to have this discussion.

3 DR. MORGAN: I agree, I agree.

4 CHAIR REKOW: Okay. Thank you.

5 DR. MORGAN: But if the argument is that
6 the bone of the skull is different elsewhere, and if
7 you accept that argument, then I would suggest the FDA
8 as a unit should go back to their medical
9 counterparts, their orthopedic counterparts, and
10 restrict the use of that product by any plastic
11 surgeon or orthopedic surgeon. That's the argument.
12 I don't accept the argument that the bone of the skull
13 is different than the bone elsewhere. I'm sorry. I
14 just don't accept it, and if you do accept it, then
15 the Orthopedic Branch should restrict the use of all
16 their approved products to only non-skulls.

17 CHAIR REKOW: Clearly, the progenitors are
18 different.

19 DR. MORGAN: Oh, yes.

20 CHAIR REKOW: The issue is whether or not
21 the mature bone is different from immature bone.

22 DR. MORGAN: Which is true, yes.

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1 CHAIR REKOW: Okay.

2 DR. MORGAN: I agree with that. So
3 without any questions or --

4 CHAIR REKOW: So are there questions for
5 any of the Panel, any of the presenters, any of the
6 groups? Would anyone else from the audience like to
7 make any comments or statements? I appreciate all of
8 what you have done. I applaud Dr. Uhr for the most
9 remarkable slides we have seen for awhile, and surely
10 a lot of useful and valuable information has been
11 conveyed this morning. I thank you for your time and
12 the considerable energy that went into all of these
13 presentations and the thoughtfulness, and your
14 helpfulness in providing questions to us. I guess
15 now, we break for lunch and the Panel discussions will
16 resume around 1:15. Thank you again.

17 (Whereupon, the hearing was recessed at
18 12:09 p.m. to reconvene at 1:25 p.m. this same day.)

19
20
21

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1 A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

2 1:25 p.m.

3 CHAIR REKOW: We will begin with Jon
4 Suzuki. First, Dr. Suzuki, are you going to do it
5 from here or there?

6 DR. SUZUKI: It doesn't matter.

7 CHAIR REKOW: Wherever you would like,
8 sir, it's yours.

9 DR. SUZUKI: Jon Suzuki. I will try to
10 address the Panel's questions succinctly, and then we
11 can have a discussion later on if necessary. The
12 Panel questions are not on the board anymore. They
13 are not on the board anymore. Does the petition, as
14 found, adequately describe the risk to the health of
15 the device, and provide appropriate controls to these
16 risks? I believe the answer to this question is no,
17 and other guidelines that may need to be spelled out,
18 especially indications, including matters to OP and
19 including the possible degradation of the product.
20 And with respect to appropriate controls for these
21 risks, perhaps the indications and the reeducation of
22 the clinician needs to be at least identified more

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1 specifically.

2 And on Question 2, what modifications
3 would you make to the risk to the health presented by
4 the device with respective modifications and controls
5 perhaps identifying that the risk of infection needs
6 to be identified, and especially the sterility of the
7 product and its use in infected sites needs to be
8 further elaborated, especially in periodontal sites
9 where the infection would be different than that of
10 skeletal bone sites.

11 With respect to the controls, we're
12 looking at the form, the shape, the size and other
13 parameters I think need to be further identified and
14 defined, and that probably is going to be left up to
15 other FDA Panel members and other FDA investigations
16 to determine what that threshold is, a maximum and a
17 minimum control for the regulation of these particular
18 products.

19 We will skip the part of classification
20 questionnaire, but we'll spend more time on that
21 later, Madam Chairman, I'm assuming, so I'll go onto
22 Question 4. With respect to recommended

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1 classification and changes and, especially recommend
2 to the labeling of these devices once again to
3 reiterate the importance of considering infections and
4 the possible acidity of the site, as a role in the
5 degradation and/or signed-ability of the product, and
6 also the potential risk of infections if it's not
7 already included on the existing labels needs to be
8 identified. And that concludes my initial rhetoric,
9 and Dr. Glowacki has some follow-up comments, too.

10 DR. GLOWACKI: Yes. This is Julie
11 Glowacki, and my comments come from the point of view
12 of not being a clinician, so I'm actually going to be
13 asking the other Panels for some clinical input down
14 the line. But with respect to whether the petition,
15 Question 1, adequately describes the risk to health of
16 the device and appropriate controls for this, I view
17 it as the petition was filed to do one thing.
18 However, we are here as a Panel that is voting on a
19 reclassification of the current rule, which includes
20 other materials, other indications.

21 So the petition does not address the
22 issues of the classification, but I think gives me a

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1 way of looking at how much information is available
2 for us to feel that there are some materials within
3 the current rule that do not pose a Class III, a
4 continuation of a Class III.

5 And so with respect to the description of
6 the device being one of the major issues here, that I
7 think I will be feeling comfortable on the basis of
8 the information that we're given and, moreover, solely
9 on the petition that Beta TCP is really what we ought
10 to be reclassifying, and to that end, a more precise
11 description of the device needs to be provided, and
12 that concerns a composition, the form, is it granular,
13 is it in blocks, is it a single phase?

14 I think we have not been given enough
15 information to say that biphasic materials perform
16 with the same degree of fidelity with respect to
17 efficacy as does pure Beta TCP. I think we can talk
18 about some of the standards that are out there with
19 respect to elemental analysis, x-ray diffraction,
20 provide the information about the nature of the
21 material.

22 I think we needed more clarity than what

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1 was in the petition for the intended use or
2 indications, and I would feel more comfortable talking
3 about intraosseous applications of this material. I
4 think the orthopedic literature, as well as what the
5 experience has been in oro-periodontal maxillofacial
6 uses of these types of materials is that it cannot be
7 implied that the material is providing the physical
8 properties of cortical bone, so that stability needs
9 to be an issue. And I think one doesn't want to give
10 the clinicians the impression that you can use this in
11 discontinuity defects.

12 So I am just talking about some of the
13 applications that everybody is comfortable with, and I
14 think it's primarily intraosseous. We were provided
15 some information about untoward results if the
16 material is inserted into an endosseous defect
17 simultaneously with an endosseous implant, and that
18 that seems to be something to be avoided, that there
19 is literature recommending that Beta TCP be used first
20 to promote bone formation and subsequent insertion of
21 a dental device.

22 I think all of these things with respect

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1 to intended use, indications and precautions against
2 potentially very damaging misuse need to be put into
3 guidance documents. I would hope that there would be
4 a precaution against the use in infected sites, that
5 there would be a precaution against overfilling or use
6 in discontinuity defects and information provided to
7 the clinician about how to remove excess.

8 One can imagine a situation where the
9 cortical bone structure might be very, very weak and
10 if someone were very, very aggressive in implanting
11 this material, there could be potential fractures to
12 thin walls of bone.

13 With respect to whether the material we're
14 considering is in granular or block form, again,
15 looking at the orthopedic guidance document as a guide
16 here, there ought to be information provided to the
17 clinician on whether the block can be cut or trimmed
18 or reshaped or made smaller to fit into a disk, into a
19 particular defect.

20 Some of the other materials that are out
21 there are very, very brittle, provide lots of debris
22 that is very difficult to get rid of, and I think that

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1 information ought to be in the clinician's insert.
2 Precaution against concurrent use with implants,
3 information about the suitability to mix this material
4 with other materials, I think, ought to be provided.
5 This material's potency as an osteoconductive material
6 is in large measure due to its rate of resorption, and
7 if it's mixed with other materials that interfere with
8 that, I would think that that would be a potential
9 problem. So adding mixtures I would worry about.

10 Some people, I understand, are using Beta
11 TCP or have used it as kind of hamburger helper, mixed
12 with autogenous bone graft inadequate to fill in the
13 material, so we think we need to see some information
14 about whether that would be an indication.

15 Let's see. Oh, I think also because of
16 some of the adverse information that we saw on what
17 happens when this material gets into the bloodstream,
18 one would want to be sure that there were precautions
19 to avoid soft tissue nerves, pulp and, again, this
20 idea of overfilling the material with the potential of
21 it getting into the bloodstream. I think those are
22 things that are different in the oral dental

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1 application than in orthopedic.

2 I think that it should be possible, just
3 sort of jumping ahead, that talking about the risks,
4 which were not really that adequately dealt with, I
5 think, in the petition, the risk of causing an
6 infection or using the material in an infected or
7 previously infected site has to be addressed.

8 In general, I feel that we may, by the end
9 of the day, consider that Beta TCP is -- there is
10 enough information about its use and the properties
11 that contribute to its successful use and to its
12 safety, so that it could be reclassified in Class II
13 with some special controls.

14 And one other thing, back to the question
15 about the clinical input. I would really like to hear
16 the clinicians' views about who should be able to put
17 this material into people. Is this something that a
18 dental degree would give enough still to be able to
19 follow those instructions and to use it safely? Does
20 advanced training come into the use of this at all?

21 CHAIR REKOW: Is that all?

22 DR. GLOWACKI: That's all.

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1 CHAIR REKOW: Well, let's have some
2 conversation and discussion. It seems to me, if I can
3 put this into some categories, the questions that are
4 the most compelling and may form the basis for the
5 conversation is do we look at the form that the
6 material is presented? Is it block? Is it granules?
7 Is it both? Are we looking at all the TCPs? Are we
8 looking at only the Beta TCP? What is a list of
9 precautions and indications, and then what is the
10 level of training to be able to utilize it.

11 Is that a fair basis to form the
12 conversation around? Before I start driving any
13 conversation thought, are there questions and issues
14 that you would like to address? Would some of the
15 clinicians like to address some of the questions that
16 Julie addressed?

17 DR. PATTERS: Mark Patters. Let me say
18 that I don't recall ever being at another Panel
19 meeting that had such a dearth of scientific data to
20 try to make a decision with. As far as I'm concerned,
21 most of the papers that were provided in the petition
22 are case reports and uncontrolled studies. So there

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1 is really not a lot of scientific data to even say
2 that this material is safe and effective.

3 However, I would say that clinicians
4 generally regard it as safe, but I don't know that it
5 has been definitively proven as safe through carefully
6 controlled clinical trials, so I regard it as safe.
7 There have not been, as we have heard before, adverse
8 reactions reported from the use of this material. On
9 the other hand, I don't believe the material is widely
10 used enough to be able to gauge what adverse reactions
11 might occur. So I don't see that we have a lot of
12 data here to help us. It's just that, as a clinician,
13 it seems that this material is regarded as safe, but I
14 have not seen any data demonstrating it.

15 DR. GLOWACKI: I, too, was disappointed by
16 it. Ms. Glowacki again. I was disappointed by the
17 papers that were provided in the petition, but I did
18 take an opportunity to go onto PubMed and look up my
19 own references on this, and found that sure, you know,
20 there are a couple of small studies there that could
21 give this material versus other materials or that use
22 this material for other studies, adding in platelet-

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1 rich plasma or as a carrier for Beta TCP.

2 And with respect to the evidence-based
3 practice of medicine, I think Dr. Patters makes a very
4 important point. Yet, the general level of
5 experience, and I think I am understanding him
6 correctly, is that safety and efficacy can be defined.

7 Do you disagree with that?

8 DR. PATTERS: In general or for this
9 product?

10 DR. GLOWACKI: For Beta TCP.

11 DR. PATTERS: That can be defined, yes, I
12 agree, but the question is have they been?

13 DR. GLOWACKI: Yes.

14 CHAIR REKOW: David?

15 DR. COCHRAN: I have used this product
16 myself clinically or not this particular, but a TCP
17 product. We have used it in different clinical
18 applications. We have used a lot of other different
19 kinds of bone graft fillers, if you will, or bone
20 replacement grafts, BRGs is what we tend to call them,
21 and I feel like, Mark, that probably there is a lot of
22 experience over many years with this material and

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1 similar type materials that I don't think we need to
2 worry so much about the safety of this material in
3 humans for human use, and so I would agree that, from
4 a clinical point of view, it can be a useful material.

5 We have used it not only intraosseously,
6 but as on-lay type materials with flat coverage with
7 periosteum and flat mucoperiosteal flaps over it, and
8 there certainly does not seem to be any adverse
9 reactions. Histologically, we really don't see that
10 either. Clinically, we don't see that as a problem.
11 We have gone back and placed endosseous implants in
12 this type of material, and have really not had any
13 problems with the osseointegration around the
14 implants. So I see it from a safe point of view as
15 not a problem.

16 CHAIR REKOW: This is Dianne Rekow.
17 You're talking about the granular form, right, not the
18 block form or are you?

19 DR. COCHRAN: As regards to the TCP, it's
20 granular form that we have had experience with.

21 CHAIR REKOW: Okay. David? Richard?
22 Sorry.

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1 DR. BURTON: I would agree. I think that
2 the safety issue is sort of one side of it, but I am
3 not sure that when I look at this, and certainly in
4 the case study format that we have here though, that
5 some of the efficacy has been really established. I
6 mean, I think we have sort of lumped them together,
7 but in reality, they need to be separated, as well. I
8 think everybody says well, gee, this is really, you
9 know, it's a good product. It's not going to hurt
10 anybody. It doesn't seem to do anything terrible. It
11 doesn't fall out. It doesn't have marked adverse
12 reactions.

13 The real question is also that there is
14 some question of efficacy in terms of being a
15 reasonable product for that, and then I think it goes
16 back, what was mentioned earlier also, is going to be
17 the clinical indications for this, because my
18 experience has been that once you get a material out
19 there, people end up sticking it just about anyplace
20 you can think of to put it, and then again whether or
21 not we know now that this particular material needs a
22 certain amount of either bony contact, you mentioned

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1 continuity defects.

2 Sinus lift situations, we all know, have
3 very poor vascular supplies to those, and does it have
4 a sufficient vascular supply to such that it's also
5 conductive prostheses and actually functions? So, I
6 mean, I think that yes, I would certainly agree that
7 the safety probably has been established. I just have
8 some questions regarding what its efficacy is and then
9 how that translates into what clinical applications
10 it's appropriate for, given the information we have,
11 at this point in time.

12 It might be, that later on, that those
13 clinical indications might be expanded once there was
14 further usage and research with it once it was in
15 clinical applications, but I'm not sure that that's
16 been really defined in anything that I see that has
17 been presented thus far.

18 CHAIR REKOW: Jon, do you want to --
19 Elizabeth?

20 MS. HOWE: Elizabeth Howe. I would just
21 like to make an appeal on behalf of consumer issues,
22 and make one statement that it is certainly exciting

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1 to have products that are more accessible, certainly a
2 lot cheaper, which would encourage patients to seek
3 treatment, less invasive, a lot less risk, a lot less
4 recovery time.

5 But given all of that excitement for such
6 a product, some of the concerns would be having a
7 standard of quality that patients can be assured that
8 they are getting a quality product, certification for
9 the person that is providing that treatment to know
10 that it's being handled properly and finally, any
11 contraindications for patients who have special needs
12 because of a disease process, if it could be, I think
13 somebody mentioned, somebody who is post-menopausal,
14 if there are any studies on at what point this product
15 is not appropriate for certain patients.

16 CHAIR REKOW: Do you have anything you
17 would like to add, Dan?

18 MR. SCHECHTER: I guess from an industry
19 standpoint where, as a whole, we're always interested
20 in the least amount of obstacles and burdens to bring
21 a product to market, so generally we would always be
22 in favor of a lower classification, going from III to

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1 II. And I guess from a practical standpoint, this is
2 almost a question for FDA, Susan, perhaps.

3 Given that the general feeling is that
4 there is kind of a dearth of scientific evidence here
5 that we can base maybe specific recommendations on,
6 would it be appropriate for the Panel to, in general,
7 reclassify, recommend that special controls for
8 certain parameters exist and then leave it up to FDA
9 to state those more specifically? I'm just asking the
10 question. If we can kind of defer some of the
11 specific issues or is that issue for a further Panel
12 meeting, which I wouldn't advocate as an industry rep?

13 DR. RUNNER: You could certainly. We take
14 all of your comments during the Panel process into
15 consideration when we're developing the guidance
16 documents, any labeling recommendations, any
17 contraindications and warnings. So you wouldn't
18 necessarily have to vote on each and every
19 contraindication and warning, but give us a general
20 feeling as to what you feel would be appropriate areas
21 for us to address and any guidance or labeling for
22 this product. Does that answer your question?

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1 MR. SCHECHTER: Yes, definitely. That is
2 what I was hoping the answer was, because it doesn't
3 seem like we're going to get to the point where, you
4 know, we can say here that it's got to be 97 percent
5 or you can't have more than .5 percent Alpha,
6 etcetera. So, you know, I would encourage the Panel
7 to go as far as we can with whatever the Panel is
8 comfortable with.

9 CHAIR REKOW: I want to remind everyone,
10 too, that we can engage the people from the audience
11 that have presented, so if questions come up that can
12 be clarified by them, we have the opportunity of
13 calling on them. Yes, Susan?

14 DR. RUNNER: The other comment I wanted to
15 make about indications, you are voting on the
16 indications as stated in the present regulation and
17 that would be included from the original Miter PMA.
18 Any additional indications that might come to FDA
19 would, of course, have to be supported with
20 appropriate data. For example, I think, sinus lift
21 you mentioned, I don't believe that is in any of the--
22 it's not in the original classification, per se, and

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1 is also not in the original Miter PMA and, therefore,
2 theoretically, we could request clinical data to
3 support those types of indications.

4 DR. BURTON: Dianne? Richard Burton. I
5 don't think we have the original PMA to know what
6 their indications were.

7 CHAIR REKOW: Well, I can read what this--

8 DR. BURTON: Oh, okay. You have it?

9 CHAIR REKOW: Michael has got it. He is
10 way ahead of us, and so he just handed me this. You
11 want to know. This is Paragraph 872.3930, and it's on
12 tricalcium phosphate granules for dental bone repair.
13 The identification is tricalcium phosphate granules
14 for dental bone repair is a device intended to be
15 implanted in the upper or lower jaw to provide support
16 for prosthetic devices, so it's granules, it's TCPs in
17 general.

18 DR. BURTON: That's the CFR and not the
19 PMA.

20 CHAIR REKOW: Oh, I'm sorry. Yes, this is
21 the CFR.

22 DR. RUNNER: I think Dr. Mulry has the

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1 indications from the Miter PMA.

2 CHAIR REKOW: So while they are looking
3 that up, again, the discussion that's in the CFR is
4 granules, all TCPs in the jaws to support prostheses.

5 DR. COCHRAN: Dianne, this is David
6 Cochran. I would interpret that to include sinus lift
7 procedures.

8 DR. BURTON: Yes, so would I. I mean, you
9 could put that in to be -- I mean, you could do cleft
10 grafts you know, cleft grafts on kids with this.

11 CHAIR REKOW: Yes.

12 DR. BURTON: Within and meet those
13 indications. So, I mean, my problem is that those are
14 almost so broad that, again, you're sort of opening
15 the door perhaps to some situations that would not be
16 appropriate, in fact, because you could be doing that
17 to support a prosthesis and you're taking out, you
18 know, periodontally infected teeth that you want to
19 preserve the ridge and putting this material into an
20 infected site, and still would meet those indications.

21 CHAIR REKOW: Do you have the PMA?

22 DR. RUNNER: The PMA was originally

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1 cleared for periodontal alveolar bony defects. That's
2 very broad, but this is a very early PMA. It was also
3 indicated for use in fresh tooth extraction sockets
4 and to provide additional stability to fill bony
5 voids.

6 DR. GLOWACKI: Can you repeat the last
7 part, because I didn't hear you?

8 DR. RUNNER: To provide additional
9 stability and to fill bony voids.

10 DR. GLOWACKI: This is Julie Glowacki.
11 That statement, I think, we all can understand, but
12 the other statement about to support prostheses is an
13 incompatibility, and I, for one, would like a little
14 bit of help on saying which are we looking at here?

15 DR. RUNNER: Well, unfortunately, the
16 regulation is what it is and it was written some time
17 ago, and it's very broad and it's open to a
18 significant amount of interpretation. I can tell you
19 than in the Dental Branch, we have interpreted that
20 not to include bone filling materials around
21 endosseous implants and whenever endosseous implant,
22 an indication for use around endosseous implants have

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1 been requested, we have asked for clinical data to
2 support use around endosseous implants.

3 DR. GLOWACKI: Ms. Glowacki. So as a
4 follow-up to that then, is this an opportunity to help
5 really sharply define what education --

6 DR. PATTERS: I don't even want to do
7 that.

8 DR. RUNNER: I don't think that we can.
9 The regulation as it stands is as it stands. I think
10 you can make recommendations in terms of how you would
11 like the Dental Branch to interpret that regulation,
12 but I think as it stands, it stands.

13 DR. PATTERS: Mark Patters. Susan, does
14 the PMA, which the Panel has not seen, provide
15 clinical data to show the effectiveness of TCP in
16 periodontal defects?

17 DR. RUNNER: Yes, the original PMA did
18 have clinical data. I can't -- it was a very early
19 PMA in the history of FDA, so I can't state that it
20 was to the level of subsequent PMAs in terms of data,
21 but it did have clinical data.

22 DR. PATTERS: To your knowledge, is that

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1 data published?

2 DR. RUNNER: I don't think so.

3 DR. PATTERS: That's why I don't know it,
4 I guess.

5 DR. COCHRAN: David Cochran. I think just
6 to help explain the clinical indication is, I think,
7 probably when that was written, it was used
8 predominantly just to fill extraction sockets to help
9 maintain the ridge to support complete dentures
10 probably. I would assume that's when that was done,
11 and the endosseous implants came to vogue much later
12 than that and probably weren't included early on.

13 DR. RUNNER: You know, the original data
14 on that PMA was in 1980.

15 CHAIR REKOW: So if I understand it, we
16 really have been given some direction in terms of how
17 to focus, and that is on granules and TCP, because the
18 reg doesn't limit it to Beta TCP. Do you want to, as
19 a Panel, add that limitation of Beta TCP, as opposed
20 to TCP in general? I'm sorry, yes? Yes, please.

21 MR. DRISKELL: I would like to enlighten a
22 few people on the Committee.

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1 CHAIR REKOW: Would you go to the
2 microphone, please, and identify yourself?

3 MR. DRISKELL: I'm Tom Driskell. Well,
4 actually, you might remind me of some of the things
5 that you asked questions on, but I can speak to the
6 indications to some degree. First of all, I would
7 like to point out that any type of a material or a
8 device like this that we have ever put out, we had a
9 package insert in there that said what it was to be
10 used for, and it had plenty of contraindications in
11 it, because we don't want this stuff to fail, and you
12 see that package insert before you ever get -- I mean,
13 when we apply for a 510(k), we would have a copy of
14 that verbiage that was on the package insert. It's to
15 protect us and it's to protect the doctor.

16 CHAIR REKOW: Right.

17 MR. DRISKELL: And I think it's very
18 important that you keep that in mind, because you
19 don't really have to cite all the indications, but I
20 think in the package insert, it's got to say what it's
21 being used for or if that isn't in the regulations, it
22 ought to be. So then you have a chance to oversee

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1 what the manufacturer wants to do with it, and the
2 original PMA when we did fill two sockets, what we had
3 particularly in mind, at that point, was third molar
4 sockets, which often really would benefit from being
5 filled with something, so you generally get the defect
6 back there that you, otherwise, might likely get. So
7 that was a very good use for it.

8 In fact, my daughter was the first one
9 that ever had it used on her, on anyone. By the way,
10 let me throw this in. Speaking of sinus lifts, my
11 wife had some periodontal disease and sinus
12 infections, which she didn't even know she had for
13 years, but the point is that she ended up with one and
14 a half millimeters of bone in the maxilla, and we
15 wanted to put implants in there. We used tricalcium
16 phosphate and we were able to put in 14 millimeter
17 implants, which we no longer even bother to sell,
18 because you don't need them that big, but in those
19 days we still thought we did.

20 So anyway, those have been in now for
21 about 12 or 13 years and they still look like they did
22 within a year of the time it was done. So anyway, if

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1 you have some questions like this, I would be happy to
2 give you my best information on it.

3 CHAIR REKOW: Thank you.

4 MR. DRISKELL: I don't want to -- well,
5 excuse me.

6 CHAIR REKOW: Thank you. I appreciate
7 that and I think that our frustration is that there
8 are a great many valuable clinical case studies. The
9 frustration that we're having is well controlled
10 prospective studies, which of course have a different
11 standard of information that may or may not be
12 extractable from them, but we won't go into that
13 category. And it's the issue of what is the standard
14 against which we're going to make our decisions,
15 that's our frustration, because, clearly, there is
16 lots of experience in positive results. Thank you.
17 Susan?

18 DR. RUNNER: I just wanted to remind the
19 Panel, as well, however, that the FDA regulations do
20 state that the levels of evidence include case studies
21 and all the way from experiential all the way to well
22 controlled clinical studies.

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1 CHAIR REKOW: Thank you for that reminder.
2 So we have focused ourselves a little bit. We're
3 talking about granules and we're talking about TCP.
4 Now, the question, I guess, is maybe the easier way to
5 ask the question first is can we specify enough
6 precautions or contraindications and not address what
7 they are yet, but can we specify enough to make the
8 Panel feel comfortable that the device could be
9 reclassified? Can I take a vote, David?

10 DR. BURTON: Yes.

11 DR. PATTERS: Yes.

12 DR. GLOWACKI: Glowacki, yes.

13 DR. SUZUKI: Suzuki, yes.

14 CHAIR REKOW: Well, Elizabeth is not
15 voting. Are you voting? Okay. So I don't have to
16 break the tie, but I would say yes, too. So before we
17 go to what those precautions and indications need to
18 be, I think I would like to take on the last issue of
19 do you need training beyond that of a dentist to be
20 able to use this stuff or is that intimately tied with
21 the contraindications and indications? Mark?

22 DR. PATTERS: Mark Patters. I certainly

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1 don't know every product, but I know of no product
2 that is specified in its labeling that can only be
3 used by a specialist. I know of no product that is
4 labeled that way. I don't think I would want to start
5 one, do you?

6 DR. SUZUKI: Jon Suzuki. I agree with Dr.
7 Patters and, in fact, even dental implants are not
8 specified just for certain specialties either.

9 CHAIR REKOW: Okay.

10 DR. BURTON: Richard Burton. I would like
11 to agree. I think that the kinds of indications that
12 I can see for the product would fall within the realm
13 of the general practitioner as being appropriate for
14 it. There are going to be conditions that they are
15 going to be treating, as well as specialists. So, I
16 mean, I think that to limit the availability of it in
17 that arena would be inappropriate. Yes, cruel of them
18 to say that. I know you will.

19 CHAIR REKOW: I am being suggested that we
20 go onto the classification questionnaire, because that
21 will answer lots of the questions that need to be
22 resolved. Does that also tie in enough with your risk

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1 table or do you want us to address the risk table
2 specifically? Let's do the questionnaire first and
3 then we can see if we can go back and redo the --
4 where is the questionnaire?

5 SECRETARY ADJODHA: I believe that would
6 be in the --

7 CHAIR REKOW: It was in your stuff. Okay.
8 So for the Panel, who also don't remember, it's in
9 the last pieces of what we were given in Section 7,
10 which is at the very bottom of the pile of the
11 reading, and the general device questionnaire. The
12 first question is who is the petitioner, and then this
13 is the one, right, this one?

14 SECRETARY ADJODHA: I think we need to
15 refer to Marjorie Shulman.

16 CHAIR REKOW: Marjorie Shulman.

17 MS. SHULMAN: I'm handing out new forms,
18 too, and we're going to get one up on the overhead.

19 CHAIR REKOW: Got it. Good. It's nice to
20 have somebody keeping us on track properly. Oh, I
21 see. Got it. So, Mark, let me turn it over to you,
22 please, to guide the discussion. While she is getting

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1 that set up, are there any compelling things that any
2 of the Panel would like to say? Mark?

3 DR. PATTERS: Yes, Mark Patters. I would
4 just like to address the petition from Dr. Morgan
5 where under Number 4 in his petition, indications for
6 use in the device labeling, and he has his indications
7 as bone substitute material for dental alveolar
8 procedures. I would have to say that I personally
9 think that is way too broad, dental alveolar
10 procedures.

11 DR. COCHRAN: This is David Cochran. Just
12 listening to what Mark said, I think what we're
13 actually doing is reclassifying the original PMA is my
14 understanding, and the language that's in there is
15 what is going to be what we're really discussing.

16 CHAIR REKOW: What exactly are we
17 reclassifying, the original PMA?

18 DR. RUNNER: The tricalcium phosphate for
19 dental bone repair with the indications as indicated
20 in the PMA and in the CFR notes.

21 CHAIR REKOW: Both?

22 DR. RUNNER: Both. It includes --

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1 CHAIR REKOW: Okay.

2 MS. SHULMAN: My name is Marjorie Shulman.
3 I work for the Program Operations Staff, and we'll
4 walk you through the forms.

5 DR. GLOWACKI: May I interrupt?

6 MS. SHULMAN: Sure.

7 DR. GLOWACKI: Just to follow-up on that,
8 Susan, Ms. Glowacki again, if we do a reclassification
9 of the original PMA and put the specifications in, so
10 that it only applies, it really only applies to pure
11 Beta TCP for certain uses, what happens to the other
12 whole field that we don't talk about here?

13 DR. RUNNER: The regulation would be split
14 such that Beta TCP could potentially be Class II and
15 other forms of tricalcium phosphate would remain as
16 Class III if that's what you so suggested.

17 DR. GLOWACKI: Thank you.

18 CHAIR REKOW: So that's part of our charge
19 today, first to look at the original PMA and then to
20 talk about --

21 MS. SHULMAN: Yes, just as a matter of --

22 CHAIR REKOW: Okay.

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1 MS. SHULMAN: Marjorie Shulman. Just as a
2 matter, we're not looking at the PMA, so to speak, to
3 reclassify. We are reclassifying looking at the
4 reclassification of the reg in which the PMA was
5 classified under. So we're looking at the intended
6 use for that PMA, and any supplements that may have
7 been cleared under that, because if the vote was to go
8 for reclassification, that would then become a Class I
9 or a Class II device.

10 CHAIR REKOW: Okay.

11 MS. SHULMAN: So the first thing we want
12 to do is agree upon exactly what intended use we're
13 looking at from the intended use from the reg and the
14 PMA, and you, as a Panel, would have to decide do you
15 want to split it right off the top and go through the
16 sheets two times and see where you end up or do you
17 feel comfortable enough to go all as one group?

18 CHAIR REKOW: This is Diane Rekow again.
19 My understanding then from what you said is that the
20 PMA is a subset of the reg, and we should just focus
21 on the reg and by default, all of the things that we
22 have discussed are included as long as it applies to

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1 the ridge.

2 DR. RUNNER: Right. I think you also need
3 to consider, however, that if you split off Beta TCP,
4 that would mean that other forms of tricalcium
5 phosphate would come in with the PMA.

6 CHAIR REKOW: Yes.

7 DR. RUNNER: If that's what you so desire.
8 You can also realize if you reclassified the entire
9 group, tricalcium phosphate, FDA would also consider
10 the other forms, because we don't have any experience
11 within requiring clinical data in most instances, as
12 well. So that's --

13 CHAIR REKOW: Okay. So --

14 DR. PATTERS: Excuse me. Mark Patters.
15 Susan, isn't there an alternative that makers of other
16 forms of TCP could ask for reclassification, rather
17 than have to come in as a PMA?

18 CHAIR REKOW: So we're talking about
19 granules and we're talking about TCP in general? All
20 right. Is the Panel willing to do that as the general
21 group for going through this questionnaire form? Do I
22 hear any objections to doing so?

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1 DR. BURTON: Could you restate that again?

2 CHAIR REKOW: Yes. We're going to keep
3 all the TCPs in their granular form as a group, and
4 address this questionnaire for that group of products,
5 I guess. Is there an objection to doing so? Hearing
6 none, I'm going to give it back to you again.

7 MS. SHULMAN: Thank you. Marjorie
8 Shulman. We'll start with the form then. The first
9 part is just housekeeping, the Panel name and
10 petitioner and everyone is able to fill out their own
11 form, but the Panel Chair will keep the main form.

12 The generic type of the device is the
13 regulation. Is that what we agreed upon?

14 SECRETARY ADJODHA: Yes.

15 MS. SHULMAN: Okay. The first question --

16 SECRETARY ADJODHA: Marjorie, can you
17 explain to them what they should put in there for
18 generic type of device?

19 MS. SHULMAN: You can just put in the
20 regulation.

21 SECRETARY ADJODHA: Oh, the exact name?

22 MS. SHULMAN: Okay.

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1 SECRETARY ADJODHA: Okay. So the exact
2 name is tricalcium phosphate granules for dental bone
3 repair.

4 MS. SHULMAN: Okay. Question 1, and we
5 can do this, you can go around and tell us yes, no,
6 and then vote. Is the device life sustaining or life
7 supporting?

8 CHAIR REKOW: David?

9 DR. COCHRAN: David Cochran, no.

10 DR. BURTON: Richard Burton, no.

11 DR. PATTERS: Mark Patters, no.

12 DR. GLOWACKI: Julie Glowacki, no.

13 DR. SUZUKI: Suzuki, no.

14 MS. HOWE: Elizabeth Howe, no.

15 CHAIR REKOW: Dianne Rekow, no.

16 MS. SHULMAN: Okay. Number 2, is the
17 device for a use, which is of substantial importance
18 in the preventing impairment of human health?

19 CHAIR REKOW: Now, we'll go backwards this
20 time. Jon?

21 DR. SUZUKI: No. Suzuki.

22 DR. GLOWACKI: Yes, only because, I mean,

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1 Ms. Glowacki, I thought implanting anything into the
2 body is done for a substantial clinical reason, but
3 maybe I don't understand these words.

4 CHAIR REKOW: Let's finish the vote and
5 see if we need to have that discussion. Mark?

6 DR. PATTERS: Mark Patters, yes.

7 DR. BURTON: Richard Burton, no.

8 DR. COCHRAN: David Cochran, no.

9 CHAIR REKOW: My read would be the same as
10 Julie's, so I would say yes, which I guess splits it.

11 So could we have some clarification from FDA about
12 what this means? Mark?

13 DR. PATTERS: If we answered no to this
14 question, and we're sure we answered no to the
15 question after it, this then could be classified as a
16 Class I device. I'm not sure this Panel wants to do
17 that.

18 DR. BURTON: Well, could we go through the
19 Question 3, which would sort of, at that point, render
20 that discussion null and void. Okay. If you split
21 Question 2, if we go to Question 3 and the majority on
22 Question 3 comes up yes, then we're already, then it

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1 would appear to me, moved over to it being a Class II
2 and then looking at some --

3 CHAIR REKOW: Okay.

4 MS. SHULMAN: Marjorie Shulman. As a
5 matter of clarification, too, you could answer no to
6 the first three, get to the question is general
7 controls enough, say no, and then you get back to 2.

8 DR. BURTON: Okay. I would go through
9 Question 3.

10 CHAIR REKOW: Excuse me? I'm sorry?

11 DR. BURTON: I would move that we go
12 through Question 3, which I think would --

13 CHAIR REKOW: Yes, let's do that, and I
14 have also had some other clarification, which may
15 resolve this. So let's do Question 3, which is does
16 the device present a potential unreasonable risk of
17 illness or injury? David?

18 DR. COCHRAN: Cochran, no.

19 DR. BURTON: Burton, yes.

20 DR. PATTERS: Patters, no.

21 DR. GLOWACKI: Glowacki, yes.

22 DR. SUZUKI: Suzuki, no.

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1 DR. BURTON: Dianne?

2 CHAIR REKOW: So the general vote is no.
3 I'm told I only have to vote if there's a tie. So if
4 that's the case, does that resolve Number 2?

5 DR. BURTON: No.

6 CHAIR REKOW: Let's redo the vote on
7 Question 2, please. Jon?

8 DR. SUZUKI: Suzuki, no.

9 DR. GLOWACKI: Glowacki, yes.

10 DR. PATTERS: Patters, yes.

11 DR. BURTON: Burton, yes.

12 DR. COCHRAN: Cochran, no.

13 CHAIR REKOW: So the answer to that is
14 yes?

15 MS. SHULMAN: Correct, Question 2 is yes.

16 DR. COCHRAN: Do I have to have my opinion
17 or their opinion?

18 CHAIR REKOW: Okay.

19 MS. SHULMAN: Okay. Number 4, did you
20 answer yes to any of the above questions? The answer
21 is yes.

22 CHAIR REKOW: We don't have to vote?

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1 MS. SHULMAN: If yes, we go to Item 6. Is
2 there sufficient information to establish special
3 controls, in addition to general controls to provide
4 reasonable assurance of safety and effectiveness?

5 CHAIR REKOW: Okay. And the implications
6 of this, of course, and the comments is that if you
7 say yes, you can classify it as a Class II and if you
8 say no, it remains a Class III?

9 MS. SHULMAN: Correct.

10 CHAIR REKOW: So, Jon, shall we start with
11 you?

12 DR. SUZUKI: Suzuki, yes.

13 DR. GLOWACKI: Glowacki, yes.

14 DR. PATTERS: Patters, yes.

15 DR. BURTON: Burton, yes.

16 DR. COCHRAN: Cochran, yes.

17 CHAIR REKOW: Okay. Good. So that's
18 unanimous. So now, we go to Item 7.

19 MS. SHULMAN: Number 7, if there is
20 sufficient information to establish special controls
21 to provide reasonable assurance of safety and
22 effectiveness, identify the special controls needed to

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1 provide such reasonable assurance for Class II. And
2 the guidance document can include a lot of the
3 discussion from earlier, so you can say that.

4 CHAIR REKOW: Okay. So the choices, of
5 course, are guidance document performance standards,
6 device tracking or testing guidelines or other things
7 that we may deem appropriate. Could you, please, for
8 me, and I apologize if you had this discussion
9 earlier, differentiate the difference between the
10 content of a guidance document and a performance
11 standard. Is a performance standard like an ASTM or
12 an ISO standard?

13 MS. SHULMAN: It could be recognized
14 standards like that. Performance standards are also
15 recognized by a rule and it goes through a rule
16 making. A guidance document may have standards in it
17 that you abide by. A company does not have to go 100
18 percent to the guidance document. However, they would
19 just have to explain why they deviated, how they
20 deviated and what they used instead.

21 CHAIR REKOW: Okay.

22 MS. SHULMAN: So the performance standard

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1 is rule making.

2 CHAIR REKOW: Okay. Could we poll the
3 Panel and see if there is substantial places that we
4 need to do that at, as opposed to initially taking a
5 vote? David, can I put you on the spot and ask you
6 your preference first?

7 DR. COCHRAN: I'm sorry. Repeat your
8 request.

9 CHAIR REKOW: Just rather than voting on
10 which one we need to do first, can we have a
11 discussion by each of you of what your preference of
12 that ranking should be, and then have an open
13 discussion about that if it's clear that we need to.
14 I think it's going to throw out a few options.

15 DR. COCHRAN: Okay. This is David
16 Cochran. My feeling is that we want to be least
17 restrictive if we can, and I think the guidance
18 document, from my understanding, would do that and it
19 sounds like from what the FDA can do in a guidance
20 document, they can help direct the issues, which we
21 have concerns about.

22 MS. SHULMAN: If I can just clarify one

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1 thing, too. Dr. Betz just reminded me. There was the
2 risk table that was discussed earlier in the
3 presentation. If you want to refer to that or we
4 could put it back up there. It may help identify the
5 risks or what could mitigate them.

6 CHAIR REKOW: Okay. What is the
7 preference of the Panel? Do you want to do that or
8 you want to try to sort through it first, and then go
9 back to the risk table?

10 DR. BURTON: Keep going, I think.

11 CHAIR REKOW: Keep going this way and go
12 back to the risk table? Make sure to use that as our
13 backup check. Okay.

14 MS. BLACKWELL: Do you want to see the
15 risk table?

16 CHAIR REKOW: No.

17 DR. BURTON: No.

18 CHAIR REKOW: Not right now. We will go
19 back to it though, because I think it's a useful
20 piece. Richard?

21 DR. BURTON: I would agree with that. I
22 think that in looking at what those guidelines are, I

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1 think that the guidance document, I think, is what
2 people are really, truly going to look at. I think
3 that that's really just the way to go, and I think the
4 way we can address that most effectively.

5 CHAIR REKOW: Mark?

6 DR. PATTERS: Patters. I think,
7 obviously, the guidance document is necessary, but I
8 would give some consideration to device tracking if we
9 are not 100 percent satisfied that adequate studies
10 have been done to show safety.

11 CHAIR REKOW: Okay.

12 DR. GLOWACKI: Glowacki. I think from the
13 general discussion that's going on, that it should be
14 possible that guidance documents would cover it all.

15 CHAIR REKOW: Jon?

16 DR. SUZUKI: Suzuki. I believe I agree
17 with everybody else that the guidance document is
18 probably -- that that's the way to, at least, approach
19 this question, and I don't really believe, at this
20 point, that device tracking is that critical of
21 testing. That's just my opinion at this point.

22 CHAIR REKOW: So clearly, everyone is

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1 pretty comfortable with the guidance document, and we
2 need to probably come back to whether or not we need
3 some special tracking. Can we do that as we go back
4 to the risk table or how would you like us to proceed?

5 DR. RUNNER: I would just -- Marjorie,
6 could you comment on tracking in terms of what kind of
7 devices, at this point in time, are tracked, as
8 opposed to not?

9 MS. SHULMAN: I didn't do my homework.
10 Very few devices are tracked actually.

11 DR. RUNNER: I think, in general, tracked
12 devices actually put quite a burden on the
13 manufacturer in terms of keeping records of who
14 devices are sold to and who they are they implanted
15 in.

16 MS. SHULMAN: Correct.

17 DR. RUNNER: And I think that for a
18 device, usually, for example, TMJ implants, which have
19 had a history of having significant problems are
20 tracked devices, and there are very few other ones.
21 In my opinion, it would probably be very unwieldy to
22 track a device, such as this, which may potentially be

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1 implanted in quite a number of patients.

2 MS. SHULMAN: Correct.

3 DR. BURTON: Burton. I would agree with
4 that, because when I think of a tracked device, first
5 of all, it would be something that could be
6 potentially explanted, at some point in time, so that,
7 you know, you could recover something. Whereas, you
8 know, hopefully down the road, there is nothing here
9 to explant.

10 And again, I think also, you know, if
11 you're looking at this type of product and the cost
12 factor involved, most of those that have been tracked
13 are, I would say, expensive devices, but they are also
14 things, which would be an overhead where the
15 manufacturer could afford to have a tracking system.
16 You know, this is broadly or at least potentially as
17 broadly as this could be used in terms of the
18 potential indications would be very, very difficult,
19 because if you were in practice, you would be
20 tracking, literally, it could be hundreds of patients
21 with this and probably, I'm not sure what you would
22 really gain from that.

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1 CHAIR REKOW: Susan?

2 DR. RUNNER: I think, in addition, it
3 would be significantly different from any of the other
4 bone filling materials that are on the market
5 presently without that requirement.

6 CHAIR REKOW: I see that there is also
7 this check box of other, and to specify either any
8 special things that are done in the other bone filler
9 materials that we might think of that perhaps address
10 some of the concerns that Dr. Patters has. Are they
11 simply included and integrated into the guidance
12 document? Is there a guidance document for the bone
13 filling materials in general?

14 DR. RUNNER: There is not. That's one of
15 the reasons why we gave you the risk and mitigation
16 table, because that could potentially be used in such
17 a guidance document. The only guidance documents that
18 the center has put out so far is the one that you have
19 seen for orthopedics in terms of bone filling
20 materials.

21 CHAIR REKOW: So does it seem that it
22 might be appropriate for us to go to the risk table

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1 now?

2 DR. COCHRAN: Dianne, this is David
3 Cochran. I have a question for maybe Susan. I think
4 on the market, there are so-called bio-active classes
5 that are sold. What are they classified as?

6 DR. RUNNER: All of the other dental bone
7 filling materials are presently unclassified.

8 MS. SHULMAN: We could continue on this
9 sheet, and in the next sheet we get into the risks of
10 health and that way it would be more helpful.

11 CHAIR REKOW: Okay. So can we leave the
12 other for the moment, Mark? Are you comfortable with
13 that, just making the recommendation at the moment, a
14 guidance document, knowing that we are likely to come
15 back and revisit at least a part of this?

16 DR. PATTERS: Yes, I'm comfortable. My
17 concern was if the Panel had doubts, that was -- but
18 if you don't, you don't.

19 CHAIR REKOW: Okay.

20 DR. PATTERS: My personal concern is that
21 the lack of reports of adverse reactions may just stem
22 from the lack of broad base use, and once it's in

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1 broad base use, we maybe can see them and will we
2 recognize the problem without any type of control?

3 CHAIR REKOW: Okay. Thank you.

4 MS. SHULMAN: Number 8 is regarding the
5 Regulatory Performance Standard, but that was not
6 chosen, so we can skip that. Number 9 is also a
7 question about the performance standard, so we can
8 skip that. Number 10 is a question if it was to be
9 classified or stay in Class III, which is wasn't, so
10 we can skip that. So we can go to the next page.

11 Number 11, identify the needed
12 restrictions. There are three other restrictions and
13 another. The first one is the basic prescription
14 labeling, and the other two used only by persons with
15 specific training or experience in its use and use in
16 only certain facilities adds upon the prescription
17 labeling. So the first question is identify the
18 needed restrictions, and the first one is only upon
19 the written or oral authorization of a practitioner
20 licensed by law to administer or use the device, and
21 then the other two. We have been on those.

22 CHAIR REKOW: Okay. I have forgotten

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1 which way we were going. David, do you want to go
2 first?

3 DR. SUZUKI: Jon Suzuki. Oh, sorry.

4 CHAIR REKOW: Go ahead.

5 DR. PATTERS: Jon Suzuki. Answer 1, which
6 is only upon written or oral authorization of a
7 practitioner licensed by law to administer or use the
8 device.

9 DR. GLOWACKI: Julie Glowacki, yes to the
10 authorization with the licensed practitioner.

11 DR. PATTERS: Patters, I agree with that.

12 DR. BURTON: Burton, concur.

13 DR. COCHRAN: Cochran, with a question.
14 Does that mean like a licensed dentist or are we
15 talking about a prescription, per se?

16 MS. SHULMAN: A prescription per se.

17 DR. COCHRAN: I don't think that's our
18 understanding on the Panel.

19 CHAIR REKOW: No, I don't think so either.

20 DR. RUNNER: I think what -- this device
21 would not be -- you would not write a prescription for
22 this device and give it to your patient to go get it.

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1 In other words, you wouldn't need a licensed
2 practitioner to obtain the device to implant it.

3 CHAIR REKOW: I think, if I may, rather
4 than taking another vote, I know I'll be corrected if
5 I'm not correct, that a person who is a licensed
6 dentist with all of the abilities and assurances that
7 they can practice dentistry could use this product.
8 Is that the consensus of the Panel? So however you
9 have to say that.

10 MS. SHULMAN: That would be the first
11 block.

12 CHAIR REKOW: That's what we thought.

13 DR. COCHRAN: Well, then my answer is
14 affirmative.

15 CHAIR REKOW: Okay. All right.

16 MS. SHULMAN: Okay. Now, we can move on
17 to the supplemental data sheet and the generic types
18 of device, Question 1, was whatever you said.
19 Question 2, the Advisory Panel is the Dental Products
20 Panel. Question 3, is device an implant?

21 CHAIR REKOW: Can you read us whatever
22 CFR 860.3? I don't know how I survive with all these

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1 numbers. So we have a definition of an implant. An
2 implant means a device. For those of you who have the
3 handouts, that's on page 11. An implant means a
4 device that is placed into a surgically or a naturally
5 formed cavity in the human body. The device is
6 regulated as an implant for the purpose of this part
7 only if it is intended to remain implanted
8 continuously for a period of 30 days or more unless
9 the Commissioner determines otherwise in order to
10 protect human health.

11 What does that last phrase mean? Like in
12 an emergency, something can happen? So if it's in the
13 body for over 30 days, I guess it's an implant.

14 DR. PATTERS: Right. Yes.

15 MS. SHULMAN: Correct.

16 CHAIR REKOW: So the breakdown products
17 that we have seen, that's everything is over 30 days,
18 right? I'm getting an affirmative nod from the
19 corporate people, so I guess that makes it an implant.

20 MS. SHULMAN: Number 4, the indications
21 for use in the device's labeling. We can fill out
22 what was in the regulation and approved PMA.

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1 DR. RUNNER: I actually have the actual
2 list now of what was approved in the PMA, and I could
3 read them for you again if you would like. The Miter
4 PMA had five indications, use in defects after
5 extrication of dental alveolar cysts. In
6 periodontics, for filling of two-wall bone pockets, as
7 well as bifurcations and trifurcations of the teeth.
8 Three, augmentation of the atrophied alveolar ridge.

9 CHAIR REKOW: Say that one again.

10 DR. RUNNER: Augmentation of the atrophied
11 alveolar ridge. Four, defects around an apicoectomy
12 and five, filling of bone defects after surgical
13 resection of impacted teeth.

14 SECRETARY ADJODHA: Susan, seeing that the
15 Panel has recommended so far Class II, shouldn't we
16 use the indication for the intended use in the reg?

17 DR. RUNNER: I believe the intended use in
18 the reg is just a description of the generic class of
19 device.

20 SECRETARY ADJODHA: Okay.

21 DR. RUNNER: These are the indications
22 that would be --

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1 MS. SHULMAN: Right. So it's the intended
2 use of the reg and the indications that were cleared.

3 SECRETARY ADJODHA: Okay. Thank you.

4 CHAIR REKOW: So that does not -- does it
5 or does it not include sinus lifts?

6 DR. RUNNER: It does. I will read them
7 once again. Use in defects after extrication of
8 dental alveolar cysts. In periodontics, for filling
9 of two-wall bony pockets, as well as bifurcations and
10 trifurcations of teeth, augmentation of the atrophied
11 alveolar ridge, defects around apicoectomies and
12 filling of bone defects after surgical resection of
13 impacted teeth.

14 CHAIR REKOW: So to you periodontists,
15 does augmentation of an atrophied ridge include a
16 sinus lift?

17 DR. BURTON: No.

18 DR. RUNNER: We have not interpreted it as
19 such.

20 CHAIR REKOW: Thank you.

21 DR. BURTON: Burton. I would say that it
22 wouldn't. The other thing is though that that's even

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1 more restrictive than, at least, what I have been
2 hearing at least from manufacturers, because, I mean,
3 there it limits it down to saying, you know, surgical
4 extractions of third molars, which would then not make
5 an indication for use, let's say, in general surgical
6 -- just general extractions for ridge preservation
7 would not be an indication within what was given
8 there. You know, that's a pretty tight limitation to
9 say that it has to be surgical extraction of third
10 molar or an impacted tooth. I mean, that's, you know,
11 an impacted cuspid.

12 DR. RUNNER: But it's also a combination
13 of the intended use, which sort opens the door wide if
14 you look at the intended use definition in the CFR,
15 because the intended use in the CFR says tricalcium
16 phosphate granules for dental bone repair is a device
17 intended to be implanted into the upper or lower jaws
18 to provide support for prosthetic devices. So our
19 interpretation of that couldn't be --

20 CHAIR REKOW: Okay.

21 DR. BURTON: But not sinus lifts.

22 DR. PATTERS: Patters. I am somewhat

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1 disturbed about those periodontal indications. It's
2 my understanding that if we include an indication, we
3 are saying that there is scientific data to support
4 that use, are we not? If there is scientific data
5 that shows any bone filling material to be effective
6 in the treatment of bifurcations and trifurcations, it
7 has escaped my notice.

8 CHAIR REKOW: Yes.

9 DR. COCHRAN: This is Cochran. I'm not
10 sure that probably any device has scientific data for
11 every particular indication in the world out there
12 that it's used for, and it sounds like the regulation
13 is to use for dental alveolar surgery, and I would
14 hope that we would allow the clinician to have some
15 say in how the product is used if they think it's
16 going to benefit the patient. I favor the regulation.

17 CHAIR REKOW: Mark?

18 DR. PATTERS: Patters again. I think that
19 if it's labeled for this use, that that states that
20 there is scientific data to support it. So I am very
21 uncomfortable with filing a label that says this is
22 useful in periodontal defects and bifurcations and

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1 trifurcations.

2 DR. RUNNER: Unfortunately, when this came
3 and it was approved back in the '80s, I assume it went
4 before a Panel, at that time, it was determined that
5 there was scientific evidence to support that
6 indication and it was approved, at that time. We have
7 to --

8 DR. PATTERS: But that's not like getting
9 the Ten Commandments though, is it? I mean, just
10 because it was carved in stone in 1980 doesn't mean
11 that the pillars have not been broken, does it?

12 MS. SHULMAN: Those were the approved PMA
13 indications.

14 DR. PATTERS: But further data might show
15 in the future that those indications were not
16 appropriate. Is that not true or is it like the Ten
17 Commandments?

18 DR. RUNNER: I believe that if we were to
19 take an indication off, we would probably have to have
20 some evidence of medical device problems with the
21 issue that would be submitted to the Agency that this
22 indication should be eliminated, and to date, we don't

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1 have that data, so it is sort of like the Ten
2 Commandments.

3 DR. PATTERS: You know, I have no problem
4 with the clinician making a determination as to how to
5 use the device, but I have a problem with labeling it.

6 That is when you label it, you are stating that it
7 has been shown to be effective, and perhaps there were
8 data in 1980, but it has escaped my notice. That's
9 all I can tell you. Perhaps David could recite it for
10 us.

11 DR. COCHRAN: No.

12 DR. PATTERS: Or perhaps Dr. Suzuki who is
13 very familiar with that literature.

14 MS. SHULMAN: Marjorie Shulman. Right
15 now, that is an improved indication that is out.
16 Maybe it's not being marketed, at this time, but it's
17 an improved indication that is out on the market.

18 DR. SUZUKI: This is Jon Suzuki. I do
19 tend to agree with Dr. Patters' concerns about the
20 labeling, but I think if we go the route, as already
21 alluded to by Dr. Cochran, it really is up to the
22 clinician jurisdiction, clinician judgment, and if he

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1 feels he can utilize them in these types of defects
2 like bifurcations and trifurcations, then more power
3 to him.

4 But in their education, they learn the
5 risks and the benefits, and most astute clinicians
6 would probably go to the literature and know that it
7 doesn't work in certain situations. So I do see Dr.
8 Patters' concerns, but I would like to see us accept
9 them the way they are, I guess.

10 DR. PATTERS: Well, again, I would like to
11 see it say that it can be used in periodontal defects
12 and leave it to the clinician to decide what type of
13 defects, rather than say that it is labeled for use
14 and treatment of trifurcation and bifurcation
15 involvements, because that's very different to me.

16 DR. SUZUKI: This is Suzuki. What would
17 it take to add that clause?

18 MS. SHULMAN: A more specific indication?

19 DR. COCHRAN: I guess, a procedural
20 question would be are we really -- is this language
21 with those indications, is that going to be on the
22 labeling of this product or will it just fit into the

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1 regulations as whatever that CFR thing is you're
2 talking about?

3 MS. SHULMAN: Marjorie Shulman. It would
4 not only be on the label of a product if a company
5 came in for that indication for the labeling of their
6 product.

7 DR. PATTERS: But there is nothing to
8 prevent them from doing so if it's in the labeling.
9 They don't even have to show data, I mean, if it's in
10 the regulation.

11 MS. SHULMAN: Under pre-market
12 notification, under Class II, we could ask for data.
13 We could ask for clinical data.

14 DR. RUNNER: And you could --

15 DR. PATTERS: But if it's already a known
16 indication, why would you do that?

17 MS. SHULMAN: It's a known indication.

18 DR. PATTERS: Because, like I say, I'm
19 uncomfortable with it.

20 MS. SHULMAN: It's an improved indication
21 for the one company who has the approved PMA. Anyone
22 else who is to introduce this into the market would

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1 require a new 510(k) and would require anything that
2 was to be in the guidance document, any clinical data
3 that we might need, any special labeling, anything
4 like that.

5 DR. RUNNER: And I think you could
6 recommend to us that you feel that it would be
7 important to specifically require data when they were
8 making a claim for bifurcations and trifurcations, and
9 we could certainly ask for that.

10 DR. PATTERS: You guys always have a way
11 out.

12 CHAIR REKOW: Richard?

13 DR. BURTON: Richard Burton. One of the
14 things that has changed in the world since 1980
15 though, which concerns me a little about this is we
16 have split off in so many areas, pediatrics. I do a
17 lot of pediatric surgery, and my concern is that this
18 also opens -- I mean, again, I would say it's one
19 thing in adults, but, you know, I would have a lot of
20 heartburn with people using this type of material in
21 some pediatric situations that would fall within those
22 accepted guidelines. I mean, is there any way you can

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1 add this, you know, for -- I would say things now
2 oftentimes have a young age limit sometimes built into
3 it, but, you know.

4 MS. SHULMAN: Marjorie Shulman. I would
5 have to look at the labeling that was actually cleared
6 in that PMA. If it wasn't cleared for pediatric,
7 pediatric use is a new indication for use. New
8 indications for use require new 510(k)s, and there
9 would be a new 510(k) and we would get data.

10 DR. BURTON: Because again, you could have
11 -- it might be a fine product if you want to put it in
12 a cyst. I'm not sure you would want to put it into a
13 cyst in an 8 year-old kid, because I think that,
14 again, you know, they are not the same use. We didn't
15 split those things out. It was sort of a little more
16 across the board, but I don't know whether that could
17 be looked at. At least, I would certainly recommend
18 doing that.

19 CHAIR REKOW: Okay. I guess on the form
20 under indications for use, we say whatever is in the
21 regulation and the PMA with concerns as noted in the
22 discussion, especially relating to pediatric and

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1 labeling would deal with those. Is that adequate?
2 Yes?

3 DR. GLOWACKI: I have a question about the
4 failure to osseointegrate.

5 CHAIR REKOW: Can we go down to the --

6 DR. GLOWACKI: Oh, I'm sorry.

7 CHAIR REKOW: We'll go one by one.

8 DR. GLOWACKI: Oh, I'm sorry.

9 CHAIR REKOW: Okay. I'm sorry.

10 DR. GLOWACKI: Yes.

11 CHAIR REKOW: Infection of the soft tissue
12 and/or bone, the guidance document could deal with
13 that, as well as the sterility review question. What
14 is the sterility review? Is that like a
15 specification?

16 DR. RUNNER: It's a guidance document.
17 Well, first of all, we would review all information
18 about sterility of the device, and guidance on how the
19 company --

20 CHAIR REKOW: Okay.

21 DR. RUNNER: What about performing those
22 tests.

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1 CHAIR REKOW: For adverse tissue
2 reactions, aside from failure to osseointegrate, which
3 may be a separate issue. The FDA has an ISO standard
4 and there is biological information of medical devices
5 and evaluation and testing, which is standard
6 procedures, which would again be in the guidance
7 document, I assume. Adequate? I'm getting
8 affirmative nods from everybody, just for the record.

9 Incomplete or lack of bone formation, and
10 here the data would be obtained either through
11 performance testing, animal and/or clinical data, as
12 well as directions for use. Is that adequate? My,
13 what an accommodating group we have here.

14 MR. SCHECHTER: Dianne?

15 CHAIR REKOW: Yes, sir?

16 MR. SCHECHTER: This is Dan Schechter.
17 With, I guess, the last four categories on the risk
18 table, it talks about performance testing. Is it
19 FDA's position that every 510(k) under this category
20 regardless of indications is going to require clinical
21 data, either animal or human?

22 DR. RUNNER: No.

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1 MR. SCHECHTER: Okay. Just checking.

2 CHAIR REKOW: So having said that, can
3 you --

4 DR. RUNNER: I think that would depend on
5 the indication for use that was proposed by the
6 company.

7 CHAIR REKOW: Okay.

8 DR. PATTERS: Susan?

9 CHAIR REKOW: Yes, Mark?

10 DR. PATTERS: Patters. Susan, can the
11 performance testing be put in the guidance document?

12 DR. RUNNER: Yes.

13 CHAIR REKOW: Okay. The next one is a
14 failure to -- let me go back and make sure that we
15 took care of incomplete or lack of bone formation.
16 Everybody is okay with that? Okay. Failure to
17 osseointegrate, to be controlled again by performance
18 testing, directions for use in animal and/or clinical
19 data. Julie had a question about that.

20 DR. GLOWACKI: This is Julie Glowacki.
21 I'm not sure that that concept has any relevance,
22 osseointegration, if we're talking about resorbable

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1 materials. Now, I may in a spiralling argument here
2 with respect to are we talking about resorbable forms
3 or biphasic and so forth? So I just wanted to raise
4 that as a point of clarification.

5 CHAIR REKOW: Yes. It's an interesting
6 one. If it's in for 30 days, but it's going away,
7 does it osseointegrate? Dr. Betz, you have a comment?

8 DR. BETZ: This is Dr. Betz.
9 Unfortunately, this is my baby right here and I stole
10 it from the draft guidance that the orthopedic people
11 did. Failure to osseointegrate maybe doesn't have
12 anything to do directly with the bone itself, with the
13 grafting material itself, but my concern in putting in
14 and separating to get out from incomplete or lack of
15 bone formation was related to the fact that the bone
16 that is generated therefrom may or may not
17 osseointegrate and, therefore, I threw it in just to
18 make sure you guys were on your toes and you would
19 want to consider that as a possibility. It may not
20 apply in your opinion. That's your choice.

21 CHAIR REKOW: Can you help me understand
22 better the difference between lack of bone developing

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1 and lack of osseointegration?

2 DR. BETZ: Well, my concern was that the
3 bone that is generated may or may not have properties
4 that would permit it to osseointegrate.

5 CHAIR REKOW: Permit what to
6 osseointegrate?

7 DR. BETZ: It's a big unknown. We don't
8 know whether bone generated like this will
9 osseointegrate as such.

10 CHAIR REKOW: With the natural bone that
11 is remaining? Osseointegrate with what?

12 DR. BETZ: With the dental implant.

13 CHAIR REKOW: Oh.

14 DR. BURTON: Burton. I know what Dr. Betz
15 is alluding to. There have been some various studies
16 at different times looking at both autogenous and
17 allogeneic materials, and whether the bone that seems
18 to be developed from that doesn't seem to have quite
19 the same capabilities as some native. That has been
20 one of the tradeoffs between autogenous bone and
21 various allogeneic, you know, various allogeneic
22 materials has been -- yes, it sort of forms bone, but

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1 it doesn't seem to function quite as well or whatever
2 as that. And I think what you're saying is does the
3 bone -- you know, there's a risk from this that the
4 bone that would be generated by it may not be of the
5 same quality that would support osseointegration that
6 native bone would.

7 DR. BETZ: This is Betz again. I agree
8 100 percent. That is also related to weakness, newly
9 formed bone, you know, at the bottom. We don't know a
10 lot about the nature of the quality of bone that you
11 get, and the last thing I would want to do is have
12 somebody and my wife, especially my wife, sink a brand
13 new implant in some very freshly generated bone and
14 have to go heck in a hand basket and then have to
15 explain to her why, my dear, you have to do this
16 again.

17 CHAIR REKOW: Julie?

18 DR. GLOWACKI: Julie Glowacki. Then I
19 think it's a matter of grammar, rather than anything
20 else, because the way this table is set up, I think
21 you're talking about this implant material.

22 DR. BETZ: Right.

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1 DR. GLOWACKI: So could I make a
2 suggestion to say failure to support osseointegration
3 of devices?

4 DR. BETZ: This table is yours to do with
5 as you see fit. That's fine with me.

6 DR. GLOWACKI: Let's make it go back.

7 DR. COCHRAN: I would like to make a
8 comment. This is David Cochran. In a lot of the more
9 recent literature, we understand that the quality of
10 the bone is fine that's being stimulated, but a lot of
11 it has to do with the nature of the implant surface
12 itself, and that may be a lot more overriding a factor
13 whether you actually have osseointegration of the
14 implant or not. So I am not sure. I would agree with
15 Julie. I think it's a matter of what we're saying,
16 because the way it's sort of stated now is like does
17 this new bone integrate in the old bone? But you mean
18 it to be a dental implant.

19 DR. BETZ: Yes, sir.

20 DR. COCHRAN: Yes. And I'm not sure if we
21 should really comment. I mean, I think what you're
22 trying to say is if you want to use it in support of a

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1 dental implant, that you need to have data that
2 suggests that when you use it, you do enhance
3 osseointegration of the implant.

4 CHAIR REKOW: And you could go one step
5 further to the last item. It's stiff enough to do
6 that.

7 DR. COCHRAN: I don't know if stiff is the
8 right word.

9 CHAIR REKOW: Right, it isn't.

10 DR. COCHRAN: But osseointegration is bone
11 to implant contact at a light microscopic level, but I
12 think that's a little different issue. So I would
13 think we just need to work on the wording of that to
14 get the meaning across of what you really want to say.

15 DR. BETZ: Yes. This is Betz again. I
16 just want to make sure you guys were awake.

17 CHAIR REKOW: While you're standing there,
18 you want to help us with the last item, because it's
19 going to be the same issue? When you talk about the
20 weakness of the newly formed bone, is that also
21 relating to in support of endosseous implants or are
22 you talking about in general there?

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1 DR. BETZ: In my opinion, I would consider
2 it in general.

3 CHAIR REKOW: Okay.

4 DR. BETZ: But including related to
5 implants.

6 CHAIR REKOW: Okay. Thanks for the
7 clarification. We'll get there. So if we make the
8 change to, say, something like failure to support
9 osseointegration of endosseous implants or something
10 like that to clarify.

11 DR. BURTON: It would seem to me that we
12 could almost take all three of those, the areas
13 incomplete or lack of bone formation, failure support
14 osseointegration, weakness in newly formed bone are
15 really all sort of one thing, and they all have the
16 same outcomes across from there. They all say
17 performance testing, animal and/or clinical data, that
18 those could be rolled into maybe one statement, which
19 was just really, you know, incomplete or weak bone
20 formation, which may fail to support osseointegration,
21 make it into one. I mean, you have just brought out a
22 bunch of lines.

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1 CHAIR REKOW: Say incomplete or inadequate
2 maybe.

3 DR. COCHRAN: I would have the opinion
4 that we ought to get rid of the last one. I don't
5 think we do any testing for weakness of the bone. I
6 don't think that's the appropriate language at all
7 there.

8 DR. BURTON: Yes. I mean, that's really
9 an orthopedic term, because what it is is when they
10 used this to deal with a gap issue was whether it was
11 strong enough to support function. It would appear
12 that we're really not doing that.

13 DR. COCHRAN: We don't do that.

14 CHAIR REKOW: Especially with granules.

15 DR. COCHRAN: Right.

16 CHAIR REKOW: It's a good trick if you can
17 do that.

18 DR. COCHRAN: We would drop that last one.
19 I don't think that's appropriate.

20 CHAIR REKOW: So what if we just made that
21 heading incomplete or inadequate bone formation?

22 DR. COCHRAN: Yes.

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1 CHAIR REKOW: Because that then gets you
2 to the applications.

3 DR. COCHRAN: Yes.

4 CHAIR REKOW: It addresses some of the
5 alveolar ridge stuff underneath prostheses, and it
6 lets the test be driven by what the application --

7 DR. COCHRAN: In that Number 4 that we
8 have, the fourth block down.

9 DR. BURTON: Yes. But I would say, you
10 know, incomplete or what was the other word you used?

11 CHAIR REKOW: Inadequate.

12 DR. BURTON: Inadequate bone formation,
13 which may not support osseointegration.

14 CHAIR REKOW: No, I would actually go
15 back, if I may, I'm sorry. Sometimes I get too pushy.

16 Take the first, the second and the fourth one and
17 collapse them into just saying incomplete or
18 inadequate bone formation, and let the application
19 drive the decision and the test for what that needs to
20 be, because if it's inadequate, it can't support the
21 endosseous implant. If it's too weak, it can't do the
22 other stuff it's supposed to do.

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1 DR. COCHRAN: But we don't measure
2 weakness in bone.

3 CHAIR REKOW: No, I know we don't, but
4 that's why I would just say get rid of the word
5 entirely, and just put all three of those into one
6 category that says incomplete or inadequate.

7 DR. RUNNER: So you're going to get rid of
8 5 and 7?

9 CHAIR REKOW: Oh, I'm sorry. I would like
10 to get rid of -- collapse together the incomplete, the
11 failure to osseointegrate and the weakness.

12 DR. COCHRAN: I would vote against that,
13 Dianne.

14 CHAIR REKOW: Okay.

15 DR. COCHRAN: The reason for it is that
16 Number 4, the incomplete or lack of bone, can apply to
17 other indications in this material. A lot of times we
18 have placed in an intraosseous defect without an
19 implant.

20 CHAIR REKOW: Right. I agree completely,
21 but the point that I was trying to make is that if we
22 make it more generic, then it becomes a decision

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1 process for every application, because you need either
2 complete or adequate bone for whatever application
3 you're thinking about. If you're going to enhance the
4 ridge, if you're going to do it around an implant, if
5 you're going to replace a cyst, all those things
6 needed to be adequate and they needed to be complete.

7 DR. COCHRAN: My feeling is, in the
8 experience I have had, is that we are really looking
9 at very different indications when we put it around an
10 endosseous implant.

11 CHAIR REKOW: I agree.

12 DR. COCHRAN: Versus when we use it as a
13 bone augmentation material in a ridge.

14 CHAIR REKOW: Okay.

15 DR. COCHRAN: So my preference would be to
16 keep them separate.

17 CHAIR REKOW: Okay.

18 DR. COCHRAN: Because I think you're going
19 to see, the FDA is going to see very different data in
20 the performance testing in those kinds of things.

21 CHAIR REKOW: Okay. We just want it to
22 work. Any comments, changes, suggestions? Okay. We

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1 have the device migration or extrusion and there, the
2 answers that are given are the performance testing,
3 animal and/or clinical data and the directions for
4 use. I would like to motivate a tiny bit of
5 conversation about whether or not it's appropriate and
6 needs to be specified what the breakdown product
7 dynamics are. Dynamics is probably the wrong word,
8 but to be able to characterize the breakdown products
9 as a function of time. Does that need to be more
10 completely specified than it is or is it already taken
11 care of in the data that you would collect under this?

12 DR. RUNNER: We typically collect that
13 data as a part of these applications.

14 CHAIR REKOW: Okay. Never mind.

15 MS. SHULMAN: That would be under adverse
16 tissue reaction.

17 CHAIR REKOW: Okay. Jon?

18 DR. SUZUKI: This is Suzuki. I guess I'm
19 not reading it the same way you are, Dianne. Device
20 migration or extrusion to me means lost out of a site
21 or a pocket, as opposed to degradation of products.

22 CHAIR REKOW: Okay. Okay.

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1 DR. SUZUKI: And I getting mixed up?

2 CHAIR REKOW: You are probably right.
3 Okay. So does that take care of the risks?

4 SECRETARY ADJODHA: Well, you need to go
5 through and list each one. You should agree on it.

6 CHAIR REKOW: Okay. Okay. So will you
7 write and I'll see if I can summarize them? So the
8 first one, maybe we can just tie it to Angela's table.

9 The first one is the risk associated with surgical
10 and treatment procedures and that is as it appears.
11 There were no modifications. Yes, we're talking about
12 Question 5.

13 MS. BLACKWELL: Question 5? Okay.

14 CHAIR REKOW: The second point -- Angela,
15 maybe you can number those, so that Michael can --

16 DR. RUNNER: Dr. Rekow?

17 CHAIR REKOW: Yes, ma'am?

18 DR. RUNNER: Maybe we could just say see
19 table, table of risks.

20 SECRETARY ADJODHA: But they modify the
21 tables.

22 DR. RUNNER: See table as modified.

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1 CHAIR REKOW: So maybe we can mark up your
2 table. The second one is fine. The third one is
3 fine. The fourth one we decided. What did we decide?
4 The incomplete or lack of bone formation, we said we
5 would leave or did we want lack to be inadequate?

6 DR. SUZUKI: Suzuki. Lack to be
7 inadequate, I think, is what we agreed.

8 CHAIR REKOW: Okay. So, Angela?

9 MS. BLACKWELL: What does it say?

10 CHAIR REKOW: The next one up from where
11 your finger is. Change lack to inadequate.

12 MS. BLACKWELL: Okay.

13 CHAIR REKOW: And the next one down, I
14 think we modified that to say failure to support
15 osseointegration of endosseous implants.

16 DR. BURTON: Endosseous dental.

17 CHAIR REKOW: Dental implants?

18 MS. BLACKWELL: Yes, we'll use the one
19 from this.

20 CHAIR REKOW: Okay. The next one was
21 fine, and the we were going to eliminate the last one,
22 the last row, yes. Okay?

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1 DR. RUNNER: Okay.

2 SECRETARY ADJODHA: Okay.

3 MS. SHULMAN: Perfect. On the form, we
4 can move to Number 6, the recommended Advisory Panel
5 classification of priority. Classification is Class
6 II. The priority you would vote on a high, medium and
7 low, and all that means is how fast would you like us
8 to work on the regulation reclassifying the device?

9 CHAIR REKOW: Yesterday afternoon would
10 have been good.

11 MR. SCHECHTER: This is Dan Schechter. Do
12 we get to ask the petitioner what priority they like?

13 As industry representative, I endorse high priority.

14 CHAIR REKOW: Do you ever get anything
15 that isn't high priority?

16 DR. BURTON: You could try carbon dating.

17 CHAIR REKOW: Excuse me? What did you
18 say, Rick?

19 DR. BURTON: I said we could try carbon
20 dating.

21 CHAIR REKOW: Do you ever get anything
22 that isn't high priority, Susan?

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1 MS. SHULMAN: I can tell you. Marjorie.
2 We do get some things that are low priority if they
3 are Class III already undergoing 510(k), so it's not a
4 change in the regulatory path, PMA versus 510(k).

5 MR. SCHECHTER: This is Dan Schechter. In
6 all seriousness, given that there aren't many or any,
7 at this point, products in this category on the market
8 and, although, the studies we have may not be gold
9 standards studies, it does seem to be a very helpful
10 product. I would just push for a high priority, so
11 that these products can actually get back out there on
12 the market.

13 CHAIR REKOW: Is there anyone that would
14 argue otherwise?

15 SECRETARY ADJODHA: Did we vote on what
16 classifications?

17 CHAIR REKOW: Oh, I guess Michael has just
18 brought up that we didn't formally vote on which
19 classification --

20 MS. SHULMAN: We'll vote on the sheets
21 when completely done.

22 CHAIR REKOW: Okay. I'm sorry. So I'm

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1 hearing the priority should be high. David?

2 DR. COCHRAN: I think medium would work,
3 as well, for fairness to the FDA, but I don't really
4 care how we go on this one.

5 MS. BLACKWELL: We can't go any faster.

6 DR. BURTON: It's sort of like the mule.
7 It only has one speed. You can dangle carrots or a
8 whip.

9 CHAIR REKOW: Rather than putting anyone
10 on the spot, is there anyone who will --

11 DR. GLOWACKI: I'll go on the spot.

12 CHAIR REKOW: Go ahead.

13 DR. GLOWACKI: Julie Glowacki. I think,
14 you know, having made this recommendation for
15 reclassification is absolutely no reason to suggest
16 any delay, and I think we ought to say high.

17 CHAIR REKOW: Any other comments,
18 suggestions? All right. I will take that as
19 affirmation.

20 MS. SHULMAN: Okay. Number 7, if device
21 is an implant or is life sustaining or life supporting
22 and has been classified in a category other than Class

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1 III, explain fully the reasons for the lower
2 classification with supporting documentation and data,
3 and we may say as discussed in the Panel meeting if
4 you so wish.

5 CHAIR REKOW: Is there anyone that would
6 like to explicitly state all of our things, as opposed
7 to saying as discussed in the Panel meeting?

8 MS. SHULMAN: Okay. Number 8, summary of
9 information, including clinical experience and
10 judgment upon which classification recommendation is
11 based. You can also say as discussed in the Panel
12 meeting.

13 CHAIR REKOW: Anyone want to say other
14 than that? Hearing nothing, we'll go on.

15 MS. SHULMAN: Number 9, identification of
16 any needed restrictions on the use of the device, for
17 example, special labeling, banning prescription use,
18 anything else besides what has already been discussed
19 in the risk to health?

20 DR. BURTON: Children.

21 MS. SHULMAN: Pardon me?

22 DR. BURTON: Children, children.

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1 MS. SHULMAN: Oh, pediatric? All right.

2 CHAIR REKOW: Julie brought up a list.
3 I'll have to write and talk at the same time. That
4 never works. Julie brought up a series of questions.

5 Do we want to go with any of these? If I remember
6 her list, it was not doing infected sites, being
7 careful about overfilling, discontinuous defects.

8 DR. GLOWACKI: Discontinuity.

9 CHAIR REKOW: Discontinuity defects, I'm
10 sorry. I guess now that we have only granules, we
11 won't worry about the block and the machinability.
12 Concurrent use with implants, I guess we have taken
13 care of that. One that we haven't addressed is the
14 suitability of mixing it with other materials, and
15 that might be either inert materials and/or biologic
16 materials, but I guess under this umbrella, it would
17 be with other inert materials, perhaps HA, perhaps
18 other forms of the TCP, and whether or not we need to
19 explicitly say to avoid various tissue types,
20 including the blood stream, and I think you mentioned
21 soft tissue and nerves and the dental pulp and those
22 sorts of things.

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1 So do we need to go with a conversation in
2 any of those? David?

3 DR. COCHRAN: This is David Cochran. My
4 comment is even on the pediatric one, we really don't
5 have any data to say anything about these or any of
6 these, at this point, and I think we almost have to
7 rely on the FDA that when they get the applications or
8 the 510(k)s, that the data they get supports whatever
9 indication you're going to use, and I would just vote
10 that we allow that to happen.

11 CHAIR REKOW: So I guess we don't have a
12 burden of proof to be able to prove that it is an
13 issue. It's a concern that we have, but there is no
14 proof and there is plenty of practical usage proof
15 that suggests otherwise. Do we need to worry at all
16 about the mixing and combinations or does more than 50
17 percent --

18 DR. PATTERS: The guidance document should
19 cover that.

20 CHAIR REKOW: The guidance document can
21 cover it?

22 DR. RUNNER: The mixing has already

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1 occurred in cleared 510(k)s in terms of --

2 CHAIR REKOW: Okay.

3 DR. RUNNER: However, if that's something
4 that you think we should look more into in terms of
5 concerns, you know, the Panel transcript is reviewed
6 and your concerns are looked at when we do write the
7 guidance document.

8 CHAIR REKOW: Okay. So I guess the answer
9 to Number 9 is nothing other than what has already
10 been discussed.

11 MS. SHULMAN: Perfect.

12 DR. GLOWACKI: This is Glowacki. Since
13 pediatric was brought up, I wonder about the
14 geriatric, extreme geriatric population, where there--
15 you know, with the prevalence of diabetes and
16 inadequate healing responses of diabetics and
17 geriatric patients that we may also want to think
18 about an upper end of the age or health status just as
19 we begin on the lower level.

20 CHAIR REKOW: Mark?

21 DR. PATTERS: Mark Patters. I think
22 that's the clinician's judgment about the surgical

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1 risks involved for any given patient, and there is no
2 reason to believe that in a perfectly healthy 80 year-
3 old patient, this device would not be helpful, so it
4 has nothing to do with their age. It's just surgical
5 judgment. Some patients are not candidates for
6 surgery. I'm not sure it's device related.

7 CHAIR REKOW: The same would be true for
8 biologic, pathologic conditions and various disease
9 states, I think. Okay?

10 MS. SHULMAN: Okay. Number 10 we get to
11 skip, because it's not a Class I device. Number 11,
12 if the device is recommended for Class II, recommend
13 whether FDA should exempt it from pre-market
14 notification. That's a yes and a no. A Class II
15 device can be exempt from pre-market notification and
16 we would not see, so you would vote yes or no.

17 CHAIR REKOW: Can I have a vote, David?

18 DR. COCHRAN: Cochran, no.

19 DR. BURTON: Burton, no.

20 DR. PATTERS: Patters, no.

21 DR. GLOWACKI: Glowacki, B, no.

22 DR. SUZUKI: Suzuki, no.

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1 CHAIR REKOW: You have it.

2 MS. SHULMAN: Okay. Number 12, existing
3 standards applicable to the device of assemblies,
4 components or device materials. We can say what we
5 have discussed earlier, though it has been presented
6 or if you wanted to add any.

7 CHAIR REKOW: Does anybody have any
8 compelling standards that we have overlooked so far in
9 our conversation?

10 DR. SUZUKI: Suzuki, nothing to add.

11 CHAIR REKOW: Angela?

12 MS. BLACKWELL: I think there is an ASTM
13 standard that's out there.

14 CHAIR REKOW: Can we say this is as
15 discussed?

16 MS. SHULMAN: We can, as discussed in the
17 Panel meeting.

18 CHAIR REKOW: Okay. And if there are new
19 ASTM standards and ISO standards, I would assume that
20 those would be applied as part of the guidance
21 document anyway.

22 MR. SNIDER: Those would be reviewed and

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1 applied.

2 MS. SHULMAN: Then you will take one final
3 vote on the forms as filled out and voted upon as a
4 Class II device reclassification.

5 CHAIR REKOW: Okay. So the question is
6 should this be reclassified as a Class II device.
7 Jon?

8 DR. SUZUKI: Suzuki, yes.

9 DR. GLOWACKI: Glowacki, yes.

10 DR. PATTERS: Patters, yes.

11 DR. BURTON: Burton, yes.

12 DR. COCHRAN: Cochran, yes.

13 MS. SHULMAN: Thank you very much for your
14 time.

15 CHAIR REKOW: Is there any other comments
16 or statements that anyone has a compelling urge to
17 make? Hearing none, I thank you all, and it has been
18 fun, as always, Susan.

19 SECRETARY ADJODHA: Onto the closed
20 session now.

21 CHAIR REKOW: Now, we have a closed
22 session. Sorry.

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1 DR. BURTON: Can we take a break first?

2 DR. COCHRAN: Take a break.

3 SECRETARY ADJODHA: Yes.

4 CHAIR REKOW: No.

5 DR. BURTON: I'm going to have to take my

6 own.

7 DR. COCHRAN: Yes, me, too.

8 CHAIR REKOW: Why don't we take a 10
9 minute break, and then we'll come back for a closed
10 session. Thank you all.

11 (Whereupon, at 3:04 p.m. a recess until
12 3:17 p.m., when the Panel resumed in Closed Session.)

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