put you on the spot a bit more. Assume that --

DR. HEUBI: I don't mind being put on the spot.

DR. GARZA: Assume for a moment that, obviously, the study was not designed -- no study will be designed to look at an adverse event and that if you do see something that has sufficient power, you always have to deal with whether or not you're dealing with an --

DR. HEUBI: Right.

DR. GARZA: Now, if you don't have sufficient power, retrospectively, with all the problems that presents, because it wasn't a hypothesis that was put forward before the study, what sort of criteria would you depend on to be able to say, well, even though you don't have the power to detect a difference, more data are needed, or given -- I wouldn't worry about the fact that you didn't have sufficient power, you don't need any additional data.

DR. HEUBI: I would feel warmer about the concept that if you have somebody independently

reviewing these adverse events, that you have at least covered all the bases appropriately to minimize the risk that somebody would be reviewing and say, well, here is an industry sponsor who has an internal committee that says this is obviously not related to the formula, whereas if you have independent reviewers who look and say this clearly doesn't appear to be related to it.

It's a safer way to deal with this than having it being internalized.

DR. GARZA: We'll go to Dr. Stallings and then Dr. Giacoia.

DR. STALLINGS: Having been at a couple of really good Children's Hospitals, too, and have served on IRBs, I think it misrepresents the real state of the world to think that investigators doing industry sponsored formula trials or any other trials or NIH trials, up until the last recent time, were fully informed and fully executed their responsibilities about adverse event reporting.

I think most people who are doing these

kinds of studies wouldn't know the definition of an adverse event. And I also know that in most settings, the IRB and, until the last six months, the CRC had no requirements for reporting, and, again, most of your studies aren't going to be done in the CRCs, many of them are not going to be done in academic settings.

DR. GARZA: CRCs are clinical research centers.

DR. STALLINGS: Clinical research centers, which have a second set of oversight. So I really worry about this.

If you're in an IRB that is a general IRB, there's limited pediatric expertise at the table. Even if you're in my IRB, which is only children, almost, I think there's excellent expertise, but I think historically the requirement to report everything -- I mean, I would get a note and it would report them once a year.

Well, if it's not regulated in the way that we look at other things, they're not being written down, they're not going in.

So I think there is a real risk that there are -- we know that there are adverse events. They haven't been reported. They very likely are not related to the formula. They are related to other things.

But I agree with Jim. We completely have no idea and I don't think we should rely on the IRBs. It is not their responsibility solely. It really goes with the principal investigator and the sponsor.

So I think this is a place where I would agree that we need further scrutiny. If we buy the concepts of this is such a unique product, it's such a unique food that it begins to behave more like a drug, and we're calling these studies that report adverse events, I think we have to think about that, because I think you have an -- historically.

Now, everything has changed in the last 12 to 18 months in clinical research. We all know that. So it's about how do we go forward.

But I know IRBs have not been managing

this.

DR. GIACOIA: This is like telling a joke and forgetting the punch line. There is a new policy in NIH that recognizes --

DR. GARZA: I hope that's not the joke.

DR. GIACOIA: What is the joke? I don't remember. But it recognizes the issue of adverse events not achieving significance in the trial and set this apart.

So I think it's a very clear cut situation here. You cannot continue extrapolating in this situation.

DR. GARZA: So your advise would be that --

DR. GIACOIA: You have enough evidence -- what we're saying here is where you can extrapolate to another population. Having had this trial, number of adverse events significance.

DR. GARZA: It presents even more complications of you are extrapolating from one population to another. I see. Okay.

DR. SIGMAN-GRANT: I was just reflecting

on what's been being said and I'm wondering if this whole idea of an independent review might be under a guiding principle, might be added to those lists. That's just a suggestion.

DR. GARZA: I can ask the person who is taking notes to please add that and we'll come back to that as a guiding principle, at least for further discussion. Dr. Dwyer?

DR. DWYER: I endorse the notion of an independent data safety and monitoring board and it seems to me if that principle is accepted, that then this issue of adverse events, as Dr. Carlson said so nicely, the hypothesis is what drives the study, not the powering of adverse events.

But any decent data safety and monitoring board will yearly or half-yearly or whatever review all of the data and look at the adverse events, and then it becomes a question of cause and effect and biological plausibility and all of these other time and time relationships and so forth that might be useful.

But it seems to me we have to answer the

second question in the context of an independent data safety and monitoring board of the type that now is usual for NIH clinical trials and it's usual in many other settings.

I do agree with the comment that have been made by all the speakers that this is new news. This wasn't typically done five or ten years ago.

So this is a departure from the usual, but it seems like the abuses or oversights of the past several years suggest that it's necessary.

DR. THUREEN: May I ask a point of clarification?

DR. GARZA: Sure.

DR. THUREEN: Would you propose that those independent boards be sponsored by the investigator at the institution or be sponsored by the manufacturer?

Since there is now a lot more discussion, since there's so many more new data safety and monitoring boards that have to be -- that are coming out, that those will have to probably be paid positions in the future to get people to agree

to do them, because of their overwhelming statistical -- department of statistics and universities.

DR. GARZA: There is the third choice that we -- as long as it's being raised, that, in fact, if you intend to bring this forward to the government, that, in fact, it should be appointed by the government, but paid for by the sponsor.

DR. GIACOIA: FDA has a proposed rule for drugs to establish data safety monitoring independent from the sponsors.

DR. GARZA: That's what I said, yes, because there was a third choice. We'll go to Dr. Hotchkiss, and then Dr. Denne.

DR. HOTCHKISS: I was going to comment that my understanding is that this is ground that has been well trod for NDA, for new drug applications and so forth, and it's surprising to me that you would not want at least that level of rigor in any clinical trial involving infants.

DR. GARZA: You're right. Dr. Denne?

DR. DENNE: This is, obviously, a

difficult area to try and provide guidance on, but it seems to me that the principal ought to be the severity and the frequency of the adverse event, just as a general guide.

Obviously, if we're talking about an adverse event that requires prolonged hospitalization, even though it doesn't reach statistical significance, that's a different level than if we're talking about regurgitation.

So I think severity should be number one and then frequency would be number two, and I'm not sure you can specify a lot more than that in terms of what the FDA should look at in terms of evaluating adverse events in formula studies.

DR. GARZA: Would that change in any way for you in terms of severity or frequency if that was provided and evaluated by the type of independent board that we've heard discussed or if it was done the way it currently is done, that would -- as long as that information would be there, that would be sufficient.

DR. DENNE: I think ultimately it needs to

be done at the FDA level or an advisory committee of the FDA. That may include the original data safety monitoring board. But in many instances, their function, they may not have all that information.

The data safety monitoring board really is when the study is ongoing, the study may be done and then the adverse events may actually be more apparent.

So, again, it may include that data safety monitoring board, but I think it has to include probably beyond that.

DR. GARZA: But my understanding is that, in fact, the data safety monitoring boards will monitor study outcomes as they are being collected.

DR. DENNE: Correct, yes.

DR. GARZA: So that you don't see them at the end. You see them with at least -- the frequency will vary depending on the length of the study, but at least two times before the end of the study.

DR. GIACOIA: And they can stop a study.

DR. GARZA: And they have authority to stop the study, that's right.

DR. DENNE: They do, but there may be an accumulation of adverse events from that last half or third of the study that may never be apparent to the data safety monitoring board.

DR. GARZA: I want to make that distinction.

DR. J. ANDERSON: To return to question two, it seems to me that -- I want to make a couple points. First, it would be helpful, when a protocol is developed, to make sure that the protocol addresses the expected adverse events that are expected in the setting in which the study is done.

It may be that in healthy term infants, the rate of adverse events under normal circumstances is so low, that the best that you can do, given the expected sample size for efficacy, is to monitor for that and assess in some qualitative way whether you think there is a problem or not.

I suspect, though, if studies are being

done in pre-term infants, where perhaps a certain level of adverse events is expected in the course of providing them nutrition, that protocols could, in fact, establish statistically appropriate monitoring rules for the kind of adverse evens that are expected in that kind of setting.

Now, to get to the issue of question two. If a clinical review suggests there are clinical concerns between the levels of adverse events between two formulas that are being compared, it does seem to me that this is perhaps a setting in which some formal post-marketing evaluation could be suggested, because the particular study may not provide sufficient number of subjects to provide a clear assessment of whether or not the level of adverse events is of concern or unacceptable.

A formal process of study in a larger number of subjects after marketing could provide that information.

DR. GARZA: How do you resolve the tension then between the language that both Chris and Beth reviewed for us earlier that says that in the sense

of Congress, there was no room for error with these foods, because they were being fed to such a vulnerable population, between saying we're not sure, so we're going to feed them anyway and find out if there are problems later versus additional studies, trying to resolve whether the motivation for post-market surveillance are real or not.

How would you help resolve that tension given the intent of how formulas are to be used?

DR. J. ANDERSON: I think no margin for error is a fallacy.

DR. GARZA: So absolute safety is not a goal.

DR. J. ANDERSON: It's not an attainable goal, no. So in all of these issues that we are addressing today, the issue is really one of balance, of what we feel comfortable with based upon the information available.

DR. GARZA: So would you then suggest, in terms of transparency, so that the public is aware that we say this product is under post-market surveillance because the FDA isn't quite sure?

DR. CLEMENS: Just to make a comment, before Ginny makes a comment.

DR. GARZA: Hold on. Let me get to Dr. Stallings, then we'll come back.

DR. STALLINGS: I was just saying in the usual model, again, if we weren't talking about a formula and you had unexpected adverse events and you thought they might be related to the study being done, you would do more studies.

You would then come up with another study that would focus on that more carefully before you would release the product.

DR. GARZA: But that's not the question we're being asked.

DR. STALLINGS: The question says if it was not powered, what would you do.

DR. GARZA: Right.

DR. STALLINGS: And if I got that, I would say, well, under current regulation, I would say I think you ought to go study it some more before you release the product, which is all you can do. You can't say you can't release the product.

But I would say we have concerns about this. Now, my big concern right now is that I am not convinced that the sponsors and thus the FDA are getting adequate stories about adverse events, so I want to increase that, and then we've got to get the skills to manage them.

But I think further study is what -- that's what you do. You don't release -- I wouldn't want one where we're halfway studied, we'll let you know after we expose --

DR. GARZA: And that is because the question says raise clinical concerns.

DR. STALLINGS: Right. I'm not talking about a little more of this or that or it was a bad virus season and you can say you think that's why. I mean, something that really raises medical significance.

DR. GARZA: Dr. Clemens.

DR. CLEMENS: Let me make a few comments, if you would. First of all, infant formula is a food. It is the most heavily regulated food in the world, if not here in the United States. It's a

safe product.

Secondly, that I'd like to know how you define adverse events, much less unexpected adverse events. In all the clinical trials that I have been involved in, we have attempted to anticipate unexpected, if you could put that in the same sentence, anticipate adverse events based on the plethora of data that are publicly available and those data which are generated from pre-clinical studies and the kinds of studies that support the next notion.

It has captured every one of our protocols and all the adverse events are, in fact, reported in each one of our studies, whether it's an IRB or a safety review board.

We also have available in the United States a complaint system that is mandated by law and each one of the infant formula manufacturers has a system set up that you have a complaint, whether it deals with the physical nature of the formula or deals with the medical issue, there is a system set up.

There is a 1-800 number available to the consumer and available to physicians and any other health care provider.

DR. STALLINGS: So it's a company 800 number.

DR. CLEMENS: It's a company 800 number. It goes to the medical staff or however it's routed within a given organization. If it's a medical issue, it goes directly to the medical team and the medical team does immediate follow-up.

So that is in place and when there is a medical issue, that issue is reported directly to the agency.

So within a very, very short period of time, the FDA knows exactly what is going on in the infant formula world.

There is, in fact, as you can see, there is a reporting structure already in place here in the United States for adverse events for commercial formulas. There's also built-in, let me reiterate, there is a reporting structure built into just about every clinical trial that I've been involved

in beyond the 18 months that Jim referred to, to anticipate, if you will, potential adverse events based on our data.

So we capture and comment on every single event that occurs in the clinical study and those data are readily available in all case report forms.

DR. GARZA: The only difference being then between what's been suggested is that that reporting system is not independent. Once it gets to the FDA it is, but before then it's not, is that correct?

DR. CLEMENS: That is not independent and all the manufacturers follow the good clinical practice.

DR. GARZA: Given that description, Chris and Beth, why does this question come up then? If, in fact, our reporting system of adverse events is so adequate and everything else is working, is the way I interpret Roger, do you have instances where, in fact, adverse events between controls and experimental groups differ and are not --

DR. YETLEY: We have had more than one instance in which the major clinical study used to provide assurances of normal physical growth has a very significant difference between test and control groups and number of reported adverse effects that are clinically significant.

DR. GARZA: What is an adverse effect? I think that was Roger's question. How would you define it?

DR. YETLEY: In some cases, it's been hospitalization. In other cases, it's been infectious diseases.

DR. GARZA: But not regurgitation or things that we might think.

DR. YETLEY: We get that, too, but I think, obviously, you take into account --

DR. GARZA: So the issue --

DR. YETLEY: We did not put this in here because it only happens once. It has happened on more than one occasion.

DR. GARZA: So there were potential differences of opinion between the manufacturer in

terms of the relevance of that difference and an independent party who may be looking at it. Is that the genesis of it? Because there was room for disagreement?

DR. YETLEY: Our question is how do we use these data, if these data are what are presented to us.

DR. HEUBI: I think the answer to your question is if you have a totally independent review group outside of industry, then you can be satisfied that somebody has carefully reviewed this and is satisfied that this is not related to the agent that's being administered.

That's been my big concern about industry monitoring its own studies and that is there is inherently a conflict of interest that, no, this can't be because of my drug or my formula. And I'm not saying that to you directly, Roger, but it's true.

That's why we don't review our own projects now. I have my own independent person that reviews my activity.

DR. GIACOIA: I think we need a balanced perspective. On the one hand, it is true, there are different degrees. Adverse effects, some are very serious and some are not very serious. Usually, the less serious are more common than the more serious.

On the other hand, if you look at the situation in drugs, they are grossly under-reported and the difficulty is that you don't have the denominator and, therefore, unless a product goes in the whole country and you have thousands and thousands of babies being given the formula, you're not going to have the true incidence.

This is something that is a problem FDA is having, they use in data -- to see if they can have a better way to handle this, but the problem is you cannot get the true incidence.

But, again, balance is important.

DR. GARZA: You're talking about post-market surveillance then.

DR. GIACOIA: Correct.

DR. GARZA: Yes. All right. Dr. Russell,

and then we'll have to give you the last word and then move on to question three.

DR. RUSSELL: This may be just saying slightly a different way what Jim has said. If you think about how this might work, the independent monitoring committee, whether it be part of the IRB or subcommittee, we would follow the same NIH guidelines to have an independent monitoring committee and the IRB would get those reports and look at them and make some kind of decision at the local basis.

But then these reports could go to the Food and Drug Administration, with the IRB's decision on how they looked at it, and based on biologic plausibility that this was due to something in the formula, the severity and the frequency, again, they could come up possibly with some kind of a matrix that would help them.

Then there could be a decision to advise to study more, a decision not to approve or a decision to approve with post-marketing surveillance, or to okay it.

DR. GARZA: So then to try to bring this at least to a temporary -- the response to this question would depend on the presence of such an independent system.

DR. RUSSELL: Yes.

DR. GARZA: It would depend on to what degree the initial protocol anticipated, obviously, within reasonable terms, the likely adverse events and if, in fact, it may color it one way or another, but there ought to be at least some component within the original protocol that speaks to the anticipation of adverse events, that the severity and frequency of those adverse events actually will then dictate sample size and other issues so that, in fact, there has been a reasonable attempt to deal with them, and that given all of that, FDA still has the freedom, if there's still some unease about the safety of the product because, despite all of that, there still is some information that is needed, you have post-market surveillance that is appropriate.

The only question I would raise is to what

degree then should the public be informed that this is or is not under some sort of surveillance in terms of informed consent.

But those are all questions that we can return to tomorrow. Are there other issues that have been missed?

DR. HEUBI: I assume there's no such thing as formula watch.

DR. J. ANDERSON: As I understand it, that's exactly what is presently in place. It's a system in place for the voluntary reporting of problems with formula, either by professionals or by the public. But the emphasis, as with Med Watch, is on the voluntary nature.

DR. HEUBI: But it goes to the manufacturer, not to the FDA.

DR. GIACOIA: Are you talking for drugs or for formula?

DR. GARZA: Let's move on then to question number three. We'll say that is under post-market surveillance and its characteristics, where does the reporting system go to and things of that sort.

Beth?

DR. YETLEY: Can I just make the follow-up comment? Med Watch System, which, of course, was designed originally for drugs, does accept and process adverse event report complaints with infant formulas. So they will come into that system, but the comments were very correct in that there is significant under-reporting and we lack both a numerator and denominator.

DR. GARZA: But the significant under-reporting is no specific to formula. It's just general.

DR. YETLEY: In general.

DR. GARZA: That's right. Now, let's go to question number three. I may fail, as a chair, to get you out of here by 4:30, but I'll try to get us as close to that as possible.

Who would like to address the issue of attrition rate? Maybe I could turn to Dr. Anderson. There are some key statistical, both philosophical and substantive issues.

DR. J. ANDERSON: In the context of a

randomized clinical trial, where the interventions are blinded, it's logical to conclude that differences in attrition are an outcome of the interventions.

And when it's an outcome of the interventions, one needs to be concerned that the information that one has from those that were made is not representative of what would happen if the individuals who did not continue with the study had continued and provided information on the outcome in that particular setting.

So in the abstract, which is all that we have to deal with here at the moment, it seems to me that large differences in attrition should be considered failures of the intervention for which there was a large attrition rate, because the goal, obviously, is to deliver the intervention that was intended, and that did not occur.

DR. GARZA: Would the reasons for attrition have any impact on that?

DR. J. ANDERSON: Sure. Of course they would, although, again, if there were large

differences, one would expect a difference in the reasons to be larger for one of the interventions over the other, and that information might impact one's willingness to be supportive or not supportive about the new formula.

DR. GARZA: What would you consider large? Three significant figures, but is it 50 percent, ten percent, 80 percent?

DR. J. ANDERSON: The FDA has asked us this question. Why don't they tell us what they consider to be large.

DR. GARZA: He's punting now.

DR. YETLEY: When I went back and looked at some of the where the issues come up, they range from probably a ten percent attrition in a treatment group maybe up to 50 percent, with a much lower rate in the control group.

So those were the kinds of examples I was coming up with.

DR. GARZA: When you say much lower rates, were those rates three to four-fold difference? Among the ten, you saw two?

DR. YETLEY: Oftentimes, yes.

DR. J. ANDERSON: That would be big. I would consider that big.

DR. GARZA: Dr. Dwyer?

DR. DWYER: I was wondering. Is this against -- are these both active treatment arms or are they against breast fed or what?

DR. GARZA: I would assume that they're against two treatment arms. Whatever the control is and the treatment.

DR. DWYER: I would assume there would be a differential dropout of the breast feds.

DR. YETLEY: The control is usually almost always a comparable formula with a long history of use.

DR. STALLINGS: The same thing without the new additive or the new -- the standard of care.

DR. GARZA: Dr. Clemens.

DR. CLEMENS: My experience, again, says that doing the clinical trials with infant formula, that a dropout rate, if you will, of 25 percent is very, very common.

People move away, change insurance policies, are tired of visiting the clinic.

DR. GARZA: But the difference is not the fact that you've got --

DR. CLEMENS: They drop out, 25 percent is very common, large differences, it's just the luck of the draw. But I appreciate whatever large is, but I'd really like to see what large is in this group of experts.

DR. GARZA: I thought we were addressing issues of large differences between the groups.

DR. CLEMENS: We can be. I just want to make sure --

DR. GARZA: Not 25 percent in both groups.

DR. CLEMENS: And a statistician would say, well, if you have a dropout rate greater than ten percent, it's not valid. But the reality is that a dropout rate of 25 percent is quite common.

DR. GARZA: So you would subdivide the question into two groups.

DR. CLEMENS: Absolutely.

DR. GARZA: What is your absolute

attrition rate and when does a study become no longer informative. For safety issues, I suppose it would concern FDA, if there are different attrition rates. So why did 50 percent of the experimental drop out when you only had ten percent or 20 percent.

DR. CLEMENS: Then you're into Ginny's comment, your intent to treat statistic falls out.

DR. GARZA: So would that solve it, if we just said analyze it with an intent to treat and if the analysis is still robust after an intent to treat analysis, then we don't worry about differences in attrition rates?

DR. CLEMENS: You still have to follow up with those.

DR. J. ANDERSON: Again, we're talking in the abstract.

DR. GARZA: That's right.

DR. J. ANDERSON: But research subjects or their parents can be withdrawn for any reason at all and there is no requirement for follow-up. In fact, they can refuse that any information be

provided at the time that they withdraw being a research subject.

So intent to treat is all well and good, but if there is no information beyond the time that they withdrew available, then you are comparing not the randomized subjects, but the randomized subjects who stayed in the trial.

I want to return to my initial point, which I don't want to get into a discussion about issues related to generalizability in the setting of a certain level of dropout. That's for another time.

But in the setting of significant differences, and we can argue about what significant differences are, between the groups, it's either by chance or it's an outcome of the intervention.

In the setting where large differences, however that is defined, occur, it seems to me it's important to know or to attempt to identify what the reasons for the differences are.

Trials can attempt to collect information

about the reason why someone has withdrawn. Is it because the baby isn't eating or they don't -- if there are differences, they're likely -- the reason for the differences may be identified by collecting information about the reasons for the attrition at the time the attrition takes place, and that may, in turn, inform whether or not the information left for the people for the people to continue on the study is relevant to the issue of whether we are comfortable with the formula or not.

DR. GARZA: So your answer to this, what I'm inferring from what you are responding, that our answer should be no, unless there are circumstances that, in fact, explain the difference in attrition rates, but the default is no. It's incumbent on trying to find out why they drop out.

If you don't have that information, then it has to be known.

DR. J. ANDERSON: I think that's right.

DR. GARZA: Let's take that as a premise and if you can speak to that, that would be great.

DR. STALLINGS: It's really echoing it.

As a non-statistician and the recipient of the data on the new infant formulas, if there was a difference, I would want to know why and I would not be comfortable with a big difference without knowing why, and I think it would need to be studied further, because my assumption as a clinical investigator would be it is -- if randomization worked, then it is a result of something that I did within the course of the study.

So I believe the answer is no. Again, whatever the difference in large -- differences in dropout is.

DR. GARZA: What I heard from Dr. Anderson is if, in the follow-up, you find out that because of just bad luck, 30 percent of your subjects moved away in one arm and 15 percent moved away in the other arm, unless the product drove them out of their homes.

DR. STALLINGS: Right. But I think a lot of the other stuff, the assumption, unless we can prove otherwise, is they were getting more stomach

aches or more --

DR. GARZA: It's no unless you can --

DR. STALLINGS: Yes.

DR. GARZA: All right.

DR. HEUBI: I agree with Johanna. I think the scenario I would envision is that here you have a group and you're studying subjects that have diarrhea during the course. They go off formula for a period of time and they can't return in the time frame available for them to go back on, they get dropped.

You don't know that information. So I think it's very important that it be determined what the cause of their dropout is.

DR. GARZA: Well, it's about three minutes to 4:30 and I think we have at least a working consensus from which we can work on this question, also, tomorrow.

We've covered all three. Are there other points that any of you would like to make before we break?

The assignments for tomorrow are that, in

fact, we go back to the three questions. We talked about matrices and other issues that we need to begin to flesh out, so that the advice we give FDA would be more substantive than yes, no, and definitive maybe, but that we can flesh them out.

Are there any questions, as you reflect on those, that would help all of our thinking processes?

DR. STALLINGS: Can we assume that the writing --

DR. GARZA: No, we don't write anything. I asked that and there was a great amount of gratitude for that. The response will be taken from the verbal record and since we are advisory, then your statements tomorrow morning will be your statements of record and the FDA will then assume that that's your advice and they will act on that advice.

But we don't have to put out a one or two sheet paragraph or language that, in fact, we have to agree on. What is required is that at the end of tomorrow, as we go around the table and you

provide advice to questions one, two, and three, that a rationale be provided with your advice and that, in fact, question number three, it would not be sufficient to say no.

We would have to know why your answer is no and what would condition it, and that would be done verbally as we go around the room. Did I get that right?

The executive secretary says it's right.

DR. CLEMENS: So, in fact, you expect some statement from each one of us tomorrow regarding --

DR. GARZA: Questions one, two, and three.

DR. CLEMENS: So if we feel more comfortable reading a statement that we put together while watching the baseball game tonight, that would be okay.

DR. GARZA: That's absolutely fine, as long as you don't give us a score in the middle of it, because then we'll start to worry. You can read it.

We do ask that you be succinct, obviously, because otherwise we're not going to get through

the three questions and all the advisory group.

DR. CLEMENS: A closing remark is that Mr. Gelardi this morning had indicated the willingness of the formula manufacturers in attendance to provide any resource at their disposal to each one of you here. I am the contact person. If you want information about how clinical trials are conducted, quality assurance measures are assessed, anything about conducting and evaluating infant formula, direct your comments to me through Dr. Garza, and I will be glad to provide that information directly to you.

DR. GARZA: Any other questions, comments?

DR. THUREEN: What time are we starting?

DR. GARZA: Tomorrow morning, we'll start at 8:30. Breakfast, I think, is there at 7:00, for those of you that are early risers. We will convene the group promptly at 8:30 and it is my hope that we will be done at least by 1:00, hopefully earlier, but we're going to aim at trying to finish up by 1:00.

Lunch will not be provided, which is an

incentive to finish, although there may be some infant formula and it will have an acceptability test.

There is nothing organized for this evening. You are free to go into Washington, if you wish, or stay here at the hotel.

[Whereupon, at 4:30 p.m., the meeting was recessed, to reconvene Friday, April 5, 2002, at 8:30 a.m.]