TRANSCRIPT - SURGEON GENERAL'S (KOOP) AD HOC COMMITTEE ON "NON-DENTAL HEALTH EFFECTS OF FLUORIDE," APRIL 18 - 19, 1983

TRANSCRIPT OF PROCEEDINGS

NATIONAL INSTITUTES OF HEALTH

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MEETING OF

THE FLUORIDE PANEL

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ORIGINAL

DAY II

Date: April 19, 1983

Location: Bethesda, Maryland

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EPA file (list of panel)

Surgeon General's AD HOC Committee on the "NON-Dental Effects of Fluoride," April 18-19, 1983

A G E N D A

FLUORIDE PANEL MEETING

THE CLINICAL CENTER, ROOM 2C116
NATIONAL INSTITUTES OF HEALTH, BETHESDA, MARYLAND

MONDAY, APRIL 18

9:00 A.M.	Introductions:	Jay R. Shapiro, M.D. Acting Director, Clinical Center, NIH
	Summary of the Issues:	Robert Mecklenburg, D.D.S., M.P.H. Chief Dental Officer, USPHS
	Safe Drinking Water Act:	Joseph A. Cotruvo, Ph.D. Director, Criteria and Standards Division, Office of Drinking Water US Environmental Protection Agency
	Epidemiology of Fluoride in Drinking Water:	A. Richey Sharrett, M.D., Dr.P.H. Epidemiology Branch, National Heart, Lung, and Blood Institute, NIH
	Fluoride Metabolism, an Overview:	Frank A. Smith, M.D. Associate Professor of Toxicology University of Rochester Medical Center Rochester, New York
	Tissue Effects of Fluoride Intake:	Vincent Vigorita, M.D. Department of Pathology The Hospital for Special Surgery New York, New York
	Clinical Studies:	Michael Kleerekoper, M.D. Bone and Mineral Division Henry Ford Hospital Detroit, Michigan; Jay R. Shapiro, M.D.

DISCUSSION

TUESDAY, APRIL 19

9:00 A.M.	Animal Studies:	James L. Shupe, D.V.M. Professor of Pathology and Toxicology College of Agriculture Utah State University Logan, Utah
	Summary of Economic Issues:	Joseph A. Cotruvo, Ph.D.

DISCUSSION

FLUORIDE PANEL PARTICIPANTS

APRIL 18-19, 1983
THE CLINICAL CENTER, ROOM 2C116
NATIONAL INSTITUTES OF HEALTH, BETHESDA, MARYLAND

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* * * AGENDA * * *

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DR. SHAPIRO: For the moment, I would like to keep the discussion off the issue of the dental problem for the moment and then come back to it.

Would someone like to suggest a definition of an adverse effect in terms of non-dental toxicity, either known or unknown?

Certainly, an adverse effect is osteosclerosis. Is there a lesser stage based on your information that you would like to--

DR. MARX: I don't think we agreed that osteosclerosis presents an adverse health effect.

DR. SHAPIRO: Okay. Well, let's discuss it. If we agree that crippling fluorisis is an adverse health effect. How would you deal with this question of the lag period that was raised or do you think that the evidence to date suggests that the lag--

DR. WALLACH: That comes under the next one, "Potential Adverse."

DR. SHAPIRO: All right. So, crippling fluorosis we consider an adverse effect. Does anyone disagree with that? Are there any others?

DR. WALLACH: What about the things Michael

brings up, the fibrocytic or arthalgic?

DR. KLEEREKOPER: That is really part of crippling fluorosis, I think, isn't it?

DR. SHAPIRO: We don't know. That might be a potential adverse effect.

DR. MARX: Oh, it is an adverse effect.

DR. SHAPIRO: Okay.

DR. KLEEREKOPER: I can't accept that as readily as a known adverse effect. I mean, if you are going to put down an adverse effect in terms of fluoride toxicity, if you want to take this to the letter of the law, an adverse effect of fluoride toxicity is death.

DR. MARX: That is an adverse effect.

DR. KLEEREKOPER: Death is; gastrointestinal hemorrhage is; gastrointestinal irritation-- if the question is "are there any adverse effects from fluoride? Is there any fluoride toxicity?" The answer is absolutely yes, all the way to death. That has been well-established by Dr. Smith's presentation yesterday.

DR. SPENCER: I would like to say that I disagree. I would say that osteosclerosis is an adverse effect because we don't know what the later effect will be.

DR. KLEEREKOPER: That is potential.

DR. SPENCER: Potential effects, yes.

DR. KLEEREKOPER: But recognized adverse effects of fluoride is clearly death, gastrointestinal hemorrhage, gastrointestinal irritation, arthralgias and crippling fluorosis. They are clearly recognized adverse effects.

DR. SHAPIRO: Does anybody disagree with those adverse effects?

DR. VIGORITA: Yes. The arthralgias, in our experience, have been transient and many things pursuant to medical therapy are transient and not considered adverse effect.

So, I would consider an adverse health effect something that triggers an allergic response that leads--

DR. MARX: But somebody that has arthralgia is compromised by it. He is not in good health if he is having arthralgia.

DR. KLEEREKOPER: Not only that, but, if someone is getting arthralgias from fluoride in the drinking water, how do you stop it? So, I can't accept that.

DR. SPENCER: I believe that we ought to differentiate these adverse effects from therapeutic

doses and from amounts in—

DR. KLEEREKOPER: That wasn't the question. The question is "Are there adverse effects from fluoride adminstration?" The answer is yes. At least, I think there are and maybe others.

DR. WALLACH: Jay, why don't you redefine what we are talking about. We are talking about fluoridation, fluoride content of the drinking water or are we talking about fluoride administration in general?

DR. SHAPIRO: I think we have to be talking about fluoride in drinking water. I don't think we have to be concerned with the pharmacological effects of fluoride right now.

DR. WALLACH: Well, then I think we probably ought to throw out the GI effects.

DR. SHAPIRO: Well, you can throw them out. Some of them, I think you may not have all the information you need. If you go up to eight parts per million, some people drinking that will have GI irritation.

DR. KLEEREKOPER: Can we ask Joe what he is asking here in this paper? This is your baby. What did you want to know about any adverse effects in health? Are you really only interested in drinking

water or are you interested in fluoride?

DR. COTRUVO: Fluoride per se and then you back down—

DR. KLEEREKOPER: To the levels. So, I think the things we have mentioned are adverse effects on health. We can take them out afterwards in drinking water.

DR. WALLACH: At all doses and all manners of administration. Is that what you are after?

DR. COTRUVO: Yes.

DR. WALLACH: Okay.

DR. KLEEREKOPER: Then osteosclerosis should stay.

DR. SHAPIRO: I think we are divided on that.

DR. KELLER: Unless the adverse effects from fluoride and then we can talk about for each one what we know about levels.

DR. KLEEREKOPER: Would you read those again?

DR. SHAPIRO: Death, crippling fluorosis, GI irritation, arthralgias.

DR. KLEEREKOPER: GI bleeding.

DR. SHAPIRO: I have GI irritation and bleeding. We are not talking about the cardiac

effects. Those are potential. Osteosclerosis, is there a feeling that this represents a potential rather than a real adverse effect?

DR. WALLACH: It is more potential than real.

DR. KLEEREKOPER: I don't know whether there is a component of the crippling fluorosis that is related to osteosclerosis.

DR. WALLACH: If you don't know, that makes it potential.

DR. SHAPIRO: That is the point. You don't really know what is happening. I think it is reasonable to leave it as a potential adverse effect.

DR. MARX: I would take a position that, just as dental fluorosis is a manifestation of moderately low levels of fluoride excess, osteosclerosis is the next stage and crippling fluorosis is a much more severe stage.

I haven't seen any evidence in the two studies that were cited to suggest that, if you take a large population, a small fraction of them in Texas will have osteosclerosis, but those people are not health compromised.

DR. KLEEREKOPER: That is in the States, but in India osteosclerosis may be one of the

components.

DR. MARX: It is a component of crippling fluorosis.

DR. KLEEREKOPER: Is osteomalacia a side effect of fluoride toxicity? Can you induce osteomalacia with fluoride? The answer to that question is also yes, I think.

DR. SHAPIRO: I think you would have to define "adverse" in the broadest sense of the word.

DR. WALLACH: I would say osteodoses; I wouldn't say osteomalacia.

DR. KLEEREKOPER: True clinical osteomalacia can be induced by fluoride in the right circumstances, as a direct side effect of fluoride.

DR. VIGORITA: That data has not been presented in the last two days. That has not been presented.

DR. KLEEREKOPER: Lancet, 1981. I have the paper in my bag, if you want to see it. We didn't mention it. Do you want the paper?

DR. VIGORITA: Yes, I am curious.

DR. KLEEREKOPER: It is right down at the bottom of my dirty underwear and all.

MR. SMALL: No, don't open the bag.

(Laughter)

DR. KLEEREKOPER: You really want that paper.

DR. SHAPIRO: I think, from a clinical standpoint, it is hard to say some grade of osteoid malacia or osteosclerosis is anything other than a potentially adverse effect, potential when impacted by other factors.

DR. MARX: I don't think it is a potentially adverse effect. A potentially adverse effect is something that is adverse that might occur. Osteosclerosis is an effect that we don't think is adverse.

DR. SHAPIRO: Are you sure that in children it is not adverse? Does it limit the rate of skeletal growth if it occurred in a child?

DR. MARX: Osteosclerosis I don't think is adverse. Compromise of skeletal growth, if it occurs, is adverse. I don't think osteosclerosis is adverse.

DR. SHAPIRO: But we don't know--

DR. MARX: If you want to say that delayed skeletal maturity is a potential adverse effect--it is undesirable and we don't know if it occurs.

DR. MARCUS: What Jay is trying to get you to address is whether you know in your heart that the lesion of osteosclerosis does not, in itself, cause

the delay in skeletal maturation, not that skeletal maturation is--

DR. MARX: For my part, I don't think that osteosclerosis, per se, is bad.

DR. SHAPIRO: Look at it from this standpoint. If it doesn't naturally happen and you are inducing it by permitting this contaminant in water, does that--

DR. MARX: But you could say the same thing for dental mottling. It doesn't normally happen. Mild changes in the dental composition don't imply that the skeleton is compromised. I would say the same for osteosclerosis.

DR. ROWE: If those same changes were occurring in your daughter, you wouldn't be upset about it?

DR. MARX: No.

DR. SPENCER: If you were taking an x-ray of someone who lives in an area--

DR. MARX: Let's also say that these sclerotic effects have been observed at age 50 and beyond. In these communities were there is life-long exposure, nobody decided to change.

DR. ROWE: If it were my daughter, I would be concerned. We can say all of those things, but

when you see a change occurring in the bones that we don't know what its implications are, but it is clearly recognized as two standard deviations from the norm--

DR. KLEEREKOPER: Let's get away for a minute from the drinking water. Can you induce osteosclerosis in humans with fluoride? And the answer to that is yes.

Can osteosclerosis, either on its own or induced by fluoride, cause adverse effects on health and the answer to that, in my opinion, Steve, is yes. I think it does cause certainly marble bone disease which is a form of osteosclerosis. Now, that may not be the same disease that you can induce with fluoride. I am not sure of that. That is clearly causing adverse effects.

DR. VIGORITA: Marble bone disease refers to osteopetrosis. It is a completely different entity. If you are going to use the terms on record, you have to use them correctly.

DR. KLEEREKOPER: Let me put it this way. There are osteosclerotic diseases that do have adverse effects. Whether it is the same disease that is induced by fluoride or not, I really don't know.

DR. SHAPIRO: Let's just say, because we

really don't have the information to come off of this, that osteosclerosis occurs and we really don't know whether it is potentially adverse or not. We don't have the data.

DR. MARX: But we can still vote on it. That is what we are here for.

DR. SHAPIRO: All right. Let's have a vote. How many feel that osteosclerosis should be included as an adverse effect?

DR. MARCUS: As a potential--

DR. SHAPIRO: No. I said adverse effect. Who believes that osteosclerosis is a known adverse effect, that there is something wrong with having it?

DR. SHUPE: May I ask a question. I will go back to the work of Lente and some of them where he broke down osteofluorosis into the chemical, the sclerotic, pleurotic, the malacic and he based it into degrees. The problem I am having is to define what you mean by osteosclerosis.

DR. MARX: What we are talking about is is it a healthy animal or an unhealthy animal. We are not talking about the histology and we are not talking about the chemistry, but whether the animal is in bad health.

DR. VIGORITA: I would like to make a

comment because I see what Dr. Shupe is saying. If the osteosclerosis in fluoride refers to the changes that Dr. Shupe showed and Riggs has referred to as calcified ligaments, I think that is an adverse effect on health.

We have not observed that in our experience and we haven't discussed it in this group from others' experience. So, I wouldn't consider that without the calcified tendons an adverse effect on health.

So, perhaps the blanket statement is unfair. Maybe we want to modify it.

DR. MARCUS: My interpretation of the discussion is osteofluorosis is a histologic change which is an increase in trabecular width and some of the things you showed yesterday. That is what I think we are talking about. We are not talking about any disease which is radiologically apparent. We are already recognizing that. That is osteofluorosis. Is that what you called it?

DR. SPENCER: Talk about radiologically again.

DR. MARCUS: We have already talked about that as an adverse thing. That is agreed on. We have moved that aside.

bone fractures

DR. SHAPIRO: No, no. We have not agreed that early radiologic change is an adverse effect because in everything we read nobody says it is an adverse effect.

DR. MARCUS: How far do you want to take this definition of what we are voting on.

DR. KLEEREKOPER: To me, adverse effects of skeletal disease are either pain and invisible fracture. I don't know of any other clinical manifestation of skeletal disease.

DR. MARCUS: Growth abnormalities.

DR. SHAPIRO: That can happen to.

DR. KLEEREKOPER: What do we know about fractures in bones treated with fluoride? What do we know about the strength?

DR. SHAPIRO: These articles all say that there is nothing to say that it occurs. It has not been cited.

DR. KLEEREKOPER: What do we know about pain as a symptom in these patients who get even severe radiographic changes?

DR. SHAPIRO: It can occur after very, very prolonged levels of fluoride. But at ambient levels it occurs in a very, very small level.

DR. KLEEREKOPER: But it is not something

that occurs.

DR. SHAPIRO: And it may not be related to fluoride.

DR. KLEEREKOPER: So you have no fractures, no pain, no tenderness.

DR. SHAPIRO: That is right.

DR. KLEEREKOPER: I think from that point of view, it is not an adverse effect on health. If you wanted to include the exosdoses as part of the osteosclerosis symptom, then you have a different ballgame. I am not sure I can, but just taking osteosclerosis, leaving the joint component out, osteosclerosis doesn't have pain, tenderness or fracture.

DR. VIGORITA: I think I have a way out of this. If we said something to the effect of a radio-dense skeleton--that is implying an x-ray change--a radio-dense skelton, as seen in association with the fluoride, without soft tissue changes, does not appear to have an adverse effect on health and that gets us away from the calcified ligaments, from potential soft tissue changes and confines it to a Roentgenographic radio-dense skeleton because I can certainly accept that.

DR. SHAPIRO: Okay, but again you are

Radiographic change
no pain, no fracture,
no tenderness
∴ not a health effect

talking about something that has not generally been observed.

DR. VICORITA: Well, osteosclerosis, I believe, we are referring to Roentgenographic radio-density.

DR. KELLER: I think there is evidence. It is controversial and it has not even been repeated that often. But there is evidence to the contrary, that radio-dense skeletons are protected against fractures, at least. Now, I don't know about pain.

The North Dakota study certainly indicated less compression fractions in women, I think it was, accompanied with radio-dense skeletons in very high fluoride areas.

DR. MARX: But, again, we are not trying to address protective levels.

DR. KELLER: I understand, but we are asking the question does radio-dense skeleton, which is a clinical indication of osteosclerosis, imply adverse effects which have been defined as pain, tenderness or fracture and I am saying one of those three not only doesn't imply an increase in fracture, it implies the reverse, a decrease in fracture.

DR. MARX: How about something in the line of osteosclerosis, as has been observed in water

levels up to eight parts per million, is not associated with adverse health effects. That leaves open the fact that osteosclerosis is a part of crippling fluorosis. But the degrees that have been seen, which are relatively mild, have not been associated with that.

DR. SHAPIRO: So, what you are saying is you don't think it should be listed as a potential adverse effect?

DR. MARX: Getting back into the definition of what is a potential adverse effect, fracture is a potential effect; pain is a potential adverse effect; I don't think that a radiographic change is an adverse health effect.

DR. SHAPIRO: All right. Are there other--the value of the potential, by the way, I think is highlighting some possible changes and perhaps later on leading to some recommendations about information that we would have to get, for example, in terms of cardiotoxic, in terms of impairment of skeletal growth in children who have early changes.

DR. WALLACH: I would also include the possibility of reduced turn-over of the young skeleton and the retention in the skeleon of other

adverse effects.

DR. SHAPIRO: Going along with Joe's suggestion, what is the highest no observed adverse effect exposure level? Now, remember, the water group when they discussed this they sort of split. Half of them--

DR. MARX: Before we address any of that, we have got to decide whether we consider dental to be an adverse health effect because that is the threshhold effect for a lot of things.

DR. SHAPIRO: We don't know what bone looks like, unless Jim tells us the answer, we really don't know what bone looks like when you have a level of dental change which is acceptable at the two part per million level? Is that right? Over two parts per million in the drinking water, you are going to get more than grade two mottling in a small percent.

DR. COTRUVO: In a small percentage.

DR. SHAPIRO: We already know what that level is. That level that would be acceptable is, say, two parts per million or 2.4 part per million. What is the level?

DR. COTRUVO: Well, 2.4 is the highest.

DR. SHAPIRO: So, 2.4. Okay.

DR. MARX: So you want to qualify. We are

talking about the highest level for non-dental.

DR. SHAPIRO: At the moment, yes. We know what happens at eight. Is eight an acceptable primary level? Is the risk so small that one can generalize to the--

DR. WALLACH: You are talking about known risk or potential risk?

DR. SHAPIRO: I am talking about known risk.

DR. WALLACH: I will agree with eight for known risk.

DR. SHAPIRO: You would agree with eight?

DR. WALLACH: For known risk.

DR. SHAPIRO: Right.

MR. SMALL: I am concerned with something here that we keep going by and I would like to pin down. Joe shares this, I am sure, in the regulatory write-up the regulation refers to twice the optimal for an area which may vary. Eight PPM versus, for instance, being selected for research done in an area in Texas where the optimum was a particular level might not be equally all right some place else where the optimal is different. The multiples of optimal would be based on not only--

DR. SHAPIRO: Do you feel any concern about

this?

DR. COTRUVO: No, because our feeling, in fact, for the future, is to move away from that, to try to set a standard based on specific numeric values.

DR. MARX: I think right now what we are trying to do is establish the toxicology. We are not concerned with what is therapeutic. We just want to find out--

MR. SMALL: No, it is just the terminology to be applied later in other areas where the optimal is different.

DR. COTRUVO: Just dosages.

DR. SHAPIRO: There is nothing that we have examined that says we should go above eight. Clearly, at eight, a small percentage of the population will at least have recognizable osteosclerosis. Some of them may have even more severe disease than that. There may be a smaller percentage who are clinically more effected, have an adverse effect.

Now, is there any reason to move lower than that? Is there a reason to say or is there a reason to segregate out a certain population in which you say that is fine, but we will tell you right now, for this population, our best information is that we have

to set that level here.

DR. WALLACH: Jay, I personally feel that there is every reason in the world to go lower than that for the potential risks. Again, as a practical matter, I would set four for adults over the age of 50 and, frankly, I would stick with the two for children and young adults. That is my personal feeling, not based on known effects, but based on the potential adverse effects.

DR. KLEEREKOPER: Jay, this is something I should know, but I really can't remember off the top of my head. What is the level of fluoride in the drinking water in those communities that get clinically significant endemic fluorosis?

DR. SHAPIRO: It depends.

DR. KLEEREKOPER: The stuff Jeremy writes about for example.

DR. KELLER: Bone fluorosis or dental fluorosis?

DR. KLEEREKOPER: Bone fluorosis, crippling endemic bone fluorosis that Thiosus(?) has published widely on and many other people have.

DR. SHAPIRO: You are talking about very high intakes for very long periods of time.

DR. KLEEREKOPER: I understand, but what is

the level of fluoride in the drinking water?

DR. SMITH: Nine to ten and up.

DR. SHAPIRO: You don't know what the level is, but certainly you are talking eight to ten and above.

DR. KLEEREKOPER: Or are we talking about four and above?

MR. SMALL: No and you are talking about a tropical climate largely too.

DR. KLEEREKOPER: I understand that. The question that we are asking is what is the lowest level of fluoride in drinking water that has not been reported to be adverse effect. If you want to define that in the United States—

DR. VIGORITA: My records show that, at ten parts per million, if you drink ten liters like that Indian community did, you may develop crippling fluorosis. So, the lowest figure that I have access to from my material is ten, if you drink a lot of water.

DR. OHANIAN: I have here a 1963 by Singe that says 1.2 to 16.2 milligrams per liter showed morphological changes.

DR. MARX: Why don't you say for the group what you just mentioned about those levels from the

1 Donaldson & Juncos, 1.7 & 2.6 ppm!

Indian studies.

DR. SMITH: I was just remarking that the problem with that literature is that they tell you that the population lives in an area of the Punjab where waters contain 1.6 to 15 or 18 or 23 PPM and you never know what well the guy is using that shows this. → WRONG

Let me quote you a paper. You were speaking of '63, was it? This is a paper of '65 by Sabrun(?) et al. There is only one subject, of course, but he states that he appears to have been drinking for 43 years water of the concentrations of fluoride from 2.4 to 3.5 PPM. Now, he had polydipsia of unknown origin, but he did have fluorotic radical myelopathy.

DR. SHAPIRO: I think a possible answer is we know from the Hodge study, the one I quoted earlier, that there was no effect at three parts per million. You know on the other hand that you do get an effect between four and eight. I think there is some literature that suggests that.

Around four seems to be the level at which you don't see anything, based on the available data.

DR. KLEEREKOPER: So, to answer the question what is the lowest observed effect level, the answer, of course, is four.

Lowest observed level of 4

DR. SHAPIRO: It could be an adverse effect in an individual depending on other factors such as the amount that they are taking in every day, but I am talking about the development of radiologic change. That would occur in very small numbers.

DR. KLEEREKOPER: In endemic areas, it occurs at the level of four.

DR. SHAPIRO: Right.

DR. MARX: For osteosclerosis.

DR. KLEEREKOPER: Endemic fluorosis has been reported from communities, not in the United States, but it has been reported in communities drinking levels as low as four. No one is saying it is for 43 years with long term studies. That is what we are talking about and we are talking about people taking fluoride in drinking water from age zero to age 103. The reports outside of the United States, taking everything into consideration, do get clinically observable adverse effects certainly at four or above. There are plenty of papers.

I mean, you may say you don't like that one, but there are other papers that show you do get that at four.

DR. SPENCER: I don't believe that we can compare a report in Indian which is a tropical

country where you don't know how much water you take in, where the nutritional status is very poor, where they don't have any milk and little meat; therefore, no calcium, no phosphorus and magnesium and one cannot compare this to the high fluoride areas in this country.

DR. SMITH: I think you are going to find some populations of that sort in this country too.

DR. SPENCER: Then we should see more pathologic indication of myelopathy and fluorosis in this country. Why don't we see it in the areas of four PPM?

DR. SHAPIRO: I think that you have to conclude that we haven't looked for it and we really don't know. What we are being driven by in this argument is that slide of fluoride content in water because we know that you are dealing with a relative small number of people. That is a major part of this and also inadequate data in terms of this.

DR. MARCUS: I think we are going to be drive by the list of potential effects even further than we are by the list of well-defined effects. So, perhaps we should move on with that.

DR. SHAPIRO: Let me restate what Stanley said though. What Stanley said was he suggested that

we set a level of four parts per million for an adult population. You want to say over 50 and that might be kind of hard to work, but at least for an adult population.

Two parts per million for children and young adults, as levels at which one would think that you are approaching a mean level of safety. You still don't know what is happening at that point, but you are approaching a mean level of safety.

DR. KLEEREKOPER: That is a totally impractical suggestion.

DR. SHAPIRO: Why?

DR. KLEEREKOPER: Any family with kids, which is every community clearly, has to have a two level.

DR. WALLACH: Then so be it.

DR. SHAPIRO: Is that impractical? In other words, can you say that, if you have children in your house up to a certain age, as a primary regulation the water coming through your facet should not contain more than two parts per million of fluoride?

DR. COTRUVO: That can be done. The question of how this is all done is a matter of the law.

DR. SHAPIRO: We are just looking at the

data and I don't think we have to worry about how that would be implemented, if one seriously believes going above that and allowing children to take in four parts per million would be compromising their health. Unfortunately, we don't have the answer one way or the other.

DR. WALLACH: I hate to put this on a personal level, but how many people here, if they had a child born today or tomorrow, would want their child to drink four parts per million for most of their lives?

DR. KLEEREKOPER: And why would they not want them to drink four parts per million?

DR. WALLACH: Because of the potential adverse effects?

DR. KLEEREKOPER: No. Because of unequivocal expected dental fluorosis, unacceptable. If you ask me why I don't want my daughter to have four parts per million, I don't want her to have Stage III or IV dental fluorosis.

DR. SHAPIRO: What I am talking about is, if I know I enter toxicity for 15 percent or whatever it is between four and eight, then I don't know how you can go above that level because you get into a range that is potentially toxic for some people,

depending on variables that you can't control.

DR. WALLACH: You would have to have rocks in your head, in my opinion, to allow your child much more than two parts per million.

DR. ROWE: I think we all agree on that.

DR. SHAPIRO: How many disagree with setting a primary standard of four parts for adults and no more than two parts for children.

DR. MARX: One at a time.

DR. CARLOS: Can we define "adult", the age of adult?

DR. SHAPIRO: Post-puberty.

DR. MARX: I think Michael and I, at least, see the age cut-off as a dental issue. There is some disagreement about that.

DR. MECKLENBURG: In dental areas, the data is quite variable in this too. More recent studies now in Texas with 3.8, 3.9, they are showing no severe fluorosis at all. But there are other places that were. Only in some studies. Some don't report any of the higher level, where you know it has to be or it seems like it has to be, but, if you look across the range of studies, the comfidence interval in the studies, it appears that you are running on the range of moderate to severe fluorosis, maybe

showing up a little bit, one percent, two percent. Optimum, twice optimum, three times optimum. You are getting up maybe to three or four percent risk.

DR. MARX: Up until what age?

DR. MECKLENBURG: Around six or seven. To be safe, the Surgeon General said less than age nine, to have a safety margin.

DR. MARCUS: Even for third molars which don't come out until—

DR. MARX: That is not cosmetic though.

DR. MECKLENBURG: You see some evidence back there, but it is not significant in any respect.

DR. KLEEREKOPER: And you don't smile with your back teeth.

DR. MECKLENBURG: No, you don't smile back there. This isn't significant.

DR. WALLACH: Shall we say age 14?

DR. MARCUS: Age nine.

DR. REDDI: I think the question that Dr. Wallach brought up in terms of turn-over, if we are interested more about the norm, I would say the age of the closure of the epiphysis which might be more meaningful and more physiological.

DR. KLEEREKOPER: We have no idea what happens when you go through the accelerated growth

spurt. We have no idea, if you are talking about potential toxicity, we have no idea whether it is 18 or puberty. We have no idea.

DR. WALLACH: But the point is being made that we ought to at least pick a point at which skeletal turnover begins to slow down.

DR. REDDI: Turnover of the major growth spurt, at least for clinical parameters, I would say is the closure of the epiphysis.

DR. WALLACH: Well, while they are not all closed at 18, most of your epiphyses are closed at 18.

DR. KLEEREKOPER: As long as you are not hypothyroid.

DR. REDDI: Even in legal matters, I would say that closure of epiphysis or voting age where the person decides for himself what is good for him, even on a legal parameter because now we can decide for our children. At the age of 18, he will decide how much fluoride he wants to have.

DR. SHAPIRO: I think there is no data on that point. I think, if you are talking about a regulation that has some impact, I think you have to be very conservative in that.

DR. WALLACH: I know I mentioned every age

10354 under the sun. I guess I will settle with a
10355 recommendation for 18.
10356 DR. SHAPIRO: How many feel it should be
10357 18?
10358 DR. VIGORITA: I would like to make one
10359 comment. I think I would go along with Dr. Reddi. I
10360 mentioned just briefly in the discussion the
10361 skeletally mature individual. If we are concerned
10362 about teeth and bones are really teeth, I think that
10363 is a safe way of going, skeletally mature individual
10364 and that leaves it subject to the pediatrician of
10365 knowing when they are skeletally mature.
10366 MR. SMALL: But it is not the pediatrician;
10367 it is the water department and the medical society
10368 that is going to have to make that decision.
10369 DR. WALLACH: And this may have to be
10370 defended in court.
10371 DR. KLEEREKOPER: This is an aside and it
10372 may be the wrong question to ask. Joe, if we set an
10373 upper limit and you have a fluoridation program--of
10374 course, there are many places having fluoride
10375 added--would you then add fluoride to a level of two
10376 or what factors would you use to determine the level
10377 of fluoride you would add?
10378 DR. COTRUVO: First of all, fluoridation is

voluntary. So, the community decides whether they are going to fluoridate or not. The amount they add usually is up to about one milligram per liter because that is what is listed as the optimal and that is also economic. When you add two, it costs twice as much money. So, they generally add up to one.

So, a number of two and above--well, number one and above really wouldn't affect that at all.

DR. WALLACH: Two would not conflict with that?

DR. KLEEREKOPER: So, you do not regulate what they put in?

DR. COTRUVO: No, as long as they don't put in more.

DR. SHAPIRO: There were one or two people interested in 18. How many people are interested in nine which is the point at which teeth become--

(There was a show of hands.)

DR. SHAPIRO: And how many have any other recommendations?

DR. MARCUS: I have a recommendation, but I am very worried about breaking in the ages.

DR. KLEEREKOPER: So am I. I would like to make a recommendation that, from all the available

data, we can't state that there is no apparent adverse health effects on a water fluoride level of two parts per million or below. There may be higher levels that you can go without adverse effects on health. That high level may change as a function of age, but we don't have enough data to recommend at this stage that a higher level of two parts per million is safe for all age groups.

DR. SHAPIRO: I think you are being unduly cautious. I think there is data that allows you to make--

DR. KLEEREKOPER: At all age groups?

DR. SHAPIRO: Yes, that is my impression.

DR. KLEEREKOPER: Maybe I am unduly cautious, but--

DR. MARX: Any recommendation we make is for the time-being. If new data comes up tomorrow, then the recommendation can be changed.

DR. SHAPIRO: Let me just expand on that. Is it possible for us to come up with a recommendation that requests specific studies? Is it possible to request reevaluation. The law requires it how frequently?

DR. COTRUVO: Every three years.

DR. SHAPIRO: Every three years. Michael,

10429 the law requires this to go on every three years.
10430 DR. COTRUVO: Not necessarily like this,
10431 but a review every three years.
10432 DR. SHAPIRO: So, is it farfetched for us
10433 to recommend to the EPA that certain studies be
10434 carried out with regard to children?
10435 DR. COTRUVO: No, that is fine, in addition
10436 to your other recommendations.
10437 DR. SHAPIRO: In addition to our other
10438 recommendations.
10439 DR. KLEEREKOPER: Let me ask again a
10440 practical question. In practical terms, what is
10441 harder for the ODW to look at? A global
10442 recommendationof two or a recommendation of two up to
10443 age nine and four beyond that? Which is a more
10444 difficult situation for you to live with in a
10445 practical sense?
10446 DR. COTRUVO: They are both really okay
10447 and, in fact, the latter is good. It is perfectly
10448 fine to put qualifiers on. It is perfectly fine to
10449 say this is the outside limit that we are talking
10450 about that would protect the whole population;
10451 however, in addition to that, there are certain
10452 individuals who are at less risk or at more risk or
10453 there are certain times in their lives where they

will be at risk. It is perfectly fine to do that.

Now, ultimately, we have to pick a number, but all of that additional information helps in the application of that number.

DR. KLEEREKOPER: Let's just say that there are two options that I can personally live, two across the board or two up to age nine and four beyond that.

DR. COTRUVO: Either one of those are okay.

DR. KLEEREKOPER: And easily workable?

DR. COTRUVO: Because, let's suppose, the two across the board is obvious, but the second recommendation, two for a certain age group and four and above for another age group, really says the standard is really two because there is a large number of people who are at that age group; however, if you run into situations where you have segments of people that don't include the high risk group, you may be able to deal with that a little differently. You can be more liberal in the way you apply the thing. That kind of device is helpful.

DR. MARX: In looking at the system, they have to go with the two.

DR. MARCUS: In looking at this graph that was shown on the water content, out of the 5000

communities that were out of compliance, 68 percent of those, if we set a new level now at two, will be in compliance. I am not sure that two or three are substantially different. My own view, I would find three acceptable. That would take care of another 1000 or 940.

If we say a level of three, it would save so much money in terms of what would be necessary to put them into compliance that you could actually get involved in trying to separate age groups or do on-site, point of use. You could be dealing with point of use. You would be dealing with a very small number of communities in terms of cost efficacy which I understand we are not necessarily considering here, but I think a level of three would have a substantial impact.

Extending that to four wouldn't have much more impact. So, it would seem to me that we have already agreed that four is probably not--

DR. COTRUVO: But that is a cost benefit judgment and a risk-benefit judgment. What we would ask you to say is what are the consequences of two, three, four, five.

DR. MARCUS: Four, we all agreed that we are concerned about. The cost benefit issue wouldn't

be substantial anyway. So, I see no pressure to even consider four further. I can see some pressures maybe to consider three.

DR. WALLACH: Three wouldn't protect the individual with renal insufficiency; it would protect the polydipsic individual.

DR. MARX: We are going to have to talk about special cases.

DR. MARCUS: Do you think two would?

DR. WALLACH: I think two is more likely to protect--

DR. MARCUS: But, even if we settled at two, we are still talking about 68 percent of the problem.

DR. KLEEREKOPER: No, less than 68 percent of the problem. You have only those communities on there that are out of compliance.

DR. MARCUS: That is correct. Sixty-eight percent of the compliance problem is taken care of by a level of two.

DR. COTRUVO: Some of those are in compliance because the standard stretches over that range. Many of those 3000 are in compliance.

DR. KLEEREKOPER: Still, the bigger picture of 60,000 communities. There are only 1800 of those

60,000 that have a level currently greater than two parts per million.

Do we really have to have that rider of two to four for other age groups to take in that 1800 communities? That is really the question I am asking myself. That is why maybe I am being over-conservative, but, in the real world, that rider doesn't serve very much purpose. The people are unhappy at having a fluoride level with a primary regulation. They are going to be unhappy no matter what you say.

DR. WALLACH: It seems to me that we have three alternatives, as a practical matter, to decide upon. One is a level of two globally, a level of two up to age nine, or a level up to age 18. Why don't we address these three issues and make a decision.

DR. KLEEREKOPER: I would like to make a recommendation that it is two globally.

DR. SHAPIRO: Okay. There is a recommendation of two globally. Who is in favor of that recommendation?

DR. MARX: Can we have a little discussion? I think that is too restrictive. I think that what we are supposed to be doing is setting limits for toxic effects for the general population. Eight is a level

at which the general population doesn't have problems. I think four gives a limit of safety. I don't see any reason to be more restrictive than four.

DR. SHAPIRO: The comment has been made that we should really talk about adverse rather than adverse health effects because the health effects are really minimal. That is a good point.

DR. ROWE: Do you feel that for children too?

DR. MARX: Right now we are talking about the general population.

DR. SHAPIRO: All right. Any other discussion about two global?

(No response.)

DR. SHAPIRO: All right.

DR. KLEEREKOPER: That includes kids.

DR. MARX: I have another objection to two global. I think, if one considers bringing the level down that low, I think one should not talk in terms of a global absolute number, but something more adjusted for climate where water intake varies as well.

DR. WALLACH: I think that two across the board is very restrictive. It is not really

necessary.

DR. KLEEREKOPER: Excuse me, but what is the current level? When you say this two is restrictive, what is the current level?

DR. COTRUVO: 1.4 to 2.4.

DR. KLEEREKOPER: So how restrictive is two?

DR. SHAPIRO: No, that is optimal without being any trace of dental fluorosis.

DR. KLEEREKOPER: How is that far different from what you have now?

DR. WALLACH: We are being asked to reconsider the issue.

DR. MECKLENBURG: You really start seeing the dental fluorosis that you are concerned about in moderate to severe once you hit four time. Once you hit four times and up, then you have a very good chance of having it. I started to say earlier about asking the wrong question. It bounces around down in that list of one or two percent, three percent through most of these areas, optimum, two times optimum, three times optimum. When you get four times optimum, zoom! You know you are going--

DR. WALLACH: So, that is between .7 and 1.2 is optimal.

10604 DR. SHAPIRO: But we are talking about the
10605 limits, four times that of 2.8 and roughly--
10606 DR. KLEEREKOPER: So, I don't see how a
10607 value of two is overly conservative nor overly
10608 different from what is in there now.
10609 DR. WALLACH: Except that the older
10610 population isn't at risk for dental fluorosis.
10611 DR. MECKLENBURG: Once you are past age
10612 eight, you are not at risk for dental fluorosis.
10613 DR. KLEEREKOPER: If we allow a level of
10614 eight, for example, and I am living near an aluminum
10615 or a phosphate plant, now I can contaminate my water
10616 up to a level of eight and be in compliance with the
10617 ODW and not worry about any effects for the large
10618 population that is going to have this? That is what
10619 you are saying.
10620 DR. SHAPIRO: That is what he is telling us
10621 the states are doing. That is making any of this a
10622 secondary regulation because nobody is going to pay
10623 any attention to it.
10624 MR. SMALL: This is your drinking water not
10625 discharge water.
10626 DR. KLEEREKOPER: Nevertheless, levels go
10627 up in areas surrounding--
10628 DR. SHAPIRO: The experience seems to be in

these communities that they ignore it. Is that fair?

DR. COTRUVO: Oh, way up the line, they don't drink the water. In the lower ends, those that can easily get into compliance do; those that have to build something, don't.

DR. SHAPIRO: We differ in this discussion from the option that voted on levels to protect against dental fluorosis as a secondary regulation. We really differ. We are talking about them as a primary regulation. That is a very different story.

DR. WALLACH: You know, we have kicked this around a lot. I think we all know the issues involved and we are going to disagree with each other. I think we are just going to have to get a consensus.

DR. SHAPIRO: Okay. Do you want to talk about two up to age 18? Is there any further discussion required on that?

DR. MARX: What?

DR. SHAPIRO: Two parts per million standard up to age 18.

DR. MARX: I think what we have to discuss is some of the concepts though. I think the issue on this 18 is that some people think that the potential adverse effect of impaired skeletal maturation is something to be concerned about and that is why they

10654 are recommending age 18.
10655 I think the real issue is how many people
10656 think that the potential adverse effect on skeletal
10657 maturation should be a concern? If it is a concern,
10658 then one would have to go up to age 18. The question
10659 is how many people think it is a concern and how many
10660 don't?
10661 DR. WALLACH: I feel it is a concern for
10662 two reasons: One, the intrinsic benefits of having
10663 normal maturation in general; the second one has to
10664 do with the presence in the skeleton of the
10665 contaminants that reduce greater maturation, reduce
10666 turn-over in general, if they occur.
10667 It will lead to a greater exposure to
10668 skeleton of noxious elements. There is a whole
10669 radio-biologic effort in England at the present time
10670 to be very concerned with the presence of such things
10671 as plutonium and americium in the animal and human
10672 skeleton.
10673 I asked one of the people in that group, a
10674 fellow named Priest. I said why are you worried about
10675 this? Are you really worried that, if somebody drops
10676 a bomb, there will be enough of us around?
10677 He said there is, in fact, present
10678 contamination of our environment with these elements.

I said give me an example and he said smoke detectors and there are radio-biologically active contaminants in our environment that get into our skeletons. They are all long-lived and, if we don't turn-over our skeletons at a reasonable rate and get rid of these things in due course, we have undue and excessive radiation.

DR. REDDI: Although the levels of fluoride which were used by Dr. Shupe in his studies are much higher than what we are discussing now, in his own studies we saw that there was a clear difference between when the fluoride was initiated in the young. They had large amounts.

DR. VIGORITA: I would like to raise a question. I think we should deal in terms of physiology and not age limits per se because the concept I think Dr. Reddi referred to was that the epiphysis be closed and that the patient be skeletally mature. That isn't necessarily at age 18.

So, to be physiologic, since we are a group of scientists, I think we should use those terms and not numbers. Now, Dr. Mecklenburg referred to nine as dental maturity in most people. I accept that because I don't know, but in a skeleton it varies.

DR. SHAPIRO: Let me make another

recommendation to you. That you pick a number that allows you to have some impact at this point on the population you think may be most at risk, although you don't know, and do that with the caveat that it be studied and that at the time of the next review this be one of the major considerations in looking at that number again, insofar as it applies to children.

My own feeling would be that I would go to nine since the best information you have, at least as far as teeth are concerned, but I would make it very, very clear that we know nothing about this issue and maybe it should be 14, maybe it should be 18. Is there going to be any global impact of our postponing this issue for three years or so and the answer is that I don't think there is.

So, rather than provoke something in an area that we really have no information on, I would be a little conservative there, try to protect the relatively young in terms of a time when I know bone turn-over is particularly high and I know it is going to affect the teeth at that point which may have something to do or may not with what is happening with bone. I don't know. I can't say because I don't have the information, but make it is very clear that that is something I have to look at again.

DR. MARX: We know already that there are lots of communities in Texas and other parts of the United States where people have had relatively high fluoride consumptions throughout their bone growth and into maturity and the most that has been observed in those communities so far is a little bit of osteosclerosis.

DR. SHAPIRO: But you really don't know that. Maybe they should all be five or six. Maybe they had Heberden's nodes when they are 40 years old.

MR. HANSON: Maybe I can add something to that. In Texas, which took a stand on fluoride and said anything higher than five you had to do something else, you weren't allowed to drink that water, and really you aren't seeing any exposure above five milligrams per liter.

DR. MARX: Not anymore, but at one time they did.

MR. SMALL: And they did intense medical examinations.

DR. HUGHES: I would agree with you, except that I would take the conservative and pick the age 18 or 20, some number, when in most people the epiphysis is closed until that question can be answered.

Is there a community in which that question can be looked at?

DR. MARCUS: I think the Pima Indians are a good one because they are under constant scrutiny anyway and they live in a high fluoride area and they are known in the earlier part of the century to have a high prevalence of dental fluorosis. My recollection of the Pima data from Public Health Service is that, in fact, they are a relatively short statured group of people.

DR. WALLACH: And they all get diabetes.

DR. MARCUS: There are many confounding things.

DR. SHAPIRO: Do they have a high incidence of dental fluorosis?

DR. MECKLENBURG: I am not aware that they have a high incidence.

DR. MARCUS: There is a book from the PHS that was published around ten years ago, a nice hard-bound book that I got when I was here at NIH. It was sort of a history of fluoridation.

MR. SMALL: Frank McClure's.

DR. MARCUS: That is right and he describes these country dentists that went around on mule-back looking in mouths. He said in that book that there

was a high prevalence among the Pima.

DR. KLEEREKOPER: Certainly, nobody would have any question globally about two. I don't think anybody would have any concern about two up to age nine, whether we are allowed to talk about dental fluorosis or otherwise. Is that reasonable?

DR. MARX: I think we can have a range. I don't think we have to set an absolute limit because I think water intake varies, dependingon climate.

DR. SHAPIRO: Yes, it depends on other factors.

DR. MARCUS: Well, we are going to have to learn to set that range. I am not sure what is the fudge factor.

DR. KLEEREKOPER: I think everybody is in agreement including the dental aspects that, after age nine, four is without harm, both observed or even potential.

DR. HUGHES: No, I am not in agreement with that. I am not sure that a ten year old is going to have no harm from four. I am not sure what it is going to do to their bone turn-over rate and to the concerns that have been expressed here.

I think that that data can probably be gotten by looking at growth curves in children who

were examined in Bartlett, Texas and in North Dakota. I think that this could be gotten by somebody with a lot of energy and a lot of time to get at this data. I am sure it is available in bits and pieces.

DR. ROWE: At bone age of nine, you have about--I am trying to remember the table--about 60 to 70 percent of your total bone growth. So, you still have a lot of bone growth left to go at bone age nine.

DR. SHAPIRO: All right. How many people feel that 18, picking that one out of the air, is a more appropriate age at which to run the two parts per million up to than nine?

(There was a show of hands.)

DR. SHAPIRO: Four, okay.

DR. KLEEREKOPER: I can certainly live with that.

DR. SPENCER: I believe a study should be done as suggested and not with Indians, but in areas like in Texas and in North Dakota and to look at the growth curves. This is very important. This can be done and would not take such a long time.

DR. SHAPIRO: How many feel that they would limit the two parts by primary regulation up to age nine?

(There was a show of hands.)

DR. WALLACH: I will vote for 18.

DR. SHAPIRO: That made it five. How many for nine? Who isn't voting? Okay. Eight. The majority seems to feel that nine would be appropriate at the moment.

DR. CARLOS: Could we pin down the point Steve makes? You talked about two times optimum. It acknowledges that it depends on consumption, not on presence in the water supply. Furthermore, all recent fluorosis data are reported in terms of multiples.

DR. SHAPIRO: So, you are suggesting two is a multiple?

DR. CARLOS: Rather than two milligrams per liter. Also, it allows a little enabling of the optimum should that become necessary in the future.

DR. KLEEREKOPER: I am not sure I follow you.

DR. SHAPIRO: You are saying that two is the absolute upper limit?

DR. MECKLENBURG: No, no. In dental terms, if you were talking about two times optimal, because we know a range, depending upon temperature, would be .8 or 1.2. Generally, we are always talking in terms of times the optimum. Instead of saying two parts per

million, it is more sophisticated--

DR. KLEEREKOPER: That is daily ingestion of fluoride in drinking water.

DR. WALLACH: You are saying four times optimal.

DR. MECKLENBURG: You are saying two times optimal. It could be as low as 1.3.

DR. CARLOS: Not ingestion; presence.

DR. SHAPIRO: What we are saying is that we

DR. MARX: What we are saying is that we want to enforce the current regulation that is the primary regulation.

DR. SHAPIRO: You say enforce the current regulation of .7 to 1.2 up to age nine, two times that, up to age nine and then in comparable terms for adults over 50. You are talking two times the level of an upper limit of two.

DR. KLEEREKOPER: Why are we not saying four times?

DR. SHAPIRO: Four times the optimal.

DR. CARLOS: It doesn't really matter because we don't know what the sensitive level is there.

DR. MECKLENBURG: Once you establish that, then the next thing you do is you are in that guarded

range until you get to a point where you see things that are an adverse health effect. Then, you are either talking about ten milligrams per day or 20 milligrams a day or something like that, depending on what studies you cite. Everything else is in doubt.

DR. KLEEREKOPER: Say that again, Bob?

DR. MECKLENBURG: Isn't your range of caution then above this two times optimum up to the point where you actually have evidence?

DR. KLEEREKOPER: Four times optimum up to--you want us to give--

DR. MECKLENBURG: Your evidence of health effect begins at ten or eight to ten or 20 to 80, depending on which studies you are citing. There is your health effects.

DR. MARX: So, what is the question?

DR. KLEEREKOPER: What margin of safety is appropriate?

DR. MECKLENBURG: Well, the margin of safety is essentially above what you just agreed upon to whatever point you have evidence.

DR. MARCUS: You want us to establish the grey zone?

DR. MECKLENBURG: That is what you are doing by establishing those two limits. You have a

grey zone.

DR. KLEEREKOPER: Four to ten.

DR. SHAPIRO: Well, ten times optimal could clearly--I think everyone would agree--be a hazard.

DR. MECKLENBURG: Ten times the optimal or ten milligrams per liter?

DR. WALLACH: Ten times optimal. That is what we treat osteoporosis with. I have to define the margin of safety, not in terms of dose alone, but in terms of age at which ingestion begins at a given level. I don't think that you--I mean, as an example, older patients are being given ten times optimal now year in and year out and no one brings us adverse effects. But I don't think I would then try this in a five year old, a nine year old or even a 12 year old.

DR. KLEEREKOPER: Or even a healthy person age 50.

MR. SMALL: I was going to ask you what would be the effect of that regimen on a normal healthy person?

DR. KLEEREKOPER: We don't know. We can't talk to that.

DR. SHAPIRO: What you are going at is that I think we would say above eight parts per million is the area in which we cannot protect against an

adverse effect, although realize that it may happen lower than that, but certainly at that level that seems to be a threshhold in terms of the experience in literature.

DR. KLEEREKOPER: Would you change that for children?

DR. SHAPIRO: No, I am just talking about adults right now.

DR. KLEEREKOPER: I understand that, but, if you are going to have two levels--

DR. WALLACH: Would such a regulation put physicians using fluoride therapeutically at higher levels at risk for legal suit?

DR. KLEEREKOPER: There is a big difference between using fluoride for therapy and using a substance in the general community, an incredible difference.

DR. WALLACH: Well, we know that, but the question is what would a jury say subjected to a legal opinion.

DR. SHAPIRO: Is it necessary for us to specify the level at which we feel an adverse effect would occur, the level at which the public should be protected against? Is that necessary for us to do?

We have already established limits --

DR. WALLACH: I think we have already set the limits.

DR. COTRUVO: I will just read that section again.

DR. SHAPIRO: Margin of safety.

DR. COTRUVO: "First, known adverse health effects are compiled; second, whether any adverse effects can reasonably be anticipated, although not proven." And then, considering factors of synergism, exposure, et cetera, et cetera, et cetera.

So, if you can say firmly that the effect level for the general population is X and then, in order to extrapolate that, to take into consideration the possibility that there are higher risk individuals in the population, the safety factor should be Y. Then that leads to the final recommended number for the general population.

DR. SHAPIRO: Well, you don't pull a number out of the air, say six times the optimal level. Four times the optimal level is what we would recommend for adults and six times the optimal level might bring you into an area where you--

DR. WALLACH: Why don't we say anything greater than four because we are setting that level for all other individuals, except under age nine.

DR. SHAPIRO: We could cut it that close. I just don't know where the truth is. That is what I don't know.

DR. CARLOS: When you talk about dose, it would probably make more sense to use milligrams per liter because "optimal" has no meaning except in the case of dental fluorosis.

DR. MARX: But the multiplication of optimal is adjusted for climate and that is why it would be useful.

DR. CARLOS: Yes, but it only pertains to dental.

DR. COTRUVO: I think one way around it--first of all, there are uncertainties on determining just how much water consumption--you know, what the average water consumption is in a particular community.

Now, I am told that diabetics drinks two or three or four times as much water as the average person. They are not taken into consideration here. That is why the uncertainty factor.

So, I would say it is simpler to make your recommendation based on daily dose and then say in the application of this it can be considered, the climate, et cetera, et cetera, can be considered in

the application of this.

DR. SHAPIRO: Were that the case, we would talk about the four parts per million, four milligrams per liter and the two and phrase it as you say which I think is very helpful, that there is an optimal.

DR. MARX: I think we have a problem with the lower age range because there we can't say that we want to have the margin of safety of, say, two to four-fold because then we get into the range in which you have therapeutic effects of fluoride for prophylaxis and dental care. If we were just handling this as an environmental contaminant, we could say we begin to see fluorosis at two parts per million. So, we want a safety factor of four. We recommend that it be kept below a half a part per million.

Clearly, we have to make an allowance there. We can't just talk about safety.

DR. MECKLENBURG: This is inconsistent with the Surgeon General because, between that two and four times optimum, we do have a 50 percent increase in caries protection.

DR. KLEEREKOPER: Do we have to define "optimum"?

DR. WALLACH: I don't think we are being asked to give a figure as a multiple for a safety factor as in radiation doses. I don't think we are being asked to do that. I think we can define it in an absolute unit, milligrams per day or parts per million in drinking water and not say it has to be ten times this or five times that.

DR. KLEEREKOPER: Could you just clarify what "optimum" means to you?

DR. MECKLENBURG: "Optimum" means the protection against caries that doesn't really run any risk of showing the slightest amount of fluorosis.

DR. KLEEREKOPER: So, our recommendation for children is twice the optimum.

DR. MECKLENBURG: A lay person generally wouldn't take a lower range.

DR. KLEEREKOPER: And those optimum levels have been determined individually for each water supplier in the United States based on temperature and climate.

DR. MECKLENBURG: Right.

DR. SHAPIRO: And at twice that optimal level, you are running morbidity on the order of a couple percent.

DR. MECKLENBURG: Yes, you are just

beginning to find some clinical fluorosis.

DR. KLEEREKOPER: So, the margin of safety for—

DR. MECKLENBURG: Four times is where you would begin to see it.

DR. KLEEREKOPER: So, for children, it would be four times that and you still allow that you might have 15 percent, you are saying?

DR. MECKLENBURG: No. I think it is the other way around. I think optimal is one time. Two times is the standard and that is where you begin to see some evidence. Four times, you run a reasonably strong risk of starting to get into brown stains.

DR. KLEEREKOPER: So, tell me again what the margin of safety should be for a child up to age nine?

DR. MECKLENBURG: To avoid any reasonable chance of fluorosis at all, two times.

DR. SHAPIRO: Why can't we say we see that, in terms of the available information, as the upper limit and we don't necessarily think there should be a margin of safety because we don't know what happens after that point.

DR. COTRUVO: I think we are interpreting margin of safety differently. To our mind, a margin

of safety is the uncertainty range which one adds on in the lower direction to insure against the effect occurring. I mean, you have identified the effect in an animal population. You add a margin of safety and say we are going to one-half that or one-tenth that.

DR. HUGHES: We haven't considered renal failure, for example. That would be something to consider.

DR. SHAPIRO: I would like to consider that after lunch. I just want to end this issue and we can talk about special populations after lunch.

Is it necessary to consider a safety factor? Can we recommend it as a primary level that in children up to age nine go no higher than twice the current recommended level of .7 to 1.2, not talking about total intake, and for adults four times the optimal level of .7 to 1.2. That is, everybody above the age of nine has primary regulations. This is because of the uncertainties of exceeding those levels.

DR. COTRUVO: Joe is suggesting that we give an absolute number rather than four times the range.

DR. KLEEREKOPER: For adults?

DR. COTRUVO: For all of them.

DR. SHAPIRO: See, the thing you are getting into is that you are not improving your accuracy any at that point. You are not making the statement any firmer. You are just coming up with a number and you take some prerogative from the local area, I think, in dealing with it.

DR. COTRUVO: I think it would work the other way. I think, if there were a number that was based on daily dose--

DR. SHAPIRO: All right. That number of 2.4--

DR. COTRUVO: Well, whatever the number is.

DR. SHAPIRO: 2.4 as a maximum up to age nine, right? And then it would go as high as 4.8 up to a maximum for anyone above the age of nine.

DR. COTRUVO: For adults. Okay, but that is a very fixed range.

DR. KLEEREKOPER: If you say 2.4 parts per million as a maximum allowable level, that could occur in a very hot area with a high level of fluid intake. Then you have really exceeded what you wanted to do.

DR. WALLACH: That is what I just said. That is why I wanted to stay away from the number.

DR. MARX: What Joe asked us to do is give

an absolute number and put in a statement that it should be adjusted depending on local conditions.

DR. SHAPIRO: Then you can say that absolute number is one.

MR. SMALL: Why do we want to lose accuracy?

DR. KLEEREKOPER: What I was saying is you give an absolute number and then we said the number is twice currently 1.2. So that is 2.4 and you could have communities where there is very high temperature, high humidity and a high fluoride content with a high water consumption getting much more fluoride than you want. We are concerned about total daily fluoride consumption.

DR. SHAPIRO: Mike, they have presumably calculated that optimal number.

DR. MECKLENBURG: That table has been accepted for 20 years.

DR. SHAPIRO: Everybody knows that. If you say twice that, then that is the number, but don't fix it for everyone.

DR. MARX: If we are going to set the age zero to nine based on the issue of dental fluorosis, I don't see any reason why we shouldn't take the recommendations of the dental panel. What is wrong

with that?

DR. SHAPIRO: That is what we are doing.

DR. MARX: We are discussing whether we should give an absolute.

DR. WALLACH: There is a well-determined standard in well-defined terms now. Why don't we just leave it the way it is and say we are sticking with the current standard up to age nine and we are willing to see that standard doubled after that age and just not change any of the terminology. Every time you change it you confuse people.

DR. MECKLENBURG: I would like, if you could, review the statement that we have already have Dr. Koop sign on page one and two and see if you can live with that from your knowledge and what you have heard medically where he recommends an optimal, where he doesn't recommend over two times optimum and where he does say that there is no evidence of adverse health effects in drinking water supplies and then work out the health effects after lunch.

DR. SHAPIRO: We are saying that up to age nine.

DR. MARX: No, we are not. The panel is saying the dental effects are adverse health effects. The panel right now is saying this should be an

This statement refers to the 1982 S.G. ad hoc comm on dental fluorosis (Albertini, et al) and the NOWAC (Nat'l. Drinking Water advisory Council to the EPA) The NOWA had several meetings after 1982.

primary regulation.

DR. SHAPIRO: As far as I can see, we are saying something very different from what everyone else has said. In fact, I think we are taking a somewhat more stringent approach to this.

DR. MARCUS: Dr. Koop says he encourages communities. That doesn't sound like primary regulation.

DR. MARX: Because the Dental Panel said is should not be a primary regulation.

DR. MECKLENBURG: Not on the basis of dental. Now, if you have evidence in medical--so far, what I thought you were doing was not trying to make a dental judgment. I thought you were making a medical judgment which was fairly consistent with the dental judgment.

DR. SHAPIRO: We are making a medical judgment. The medical judgment is that twice the optimum of .7 to 1.2 for children up to the age of nine and four times the optimum for individuals above the age of nine as primary regulation and don't go to South Carolina.

DR. MARCUS: They will tar and feather you.

DR. SHAPIRO: That is right. Is there any question about that?

Crippling bone fluorosis

MR. SMALL: Would you review up to age nine, twice the optimal is guarding against some adverse health effects? Is that potential or what?

DR. SHAPIRO: Is guarding against an adverse effect of fluoride up to nine.

MR. SMALL: The law says to be a regulation it has to be against an adverse health effect, doesn't it, Jim?

DR. MARX: The adverse effect that we are concerned with is crippling bone fluorosis.

MR. SMALL: We can't change the law, can we?

DR. MARX: That is what we voted on. I thought we voted on that. I think that is what the vote was that we considered it an adverse health effect. But I think there is some disagreement on the panel. Some people think that the childhood level should be brought up to 18. That is not unanimous.

DR. MARCUS: That is correct.

MR. SMALL: What is the adverse health effect?

DR. MARCUS: Well, there were several under consideration, but I think the most powerful ones were Dr. Wallach's consideration of skeletal maturation and retention of potential toxicity from

11229 the environment.

11230 DR. MARX: That is potential. The adverse
11231 effect is crippling fluorosis and arthralgia. Those
11232 are the things we agreed on.
11233 DR. MARCUS: Maybe we agreed for different
11234 reasons. My vote for that was based on Dr. Wallach's.
11235 Yours may have been based on others, but we all agree
11236 that we voted on that for adverse health reasons.
11237 DR. SHAPIRO: The fact of the matter is
11238 that you included dental disease in your
11239 consideration.
11240 DR. WALLACH: It is also the period of
11241 greatest skeletal turn-over and maturation.
11242 DR. SHAPIRO: John, to answer your
11243 question, the panel understands that there are too
11244 many uncertainties here and, from the available data
11245 and understanding the bone turn-over is not only more
11246 rapid, but that the younger individual is perhaps
11247 more sensitive to the effects of fluoride, it says,
11248 with this uncertainty, we cannot go up to the level
11249 in the adult where we are reasonably certain that, in
11250 an adult bone with slower turn-over, there could be
11251 an adverse effect.
11252 So, in a sense, you are exerting a margin
11253 of safety for the child.

They are arguing as if there were 2 different water supplies — one for children 0-9 and another for adults. They should be arguing done

DR. MARX: I don't agree with that.

DR. MARCUS: Well, we voted on this.

DR. MARX: No, we voted on the margin, but the reason--

DR. MARCUS: So we had different reasons?

DR. MARX: My reason for voting on the low margin for age zero to nine is because I accept the cosmetic effects of dental fluorosis as an adverse health effect. My reason for taking nine as the cut-off is because I don't see the skeletal maturation thing as a recognized adverse effect.

The panel was clearly divided on that issue. I think there were five people who were not concerned about the levels we are talking about causing adverse effects on the skeleton and there were three people who thought that that was a problem.

DR. COTRUVO: That may fit into the sentence which says "must decide whether the effects may be reasonably anticipated, even though not proven to occur."

DR. MARCUS: Also, I think it is fairly close to unanimous that we all agreed that dental fluorosis problem is, in fact, has medical ramifications. Almost everybody agreed on that. Not

knowing where bone disease begins at any age, what you are saying is that if there is something going on in the teeth, then the likelihood is that there is something going on in the bone. You don't know that it is there; you don't know that it is not there.

DR. MARX: Make a proposal so that we can vote on it.

DR. SHAPIRO: Let's finalize this by asking for a vote that, up to age nine, we accept twice the current recommended levels of .7 to 1.2 and that, above that age, we accept four times the recommended level as preventing against adverse effects.

Is there any further discussion?

(No response.)

DR. SHAPIRO: All right. All those in favor?

(There was a show of hands.)

DR. SHAPIRO: All those opposed?

(There was a show of hands.)

DR. SHAPIRO: Two are opposed. Now, let's have lunch. It is twenty after. I would like to talk some more about special groups and then extent to which we can include in our proposal to the PHS and the EPA a very strong interest in expanding the amount of data that is available.

(Whereupon, the conference adjourned for lunch, to reconvene at 1:45 p.m..)

* * * AFTERNOON SESSION * * *

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1:45 p.m.

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DR. SHAPIRO: The process, as Joe explains to me, if we develop a paper--the transcript will be available in eight days.

DR. KLEEREKOPER: An edited transcript.

DR. SHAPIRO: Yes, sort of. It depends on how much time I have, but I will certainly distribute that to anyone or all. It takes a few days to make sufficient copies. I guess we would have to develop a report of this to Bob. Is that right?

DR. MECKLENBURG: Yes.

DR. SHAPIRO: To relay to the Surgeon General who would then--

DR. MECKLENBURG: The basic report will be in the form of a letter to the Environmental Protection Agency.

DR. SHAPIRO: Hopefully, with his blessing. What I will do is, after we get something together, I will circulate it to all of you and ask that you make any comments you feel appropriate and then we will

incorporate them. If it looks like there is anything wildly different, we will send it out again. So, when it finally goes to the Surgeon General, everyone has seen it and everyone has had a chance to make any corrections or modifications.

I thought perhaps we could spend a minute in any details that you would like to discuss, but one I would like to bring up is how one includes in a way likely to be effective a request to do certain studies, to have EPA take the lead as an agency, for example, in looking at some of these concerns that we have, particularly in children or in any others at the moment.

One that was discussed was the renal patient who is at risk, but I am not sure of the dimensions of that problem. But in children I think we could look at things that might be fairly easy to get ahold of like age-related height, weight, the EKG status and whatever else seems necessary.

DR. KLEEREKOPER: Perhaps the best way to establish the data base would be to go specifically to those communities you identified that have had generation exposure to high endemic fluoride levels and to document what we can in that group and perhaps try to find a comparable demographic group in a

non-fluoride area. But rather than take a global look at what potential effects are on kids in Chicago or Detroit or Palo Alto, I think it would be best to focus on those that we know for generations have had high exposure.

DR. SHAPIRO: Clearly, I think you would do it in those areas where there was natural fluoridation and that is within the EPA's mandate or PHS, for that matter.

DR. MARCUS: It would be of interest to take some modern techniques down to those areas, such as dual photon absorptiometry. You can get a determination of the incidence of bone mineral density in both the vertebral spine and appendicular skeleton and get some other information on general health.

DR. SHAPIRO: What other special populations should we be considering?

DR. KLEEREKOPER: What other studies should be looked at?

DR. SHAPIRO: What are we overlooking?

DR. ROWE: Plutonium levels in the bone, these toxic things.

DR. MARCUS: Certainly lead.

DR. ROWE: We can make those kinds of

measures now.

DR. KLEEREKOPER: Can you measure total body fluoride, calcium?

DR. SHAPIRO: I am not sure how you do that. I would assume you would use something like neutron activation or something.

MR. SMALL: How do you look at children's cell maturation? Is this by hand x-ray or by some other method?

DR. KLEEREKOPER: X-rays would be inappropriate.

MR. SMALL: Epidemiologically or clinically?

DR. SHAPIRO: You could look at wrist bones and measure maturation.

MR. SMALL: Would this involve parental consent and all that good stuff?

DR. SHAPIRO: You could get it. Usually we get it, I think.

DR. SHUPE: I was going to say one thing we observed clinically in a bunch of animals in the field was that, on a given level of intake that we were measuring and knew they were taking in, we anticipated a number three tooth, but these animals that were on high molybdenum--there were some areas

out there with high molybdenum--you would usually find a number four tooth with a little more deposition of fluoride in the bone. Those were some animals clinically in an area where they had elevated levels of molybdenum in the vegetation.

DR. MARCUS: Would it be useful to trap small animals in various locales and examine their teeth?

DR. SHUPE: Some of the animals you are thinking of, their teeth erupt continuously. They are constantly erupting. They are different than the herbivores and the horses in that.

Now, there was a fellow who has since passed away that did quite a bit of trapping of animals around the country and I don't know how meaningful this information was, but anyway these animals do tell you a lot like on lead poisoning and a lot of these other different things.

DR. CHANIAN: Talking about well water, it is not clear how relevant some of this was.

DR. KLEEREKOPER: The dentists have done a lot of field work in several communities, looking and grading teeth. In any of those studies, did anybody look at anything else and could one identify from the work that has been done the children who have got

Stage III dental fluorosis and those with Stage IV or were just numbers looked at?

DR. CARLOS: Well, the various periods of dental fluorosis, of course, were, but do you mean other medical concerns?

DR. KLEEREKOPER: Did anybody ask any other questions of the kids? Thousands of kids have been studied, have they not, in epidemiologic studies.

DR. CARLOS: Well, there have only been a few recently. These are listed in one of the documents. So, it would be a few thousand children in Illinois and Texas mostly and Carolina.

DR. KLEEREKOPER: Were there any medical questionnaires?

DR. CARLOS: Not that I know of.

DR. KLEEREKOPER: So it was just "show me your teeth"? Is that what it was?

DR. CARLOS: As far as I know.

MR. SMALL: There question was asked about whether they had used fluoride supplements or whether they took vitamins with fluoride in their early days and that sort of thing.

DR. KLEEREKOPER: And those children who were identified in the Illinois study as having Stage III or IV fluorosis are they identifiable?

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DR. CARLOS: Yes, the children are identifiable. Yes, they could be studied.

DR. SHAPIRO: Do you have rosters of those children?

DR. CARLOS: Yes.

DR. KLEEREKOPER: That may be something to look at.

DR. CARLOS: There are very few in number, of course.

DR. KELLER: The National Toxicology Program currently has sodium FLUORIDE chloride tests, chronic toxicity study phase. They are due to be sacrificed in December of this year. I just checked on this yesterday. This is rats. It may be mice.

DR. MARCUS: I was afraid you meant the kids in Illinois.

DR. SHAPIRO: Were there different feeding levels?

DR. KELLER: They have some protocols for getting the "no effect" and "subtoxic effect."

DR. KLEEREKOPER: Jim has done a superb animal toxicology study and you know what it does to animals.

DR. SHAPIRO: These were cancer.

DR. KELLER: That is one of the end points.

of course, but I am not certain that it is the only one in this case.

MR. SMALL: Mutagenesis also.

DR. SPENCER: I would like to ask, in those children who develop dental fluorosis and only a certain percentage in high fluoride areas have developed it, is there anything known about their nutritional status and about their intake of calcium, phosphorus and magnesium?

DR. CARLOS: We don't have that, no.

DR. KLEEREKOPER: That is one of the studies we could recommend they do.

DR. SHAPIRO: Well, are there any other issues that we should consider? Joe, are there things that we ought to do that we haven't done yet?

DR. COTRUVO: No, I don't think so.

DR. SMITH: Well, you mentioned the renal group and many causes of polydipsea ought to be looked at.

DR. KLEEREKOPER: Some of the renal work has been looked at. Patients with renal disease are at risk for developing bone disease. People have done studies on the effect of fluoride in the water to bone disease that patients with renal failure get. Essentially, they came out as negative studies. There

were no ill effects from adding to the water.

The other question, whether fluoride causes renal disease, is not known.

DR. SHAPIRO: I am talking about the progressive storage of fluoride in patients with renal disease in high fluoride areas.

MR. SMALL: Well, in dealing with total renal failure and dialysis, there have been recommendations made by the national group that the water be completely de-ionized for dialysis and that a unit be included for this purpose, reverse osmosis, to complete de-ionization.

In fact, I know only one, Maryland, has since issued a regulation legally requiring that procedure in dialysis. That is becoming a little moot as far as fluoride. In extracting all of the other elements, the fluoride goes out, 96 or 97 percent.

DR. COTRUVO: The limit is one-tenth a milligram.

MR. SMALL: .2

DR. COTRUVO: Two-tenths.

DR. KLEEREKOPER: But their recommendation was not based on the adverse effects of fluoride, but rather on the other elements.

MR. SMALL: There was a question about

fluoride, but there were other things thought more important.

DR. MARCUS: In Maryland, they had that accident. That is probably what drove that.

MR. SMALL: Aluminum was the first concern. → see insert

DR. HUGHES: But there are no recommendations standing with regard to renal failure short of diaylsis patients?

MR. SMALL: No, not that I know of.

DR. MARCUS: Well, I expressed some concern yesterday about older people who have diminishing GFR, but I am satisfied as of today that concerns about the added fluoride burden that that might potentially have in older people is really trivial.

DR. ROWE: As long as you keep it at four.

DR. MARCUS: Yes.

DR. ROWE: In people who have polydypsia, diabetics maybe, certainly people with DI, diabetes insipidus, again there is a very small number, though they do exist. Once in a while, you will see a whole family that has it and they don't realize it and they are drinking ten liters a day of water.

DR. MARX: If they aren't diagnosed, you aren't going to be able to do anything about it.

DR. ROWE: They exist, but it is very

small.

DR. KLEEREKOPER: There is one group of patients that I recommend and I guess most people recommend a very high fluid intake is the kidney stone population which probably has a high prevalence in the community with diabetes insipidus. It may be high in diabetes mellitus, but that is the group that maybe worth looking at.

To my knowledge, all the recommendations to increase fluid intake are associated with a decrease in the incidence of nephrophthisis and I can't imagine it is going to have any adverse effect.

DR. WALLACH: Right, except for the hyperoxyluric patients, it is unusual for children to form kidney stones. Most kidney stone formers are adults.

DR. KLEEREKOPER: We are talking about the potential harmful effects from increasing fluid consumption.

DR. WALLACH: Yes, but the point is that these are adults with dangers of high fluoride intake are smaller to begin with.

DR. SHAPIRO: Well, if the adult is living in a community where fluoride level in the water is allowed to be up around four, I don't think we would

want to see them taking four liters of fluid.

DR. KLEEREKOPER: That is a potential group at risk.

DR. SHAPIRO: Well, if there are no other matters to discuss, I think we can adjourn the meeting, certainly with my thanks for your coming here and wrestling with this very, very difficult problem.

It may be that we have helped the EPA. It may be that we will have 16 states down on our necks. Not only are we not throwing out what they wanted, but we are telling them that they have to go back and make some special arrangement for children as a matter of regulation which they didn't anticipate doing. That should set up a bit of a howl.

What is your process. When should we start to get some feedback? As soon as the Surgeon General accepts what we have said? What if he doesn't accept it? Do we have to convene again?

DR. MECKLENBURG: Probably.

DR. KLEEREKOPER: How likely is that, Bob?

DR. ROWE: He is a surgeon.

DR. MECKLENBURG: I think he will very serious consider what this committee has said. You really brought in the best information available. It

would have to be extremely seriously considered.

DR. SHAPIRO: As a pediatrician, I don't think you could argue with tightening up the rules to protect children. I can't imagine a political question that would compromise our recommendation.

DR. MARX: What are you planning to say to address this question that some people have expressed a concern about skeletal maturation?

DR. SHAPIRO: What I will do is report the fact that it was not unanimous within the committee, that there would be some recommendation framed in the letter as regards to the need for additional study in populations at risk so that there is a better answer three years hence when this might again be up for consideration.

DR. MARX: I have a question that, before this is in final form, that you circulate a draft.

DR. SHAPIRO: Oh, I said that earlier.

DR. WALLACH: You will put cardiovascular and skeletal turn-over studies in this?

DR. SHAPIRO: Yes, I think there are some things we simply don't know. I think having some idea of how these things are accepted from a regulatory standpoint, the recommendation will stand alone. We can accomplish these other things. That is something

else, but you are really going in with a recommendation that is not necessarily linked to have that information.

DR. MARCUS: I would like to establish another point which I think is important in termsof how somebody who might be not on this committee would read the report because it would seem to me that there would be two options, depending on how the report were written.

One would be that the committee was very concerned about potential hazards associated with fluoride and we singled out a group of individuals, that is children below the age of nine, for special, additional protection and I can see that somebody who might be on the outside fluoridation lobby would use that as food for his fodder.

On the other hand, another interpretation could be, depending on how it was written, that this committee was by and large unimpressed by real dangers associated with fluoride. We are being fairly cautious with children, but we are actually relaxing our concerns about everybody above the age of nine or people whose teeth have already erupted.

My impression from talking with most of the people around the room is that the second case is a

more accurate representation of the views of this committee and I think it would be a very good idea to formulate whatever the conclusions are in a way that could not be used like what happened in that newspaper article.

DR. KLEEREKOPER: One way to do that would be to say what a lot of us have said, that we regard dental fluorosis in the Stage III level as an adverse health effect and that is what the regulation has been aimed to prevent. That is really what we have done.

DR. WALLACH: Not all of us are saying that age nine is a good cut-off point.

DR. MARCUS: I understand that.

DR. SHAPIRO: It is easier to equivocate around that than it is with what the committee that framed these options before us did. They said they couldn't choose between four and eight. I think we have made a better decision.

DR. CARLOS: I think it might be well worth considering how you phrase the recommendation, the rationale for the recommendation very carefully in terms of potential adverse effect.

The reason is that we have on record the Surgeon General, the American Medical Association,

the American Dental Association all saying that there is no adverse health effect.

I think, in the case of dental fluorosis, we can't find any data to the contrary; however, I certainly accept and I think most people do that there may well be and we just haven't found it yet and that would be true of the other things you are speaking of as well. It is potential.

DR. MARCUS: I don't think that is the sense of the committee. I think that the sense of the committee is that the cosmetic effect represents an adverse health effect, that this is psychologically damaging. People walk around covering their mouths.

DR. SHAPIRO: I think the Surgeon General left a big loophole, frankly, when he raised this cosmetic issue. I think he, in effect, was saying there is still some room for doubt as to whether what we are saying is the best really that can be said.

DR. CARLOS: There is more study needed in the matter.

DR. SHAPIRO: That is right and I would seize on that, expressing the concern of the committee that we don't have all the answers.

DR. CARLOS: The concentration of research has really been around optimal levels.

DR. COTRUVO: The previous Surgeon General was even stronger on that subject.

DR. SHAPIRO: On what subject?

DR. COTRUVO: Of the psychological effects resulting from cosmetic.

DR. SHAPIRO: Did you write anything on that?

DR. COTRUVO: Yes.

DR. SHAPIRO: Could you get that to us so we could take a look at it?

DR. COTRUVO: Yes.

DR. CARLOS: It is all very well to say that you think that may be the case and I am not arguing that, but we have no data, not a shred. What I am concerned with is that we will come into conflict with statements that are already in the public record without any data on which to base the conflict.

I think we can get around the whole thing by saying there is substantial belief that there are potential health effects, psychological, structural, functional, whatever and this may turn out to be the case.

DR. SHAPIRO: I think everyone would agree.

DR. MARCUS: The word "potential" is often

interpreted by lay audiences to mean "likely" or "probably."

MR. SMALL: That is why I was saying it is too strong.

DR. KLEEREKOPER: It is still less then what I feel is going to be potentially the real adverse effect.

MR. SMALL: I think there is a skeletal maturation problem. "Potential" is a strong word for that.

DR. KLEEREKOPER: But the skeletal maturation thing is really a gut reaction. There is really no evidence to support that or substantiate it, I don't think.

MR. SMALL: You can call it potential, but there is no evidence.

DR. MARX: This is a term that the EPA has defined. They are asking what are the potential effects. They have defined the term. So, we are left with their terminology.

DR. COTRUVO: No, it is defined in the law.

DR. MARX: Right, it is defined in the regulation.

DR. SHAPIRO: What is the largest city you would fine--is it Bartlett or Lubbock or some place

where—

MR. HANSON: High levels?

DR. SHAPIRO: Yes, very high levels where you could really start to look in a prospective manner at bones from a children's hospital.

MR. HANSON: Myrtle Beach, South Carolina.

DR. KLEEREKOPER: I will take three months sabbatical and do that.

DR. MARX: If we put in the word "potential", does that take this out of the possibility of primary regulation? A primary regulation can be made for the potential?

MR. SMALL: Potential adverse effect is sufficient for a primary regulation.

DR. SHAPIRO: "The Administrator must decide whether any adverse effects can be reasonably anticipated even though not proved to exist."

Okay. If there are no other questions. Thank you.

(Whereupon, at 2:45, on April 19, 1983, the hearing adjourned.)

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This is to certify that this is a true and accurate verbatim transcription of the proceedings in the matter of a meeting of the Fluoride Panel which took place at 9:00 a.m., on April 18-19, 1983, in Conference Rm. 2C116 of the Clinical Center, National Institutes of Health, Main Campus, Bethesda, Maryland.

STENOTECH, INC.

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President

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