ORIGINAL

NATIONAL INSTITUTE FOR OCCUPATIONAL

SAFETY AND HEALTH

PUBLIC HEARING ON UPDATING HAZARDOUS DRUG LIST

Washington, D.C.

Tuesday, August 28, 2007

ANDERSON COURT REPORTING
706 Duke Street, Suite 100
Alexandria, VA 22314
Phone (703) 519-7180 Fax (703) 519-7190

P R O C E E D I N G S

MR. REED: Good morning. So thank you for coming to our public meeting this morning. This is the first public meeting that we have had and the first update of the list of hazardous drugs for NIOSH.

My name is Larry Reed, and I, along with Tom Connor, will be facilitating this public meeting for NIOSH. Also in the back we have Barbara McKenzie, who is principally involved in helping to arrange the meeting in the ongoing effort to update the list of hazardous drugs.

Also at the table here, I'll introduce a little more formally in a moment is Anita Schill, who is a NIOSH Associate and Director for Science. And we'll have a few introductory remarks from John Howard, who is on leave through I believe Labor Day.

But mostly, I wanted to sort of set the stage for our discussion and introduce Anita to give those comments or remarks from Doctor Howard. But the purpose of the meeting, again, is to

update the list of hazardous drugs from the NIOSH Alert that was finalized three years ago.

We had prepared a list of hazardous drugs, and you'll hear more about that process from Tom later on this morning. And we also promised in the NIOSH Alert that we would update this in a periodic fashion. And this is the first update of that list from 2004. So, again, the purpose of the meeting today is to hear public comment in a very detailed and ongoing process for seeking public comment and helping us then to finalize the updated list of hazardous drugs. So with that, I would like to introduce Doctor Anita Schill, who, as I mentioned earlier, is the NIOSH Associate Director for Science, located here in Washington, D.C. And Anita has a few remarks from Doctor Howard.

DOCTOR SCHILL: Thank you, Larry. Good morning, everybody. On behalf of Doctor Howard and the Office of the Director at NIOSH, I would like to thank all of you for being here and to welcome you to this public meeting, which, as

Larry said, is the first meeting to update our list of hazardous drugs and the definition of hazardous drugs. And all of these were first published in the 2004 Alert that Larry mentioned, and so this is a very exciting milestone for us to actually be beyond publication of the Alert and now to be doing the first update.

I'd also like to thank you for your willingness to participate in this public forum. Your input is critical to producing the best possible information on hazardous drugs. NIOSH has a long history of soliciting public participation and feedback from workers, employers, and other interested stakeholders, as well as our scientific peers.

This public meeting comes from or continues our tradition of working closely with those who care about our science and the impact it has on workers, work places, and work settings.

Your comments will help us to achieve our aim of increasing awareness among health care workers and their employers about the health risks

posed by hazardous drugs and measures for protecting their health.

Additionally, your participation in this public meeting will help the scientists at NIOSH fulfill our commitment to one of our core values, and that's quality. NIOSH is committed to using only the best science, the highest level of data quality, and the most transparent and rigorous review processes for our scientific work.

In addition to this public meeting, the public comment period for this definition and list of hazardous drugs will extend to September 20th. We believe that the information shared in this public meeting and the public comments we receive in our docket will improve the quality of our work and we embrace your contributions. We whole heartedly embrace your contributions and thank you very much for being here.

MR. REED: Thanks, Anita. Just for those of you who don't know Anita, she, as well as Doctor Howard, were passionately and actively engaged in the creation of the Alert, finalization

of it, so for that I'm very thankful. We have a few moments. I'd like to -- and we're relatively small. Since this is was our first meeting, we didn't know how to gauge the size of the room, so for subsequent meetings, you know, we have like this, we will adjust accordingly. But we're small enough, most importantly, that we can introduce ourselves I think, and we'll pass along the microphone. And if you would do so, please, by stating your name and organization or affiliation.

And you don't need to -- as I mentioned, the court reporter will capture the names on a separate listing that Barb has in the back. So if you haven't already signed up on this list of attendees, please do so at the break. That's going to be the official capture of names.

I also want to mention to you, too, that we have a court reporter here who is transcribing the entire proceedings verbatim, so as part of this process, I would ask that, in general, that when you ask questions and have communications with us, that you either speak from this

microphone or from the portable one that we'll have that we'll take around to you, to identify you, as well as hear more specifically the comments that you have for the transcription. So with that, I'll go ahead and grab the microphone, and then, Barb, maybe you could help me with the movement.

MR. NAUMANN: Good morning. My name is Bruce Naumann and I'm with the American Company, and I'm also participating on the Advisory Panel for this update.

MR. JOHNSTON: Good morning. I'm Jim Johnston with WYETH.

MR. McGRATH: Bill McGrath, Bristol-Myers Squib.

MS. GOULD: Janet Gould, Bristol-Myers Squib.

MS. MATTHEW-BROWN: Dianne Matthew-Brown, AFSCME.

MS. McCONNELL-MEACHEN: Mary McConnell-Meachen, Boehringer Ingelheim Pharmaceuticals.

MS. McDIARMID: Hi, Melissa McDiarmid, I'm an occupational medicine physician at the University of Maryland and was a member, as many of our colleagues from Pharma who aren't saying, in the original hazardous drug work group. So a number of us have been joined at the hip for a long time and it's nice to see colleagues here together to go to the next level.

MR. O'CALLAGHAN: Hi, I'm Jim O'Callaghan, I'm with the NIOSH Health Effects Laboratory in Morgantown, and I'm a member of the hazardous drug group.

MS. REILLY: Good morning. Cindy Reilly, I'm with ASHP, American Society of Health System Pharmacist. I am a member of the work group. I'm joined by my colleague, who stepped out for a moment, Justin Coffy, who is the Director of Federal and Regulatory Affairs for ASHP.

MR. KASTANGO: John Kastango, Clinical IQ Consultant, member of the USP Steril Compounding Committee.

MR. STEELNACK: John Steelnack with OSHA's Office of Biological Hazards.

MS. MORGAN: Good morning. I'm Theresa Morgan, I'm a reporter with Inside OSHA.

MS. SLAVIN: Hi, I'm Katie Slavin with the American Nurse Association.

MR. SIGLER: Hi, I'm Joel Sigler with Kaiser Permanente.

MS. BULL: Good morning. Jonca Bull from Genetech.

MR. BARFNECHT: Good morning. Tom Barfnecht, Abbott Laboratories, Occupational Toxicology.

MR. SCHATZ: Tony Schatz, Shering-Plough.

MR. MARVIN: Good morning. Richard Marvin with American Society for Therapeutic Radiology and Oncology.

MR. ADER: Alan Ader with Safe Bridge Consultants. I'm an Occupational Toxicologist.

MR. RALE: Good morning. My name is Hank Rale, I'm with Containment Technologies

Group, retired Eli Lilly. I was a member of the original working group on the Engineering Control Section.

MR. SCHWARTZ: Chuck Schwartz, Pfizer, Inc. I'm a member of the working group. I was not part of the Pharma Group the first time around, but I'm looking forward to working with you guys.

MR. TROUT: Hi, Doug Trout with NIOSH, and I'm a member of the NIOSH working group.

MR. BLOSSER: Fred Blosser, NIOSH Public Affairs.

MR. PACENTINO: Good morning. John Pacentino with NIOSH.

MS. REISSMAN: Good morning. Dori Reissman, also NIOSH.

MS. BENSON: Kimberly Benson, FDA.

MR. HUNTLEY: Good morning. Carl Huntley, Division of Drug Oncology Products, FDA.

MS. VERBOIS: Leigh Verbois, Pharmacologist, Food and Drug Administration.

MR. REED: Okay, thank you. NIOSH is a

research organization. We are part of the Centers for Disease Control; and as such, the work that we do is science driven and is research. The products that we develop are recommendations. So the list that we have is not a regulatory product, it is a non-binding product, it is meant as guidance, so I just wanted to emphasize that point in this process.

I also want to emphasize the point that the purpose of the meeting here is to seek public comment and input that will be transcribed and be used as part of the process that you learn more about in a few minutes about finalizing the list that we hope to do so in the next few months. Next slide, Tom, please.

The agenda is -- I share the slide only just sort of to get the flow of the day today. We are just a one day meeting and I think the size of the group will allow us to interact as much as possible.

I do have some logistics issues to discuss. Again, if you are attending the meeting,

as you are here, I would ask that you please sign your name to the list and affiliation. Barb has it in the back, that's our official record of your attendance and involvement, and also for the court reporter's purposes of correlating what you say to the transcription. Also, Barb has a second list, an important list. If you want to provide comment here, we ask that you sign a separate list. We're aware of only one official presenter at this point in time, and that's from ASHP.

But again, we have ample time throughout the day, so we would just ask that you put your name on the list and we'll go in that order for up to ten minutes of presentation and discussion on the list.

And then we have a third list I think Barb created just a few minutes ago, and that is, if you want to be engaged or want to see future interactions of this nature on the definition and list of hazardous drugs, we'll keep you on a distribution list for future involvement, so that's -- we'll get a third list.

And I guess also in terms of logistics, Barb has asked me to remind you that the restrooms are in this direction, to your right, my left. Cell phones probably won't work in the basement, with maybe one exception, but you probably know that already if you've tried to phone out.

As I mentioned earlier, we have a transcription that will be an important part of this process as we finalize the list of drugs. And since we have ample time, there will be sufficient time I think for those people who have questions, you know, of the presenters, if the presenters don't mind being asked questions. Again, we would just ask that you use the microphone and that you identify who you are for the official transcript. And the agenda that you see in front of you is very flexible and will identify the break times and the times to come back from that, so it's a very sort of informal, flexible process right now. I'm looking to Barb now. Did I miss anything in terms of logistics? She's much better at this than I.

MS. McKENZIE: No; at lunch time, if you wish to leave your stuff here, I will stay in the room, so you don't have to --

MR. REED: Okay. Next slide, please. Just a brief overview of the Alert; as Melissa actually mentioned when we were doing introductions, Melissa McDiarmid, who was a part of this effort from the very beginning and a big creation of the Alert, many of you who are here in this room were part of that effort, and it was a fairly long effort, but it was a very good and important effort that was scientifically -- that created as its principal product the NIOSH Alert.

And that effort began actually in September of 2000, in Washington, D.C., where we had a meeting of effected partners and parties, and we heard a passionate appeal to NIOSH to develop an alert that would be the scientific basis for one identifying or communicating concern about the health effects from exposure to antineoplastic agents and other medications, and also to provide recommendations for preventing

these exposures. As an important part of that effort, we recognize the importance of having a list of drugs that would be a recommended list of those drugs that we consider to be hazardous when health care workers are exposed to them over a long period of time in their work setting. So, again, that's sort of the basis for this meeting here. And it is an appendix in that we're referred to throughout this meeting, an appendix of the alert itself.

The Alert was -- again, I won't go into the details of it, but it took about four years to complete, and it was a very interesting process in the sense that it was a very large group of passionate people with one commonality, bright and passionate people, I might add.

The one commonality was worker protection. And we all I think had our differences in this effort, and we had a very sort of -- what I thought to be a very good mix of participation across labor, industry, trade organizations and associations, academia, and

government. And I think we began with 20, and at the end of our effort, we had upwards of 50 to 60 people involved in this effort.

So I would say that from that standpoint, it was unique in terms of the broad engagement of effort, in terms of developing the original draft of the Alert. Then NIOSH took this draft, very early draft of product, the Alert, finalized it through a very rigorous process -- was a very -- what we would call a highly influential product, and through a very detailed scientific effort of peer review, both scientific peer review, as well as stakeholder peer review, we finalized it through several literations. And Tom and I know that it was a very thorough process, and others who were involved in that effort. So from that was the product basis by which we are now updating the list.

Next slide. I won't go into details of this. It's a very detailed slide. But actually this is Doctor Howard's suggestion that we -- and it was a very engineer-like suggestion. So I was

surprised, but also I think it was -- turned out to be I think a very good recommendation, that we create a flow chart of the process to help us think through and see, visualize the intricate effort that would be needed to update both the definition, as well as the list of hazardous drugs.

Again, I won't focus on the details of it. Could you go back to the first slide, please? This would be the definition.

Again, we have two slides on the process, one is the definition, and again, I won't bore you with the details.

But basically, on the definition, we assess the literature from the original definition that Tom will talk about in a few moments from the Alert itself that was based principally on the ASHP definition with some minor modifications. We went through this process over the last year or two and we determined -- we assessed within NIOSH that we didn't think there was enough reason, a scientific basis for changing the definition. So

through this flow chart, we basically came down to no changes in the definition, and we then would go to step two. Going back to step -- we have two fingers here. Had we determined that there would be a change, a proposed change in the definition, we would go through this very detailed process of public comment, a public meeting, and then the finalization of this definition through a very detailed process. Next slide, please.

This slide shows the flow chart for the updating of the list itself. Basically, it's a carry-on, a continuation from the first slide, where we decided that there was no change in the definition necessary. Then we're going through this sort of detailed process.

I'll just identify some key aspects of it. Internally, you'll hear more about this in a moment, internally, we reviewed information relevant to new drugs that had been approved since 2004, the development of the Alert itself. In that, information would be the FDA warnings and approvals, an important part of that effort.

We now have a public comment meeting here that's going to be an important part of this collection of information effort.

We then also, you'll see in a moment, we have a very large group of expert panel members who will be helping NIOSH assess this information, and the information that will be assessed will be the information in the docket that will remain open, as Anita said, until June, excuse me, until September 20th, information that we gather here at this public, as well as the information that you'll hear about in a moment that was developed by an internal group of NIOSH experts that did the original assessment of information to develop this proposed list of updated drugs.

So we will have a meeting of this peer review group probably in the fall sometime. And then we'll finalize -- NIOSH will finalize this -- the updated list based upon the collected information. And if there's substantial reason to change the definition, we would possibly do that, as well, depending upon whatever information we

hear. But at this point, it's just the list of drugs that we would propose updating.

So I think that's all, Tom, for this slide. I have two more and then I'll pass it on to Tom for more sort of detailed and substantive discussion of the process itself. But I just wanted to mention to you that we had -- as part of this effort, you'll see a summary slide at the end, we had a group of internal NIOSH experts; Tom Connor, who is sitting here, who will be talking in a few moments, is a toxicologist in the NIOSH, Division of Applied Research and Technology in Cincinnati; Barb McKenzie is a biologist, also in the same division of Applied Research and Technology; Jim O'Callaghan, Jim, if maybe you could raise your hand here, is a pharmacologist who is in the Health Effects and Laboratory Division of NIOSH in Morgantown, West Virginia; lastly, we have Doug Trout, raise your hand, please, Doug, who is an occupational physician, who is in the division that I represent, the Division of Surveillance, Hazard Evaluations, and

Field Studies, he's an octoc.

So collectively, through a long effort that lasted over a year, we gathered information with this group and we developed this proposed updated list of hazardous drugs based upon the collective information that we were aware of.

I mentioned earlier that we have a panel of experts. I think they are all here, with perhaps one exception, correct, Tom?

Okay. And this panel of experts we put together, we wanted to have -- make sure that it was representative, that it was an unbiased objective or representation in the balance perspective, I should say, of the effected parties here in terms of helping us then assess the collective public comment from the docket from this meeting and from the NIOSH initial work that was done.

And then they will provide us this expert response. We plan to meet sometime in the fall, hopefully October/November range, after we have the transcripts of information and when the

panel has had a chance to analyze and read and digest all of that information.

And I'll just mention by name, Caroline Freeman from Federal OSHA, Melissa McDiarmid, you heard earlier, is from the University of Maryland, Bruce Naumann from Merck, Marty Polovish, who is not here I believe today, is representing ONS, Cindy Reilly from ASHP, Chuck Schwartz from Pfizer, Debora Van der Sluis from Genentech, also representing BIO, a trade organization for the bioengineer drugs, Leigh Verbois from FDA, Kristen Welker-Hood from ANA, and last, Vernon Wilkes from VHA.

So again, you'll hear a summary of this process, again, at the end of the presentation. But now I'd like to pass this on to Tom Connor, who will talk more about the definition and how we generated the updated list from the internal NIOSH group. So, Tom.

MR. CONNOR: Thank you all for being here today. It's good to see a lot of old faces that were involved with this process. We've been

working on this since basically -- in 2000, we started thinking about the Alert and how to do this. And, as Larry mentioned, it's been quite a bit of work to do this update.

We had -- first we said we were going to do it on a yearly basis, and then we really had to work out the process on how we were going to do that, and that really took a quite a bit of time once we developed the process, and then we had to go through and actually do the review internally in NIOSH so we could provide some information to our panel of expert reviewers.

So basically, what we did, this is the definition that we developed with the help of the NIOSH working group. I know a number of you were members of the NIOSH working group and you are familiar with it. And, as Larry mentioned, we were up to about 50 or 60 individuals at a time when we completed the Alert, so we had quite a bit of input. We basically took this definition from the ASHP definition that had been used in the technical assistance bulletin and we just modified

it a little bit, added basically the last -- the structure activity relationship criteria to that definition. Larry, if we could have the next slide.

We also -- we have not done a quantitative risk assessment on these drugs. It's been kind of a qualitative assessment, hazard assessment. We have not done a quantitative risk assessment.

We recognize that there are occupational exposure limits that are used by industry, and there are some criteria that are applied with developing definitions for hazardous drugs. We have this as part of the definition, as a foot note to the definition for further guidance in -- if individuals want to develop their own list of drugs or just guidance how we may use this information towards developing a list. Next one.

In the current NIOSH definition, we have 136. The majority, about two-thirds of these, are antineoplastic drugs. This is the appendix A in the NIOSH Alert that Larry mentioned. So, again,

about two-thirds of these are antineoplastics. The others are some antivirals, some immunosuppressant drugs, hormonal agents, and a couple of monoclonal antibodies. What we did on that list, and I think most of you are aware, this is a similar approach that OSHA had used in their guidelines for the safe handling of hazardous drugs, where we went to a number of institutions that had, for actually a number of years, developed their own list of hazardous drugs.

So we went to those institutions, and you can see the NIH Clinical Center, Johns Hopkins, Northside Hospital in Atlanta, and University of Michigan. And also with the help of Bruce Naumann and others in Pharma, they developed a list of hazardous drugs that we combined all of these into the Alert, and from those, this is how we generated our sample list of hazardous drugs.

We needed to find a more systematic approach now that we were updating the list of hazardous drugs. So what we did, we have been collecting information on all new FDA drug

approvals since the publication of the Alert in 2004. We also have been collecting -- most of you are familiar with Medwatch, I'm sure, warnings from Medwatch. Most of these have been black box warnings, you're familiar with the black box warnings.

So we collected all of these since the publication of the Alert in 2004. And we also looked at the current list of hazardous drugs from NIH. They had the most comprehensive list when we did the first go around with the Alert. So we wanted to take a look and see what new drugs they may have included. And I think, in addition to two in the first -- I mean the first two groups, we had about 15 additional drugs from the NIH list that we included. Out of this approximately 150 drugs that we gathered information for, we -- Larry mentioned the NIOSH internal group that Doug and Jim and I, and who else, Barb, I'm sorry, Barb. Actually, Barb has been very instrumental in getting all this information together for us. We haven't been able to do this work without her.

We reviewed these drugs, we did, again, a qualitative hazard assessment on these and categorized them as -- if we considered them to be a hazardous drug or if they did not fit the definition, the NIOSH definition of a hazardous drug. We came up with 62 drugs on our initial list that we considered to be hazardous drugs. The next one.

So what we are looking for, we are looking for today input from this group of individuals and information from the NIOSH docket to correlate all of this information and put it together for this panel that Larry mentioned, panel of experts, to evaluate what we did, identifying those 62 potential hazardous drugs, and have this external group review that and provide feedback to NIOSH about how they would rate or rank these drugs, whether they would be hazardous or -- all drugs are hazardous, obviously, to some extent, but whether they would fit the definition of hazardous drugs.

As Larry mentioned, we'd like to have

the meeting of the reviewers sometime in October/November and get the list finalized as soon as possible. We had made a commitment to do this every year. Obviously, we are three years behind schedule. And we have a large number, we have approximately 150 drugs on our list, on our current list. We don't foresee having this, if we do it next year, we'd have a much smaller list. And we may be able to modify this procedure a little bit if we just have a few drugs to look at. Larry.

Here is the contact information for Larry and myself. I'm sure you have that. But if you want to -- if you need to get in touch with us about anything. Larry, you wanted to say a few words to wrap it up?

MR. REED: Yeah, thanks, Tom. Other than just to reiterate, sort of this effort here is an ongoing effort that we plan to do periodically, and this public meeting is an important part of that effort. So as I mentioned earlier, I think we have one scheduled

presentation, is that right, Barb, ASHP. And so, again, if you want to make a formal presentation, we have ample time to do that today. So please make sure that your name is on the list. And we'll start with the first person from ASHP, and I'm sorry, that would be you, Judy -- Cindy.

MS. REILLY: (off mike)

MR. REED: Yes, please.

MR. REILLY: Good morning. I'm Cynthia Reilly, I'm with the American Society of Health System Pharmacist. I don't really have an official presentation, just a few comments that I wanted to start out with. ASHP is a pharmacy association that represents about 30,000 members that practice in a variety of health systems, all of which obviously are involved in handling the medications that are proposed for the list, as well as the existing list. ASHP has a long history of being involved in this process.

As Doctor Connor had mentioned, the original list was based on our technical assistance bulletin, was one of the resources that

was used in developing that. I can't say it was based on it, but it was one of the resources.

So, obviously this is an area that ASHP is quite interested in and has a long history of being involved in. So we're pleased to continue to be involved in this process.

In a personal level, as I started to look at this process, I thought back to the time when I was a practicing pharmacist, and I admire everyone who's been involved in this process. This is new for me, I've just started with this. And it's not an easy process, it's not an easy decision, as you look at the drugs and try to determine, because you obviously are dealing with the safety of health professionals, which is something that ASHP takes very seriously, that I take very seriously.

So as I started this process, I sat down and pulled many, many package inserts and did a lot of research. But basically, ASHP would -- supports the designation of hazardous drug for many of the drugs that are proposed for the

update, including those for which we have evidence that they are known hazards, the ones that have been previously designated by the National Tox Program, et cetera. However, we do advise caution with the classification for some of the medications on the list. As you know, once drugs receive that classification, there are strict guidelines for receipt, storage, preparation, transport, administration, and disposal of these products.

And all of these factors will impact health care practitioners, not just pharmacists, not just nurses, but also other staff in the facility that are involved in patient transport, et cetera. So there are a lot of individuals involved, and obviously there's cost involved, as well, for training, for facility design, for personal protective equipment.

One of the things is, we started to look at this process and seek input from our members who have been experts in this area for a while, is that some individuals have questioned the extent

of what is an occupational exposure and then what is the evidence for some of the individual agents on the list, and in many cases, that evidence is more consistent with internal dosing in the patient rather than what might be deemed from an occupational exposure.

We also had several members that have urged us to present their view that the dosage formulation is something that should be considered. Many of these products are capsules, tablets, et cetera, where the risk from occupational exposure may be limited. One of the things that we have found from our members, as well, is that they are also -- in practice, they look at this as a tiered approach. It's not an all or nothing. The way that they look at it, they will treat different agents differently. And so ASHP knows that this occurs in practice, though we also know that there's variation in how individual will look at assigning the tiers.

And we would -- and we think in some ways that adds to the confusion. When an

individual goes from one practice site to another practice site, something that was treated as hazardous somewhere may not be treated as hazardous elsewhere.

And so we would actually prefer a process where that tier was official assigned, as far as what the risk level was from exposure. Our members tell us that some institutions use a three tiered approach, whereas others, ASHP would more advocate for a two tier, simply because, for educational reasons, and then just the science base, how you determine what would be in that second tier would be difficult.

But for medications that are intact formulations, we would consider, and obviously we'll talk about specific agents later, but some of those we would consider low risk, whereas manipulation of those agents, crushing tablets, opening capsules, would be considered higher risk, and we can talk a little bit more about the particular agents when we get to that part of the meeting. ASHP would encourage people to think

about some of the practical aspects of how this will be applied in the actual work place as we move forward. That's it. Any questions?

MR. SCHWARTZ: Chuck Schwartz from Pfizer. In the toxicology world, we've been looking at controlled banding strategies based on different levels of hazard for quite some time. Am I hearing that what you're advocating is perhaps a similar type of structure be set up on the exposure, equivalent to the exposure side, where things like powders for reconstitution, liquids, things like that, might be in one band, coated tablets, capsules, other types of, you know, solid dosage forms, be in another band, and then the controlled strategy be built around the matrix of what type of exposure there is against the depth of, or not the depth, the level or degree of hazard?

MS. REILLY: Well, I'm not a toxicologist, I'm a pharmacist, and I'm not exactly sure with the structure that you're looking at, but that is something that we're

looking at and proposing. However, I think our final -- and we have draft comments that are currently posted on our web site.

Our final comments will deal a lot more with how these individual agents are handled. For instance, some of the sleep agents that are on the list, if they were to remain on the list, we would be more firm in advocating for this tiered approach, simply because, you know, when you're dealing with, and I'm blanking on the Rimalteon. The brand names are coming more to mind than the generic, which I don't want to use.

MR. SCHWARTZ: Don't do that.

MR. REILLY: I don't want to use the brand names here. But like, for instance, all the agents that are used for sleep, are used for depression, that are used widely throughout the facility, there's large training requirements that would be required for -- we're not just talking about the oncology nurses or the immunology nurses that are much more familiar with these precautions, we'd be dealing with every nurse on

every floor.

And I think if some of those agents were to remain on the list, that would really have us encouraged looking at it as a tiered approach for risk.

MR. SCHWARTZ: Okay. Thanks very much.

MS. REILLY: Anything else?

MR. CONNOR: We have struggled with this issue even when we were developing the first list of hazardous drugs. You know, we recognize -- we have a powder that needs to be reconstituting, you may have a capsule, so you have different physical forms of this. The toxicity of the drug does not change.

And this is kind of the approach that NIOSH has taken, that the inherent toxicity of the drug remains the same. But there is a different occupational exposure scenario. If you're crushing a coated tablet, then it's another form. So you could have different forms of the same drug with the same toxicity, but different exposure potential. So this -- we struggled with this

early on, and it's something that we still struggle with here. So we're looking for feedback from this group on it.

MS. REILLY: And ASHP would acknowledge that if you were to have this tiered approach, it increases the educational needs, and that is certainly a factor that should be part of the consideration, and ASHP is, of course, interested in participating in any education.

But we also have a concern that with some of these agents on the list, we already know that health care practitioners are not necessarily always consistent with the recommendations for precautions, and we worry that some of the agents on the list will actually, in some ways, could make that worse, because they're like, oh, that's not toxic, and that cavalier attitude could extend to agents that we know are toxic.

MR. CONNOR: I think the flip side of that is, if someone is handling a drug, do I have to go look up, do I need to wear gloves with this, do I don't need to wear gloves with this, and so I

think our approach has been -- we don't want to include everything as a hazardous drug, obviously, but to try to have somewhat of a realistic approach, too, because a busy nurse or a pharmacist, you know, they can't always run and look and see how should I handle this. So to handle them, we use the term like standard precautions universal cautions in the alert, so that if you're wearing gloves or protective equipment, for one, you could wear them for the other. And I know in the real world that doesn't always happen.

MS. REILLY: One of the things also that we would encourage and ASHP is very involved in this area is the use of technology. So, for instance, with CPOE and electronic medical records and medication administration records, there are mechanisms that can be useful to help in that education as far as notes on the packaging that goes up to the floor and notes on the medication administration records, so that there is -- in some ways that can help. But we recognize that

education is a huge component of this.

MR. REED: Thanks, Cindy. Barb, do we have any other presenters? Okay. Anyone who would like to present informally or ask questions about the process or -- feel free to do so.

MR. ADER: Alan Ader from Safe Bridge Consultants. I was wondering, in the development of the new list, the new, updated list, why NIOSH had not just used -- added those compounds for which FDA had required labeling in their package insert and their official labeling which required the warnings that are I would call common to hazardous drugs in the past, where they described -- referencing the various guidelines that had been previously established, like the CDC guidelines, I think they reference the Australian or New Zealand guidelines for handling cytotoxic drugs and so forth, and why they just had expanded it beyond that list.

MR. CONNOR: Well, it's my understanding, and the FDA people can correct me, but those warnings currently only apply to

chemotherapy antineoplastic agents. We have other drugs which fall outside that category which are hazardous. And the current warning that is in the package inserts, in most cases, those references are, some of them, 20 years old.

And we've had several meetings with the FDA. I failed to mention that we have been doing meetings and conference calls with the FDA group, and they can elaborate on this a bit more, to look at that warning and maybe have it extend to all hazardous drugs so it's more uniform for these types of drugs. Would someone from the FDA like to comment on that? Thank you.

MS. VERBOIS: So right now --

MR. REED: You may want to identify yourself, Leigh.

MS. VERBOIS: Oh, Leigh Verbois, Food and Drug Administration. The Food and Drug Administration is looking comprehensively at this issue. We are trying to develop guidance to lead investigators and reviewers in determining whether or not drug products need safe handling comments

within their label. We are in the process of trying to update this information. There's a guidance that we are currently working on, but that's not out for public comment yet, we hope it will be soon.

As Tom mentioned, we are -- the procedures for a proper handling comment is placed solely in chemotherapy agents at this point. And we are trying to develop criteria by which we would go forward to determine whether or not we need safe handling comments within labels. Like I said, at this point we're still in the draft stage, so -- and we are here to hear your comments so that we make sure we incorporate the information and your concerns into our guidance document.

MR. REED: Thanks, Leigh. Did that answer your question, Alan?

MR. ADER: (Nodding)

MR. REED: Okay. Any other questions?

MR. SCHATZ: Tony Schatz, Shering-Plough, occupational toxicology. I wasn't

part of the original group that put this together, but one of the questions I have reading the definition of a hazardous drug is, at what point do you look at weight of evidence and make a determination for a reproductive or tratigenicity (?) or any of the end points that are listed?

What do you look at when defining whether it's a hazardous drug under one of those?

Because as a person at a particular company, it may be my job to then assign whether a drug should be on the list or not on the list according to your criteria, and we always look at weight of evidence approach and look at the different data and different species, et cetera, and we make a decision based on that. I'd like you to comment on what that is from NIOSH's perspective, or do you just look for the word tratigene (?) and put it on the list?

MR. CONNOR: Well, we did a little bit more than that. It is a very difficult process. This is why we organized this internal NIOSH group. We went through all of the package insert

information that was available. Obviously, if something has a fertility category DRX, I mean that's kind of a red flag, we look at that. No? Okay. But it's a red flag. It didn't automatically go on there, but that would be a red flag.

Category C is somewhat difficult. Sometimes -- Category C, as I think you're aware, is very broad. You can have almost no effects, and then you can have some serious effects close to the therapeutic dose in there. So we tried to weigh that evidence.

With the gentox data, we would look at the gentox data and try to evaluate all the gentox data that was available in the package insert. I know there are different pharmaceutical companies, I have seen schemes that they use, and these get fairly complicated.

So we try to look at that data and evaluate it. The same with the carcinogenicity data, if it's a very rare tumor that you only see in a mouse, we would probably exclude that, we

would not consider the carcinogen. If there's evidence of tumors in humans, lymphomas and so forth, and then there's also evidence in mice and rats, then we would then probably include that. So we did try to weigh the evidence as much as possible.

MR. SCHATZ: Okay. You mentioned the FDA categories, and I went to a meeting actually a couple of years ago on teratology society, where the FDA was represented and there was discussion about redefining those categories. I'm not sure where we are with that, and maybe the FDA can comment on what they're doing from that front.

MS. VERBOIS: There's a specific group set up to work with reproductive categories and we're not directly involved with that. There is, as we have also heard, a move towards that, and that has been going on for quite some time, and there's substantial discussion, but we haven't heard it going any further than probably what you heard two years ago.

MR. CONNOR: Chuck, did you want to --

please. We welcome any comments. Please --

MR TROUT: My voice really carries. Do they need me at the microphone? I would caution, there are some unique circumstances sometimes around reproductive categories. I know that you can't say that, well, X perhaps, D, you can't -- it's not black and white. The tetracycline antibiotics are a category D. They would not, I don't think, fall into the category of hazardous drugs. Boy, I better hope -- I think we all hope they don't. They cause a very specific type of development effect and it's just not in the scope of -- The other thing is that, I really like the idea that we said at the first meeting, through all of the package inserts and such, was a qualitative kind of reading. And I know for a fact that in more -- well, in at least one instance, that a very rare tumor type in one strain, one sex, was the sum and substance of the evidence that put something on the list of 62 drugs that wanted to be added to the list.

So knowing that that was just a first

read-through, that was actually one of the drugs that I wanted to comment about when we get to the discussion parts of this. So knowing that that was just the first read-through of it is encouraging.

MR. CONNOR: Yeah, so basically we developed this list, and it's a proposed list. We understand that some of these may not fit in a category. We also understand some that are on the list that we did not consider. Some of the individuals on the panel may have additional information where those would be moved to the list of hazardous drugs, so I think it could go either way.

Again, we went through the package inserts, we had this committee, we reviewed it, we discussed it and tried to look at the weight of evidence and came up with a proposed list, and now we're looking for guidance from all of you people and other people in the public to comment on that list.

And if you want to have a, you know,

we're open for discussion here now. This is what we're going to do today until we run out of things to discuss. So if you have a particular one that you want to comment on, please do that, if you feel comfortable doing that now. I don't mean to put you on the spot.

MR. TROUT: Okay. The drug that I'm thinking of is one of our drugs, and I'm in kind of an awkward position here. So we have some other people who are from our company who will be providing comments on that, you know, the advocate versus a member of the expert panel. I'm a little uncomfortable commenting about a specific drug, but I wanted to use that as an example.

Other things that I was thinking about, though, as I read through all the package inserts preparing for this were mechanism of -- genesis, where the effects are clearly secondary to other effects.

There were a couple of them that, boy, when you read that, it sounds an awful lot like these tumors and rodents are secondary to

metabolic activation, which is a mechanism that's irrelevant in humans.

Any expert panel or whoever would tell you that, that they've dismissed these. Certain types of thyroid tumors, certain types of mammary tumors that are seen in rodents, and it seemed like many of them were on the list, and that was what the evidence was all about.

Also, with the reproductive end points, the way testing is done, you test to failure, to use the euphemism that we work with. So you must show FDA the level at which the effects are going to occur, okay, because the dose makes the poison. Well, the lack of dose, therefore, is an indicator of safety. We have to worry about those respects. And it seems like that needs to be brought into the picture for many of these comments. Thank you.

MS. GOULD: Janet Gould, Bristol-Myers Squib. And I just want to follow up with what Tony and Chuck just said about dose response, because before coming here to prepare, I looked

through our drugs that are on the list to try to understand why they were put on the list.

And so I was looking at, okay, if it has a positive, then on the table, that meant, you know, it was a carcinogen and animal studies or repro studies or a category D, it was -- caused developmental effects.

But then when I looked at the dose that causes it, it could be, yes, it was -- caused tumors in animals, but the dose was much higher than the one mig per kilogram that was noted in the note, or the ten mig dose, therapeutic dose. So I would like comments on the dose, as well.

MR. CONNOR: Well, basically what I said, we took a qualitative approach. We developed a list that we would like you and others to comment on, and these are the types of comments that we want back. So, again, this list is not set in stone. We developed something to work with. The easiest way to do it was to put a plus/minus because there were so many drugs, we just couldn't list out all the information on a

single table. So this is a starting point for us basically. So --

MS. GOULD: So then I guess I'm wondering, for providing comments on our drugs, would it be helpful, you know, for either arguing for or against it being on the list, to provide that. I mean the data based on the criteria and you would take a look at that, that would be a good way to go about it?

MR. CONNOR: Yes; and some of them -- obviously, some of them are very high doses, many times the therapeutic dose, but if you look at some -- we were looking at some of them yesterday, and in fertility, sometimes it's only very close, one or two times, three times the therapeutic dose, so we have to take that into consideration also.

MS. GOULD: And I guess if the therapeutic dose is like way above ten migs and it's at the therapeutic dose, that's a different situation than if it's much lower.

MR. CONNOR: Yes.

MS. GOULD: Yeah.

MR. REED: Thanks. I would just add while the next questioner comes up that if you have comments on specific chemical, excuse me, drugs, or comments on the process itself that you don't -- you would like to expand on or provide additional information, the docket is the best way to do that. And, Barb, at the break, I think we'll put that docket information on the web site up on the flow chart or the chart here.

MR. O'KELLY: Hi, Jim O'Kelly from Pharmacology Associates. A couple of points; we look at hospital's operations and we're concerned about the potential complexity of a hospital going about implementing this. We're primarily looking at RECRA on your published list already, and when we look at hospitals, they just throw up their hands because it's just too complex.

And I think one of the particular, I talked to Cindy about this on the phone, particularly to go to more and more of a tiered approach or the different categories, it's hard

for us, when you actually see what's going on in the hospital, it's hard for us to envision how they can implement the finer points within your current -- the direction you're moving.

So if there's anything you can do to simplify it with an eye to how the hospitals are actually going to implement the precautions and the -- we deal with the recommended waste disposal as one issue. So --

MR. REED: I'm sorry, just a question on that. Are you looking for guidance more on the issue of worker protection or the disposal?

MR. O'KELLY: Well, I'm trying to think of the implications within the hospital environment on how they have to respond to the entire life cycle of your drug. And to the extent that -- right now, when we look at how hospitals are currently operating within the various RECRA plus your initial list plus the other lists that are out there, we don't see the level of compliance that we would hope for, primarily because they just can't keep up with it. So I

just think that -- I would strongly encourage you to consider the operational implications within a hospital, because, you know, we're concerned that people will just say -- I can't even begin to abide.

And we generally just -- we incorporate your recommendations in our recommendations, and we're having a -- running into a challenge. The people go, you guys are being too conservative. So that's one issue, and just a couple of others.

Along with that, to the extent that there are any other lists that are out there, and I can provide you our sources if you'd like, we would encourage you to make sure that you're integrated with those other lists because there's frustration in the community with the differences between the list of carcinogens in particular.

And one of the things as I came in, you mentioned your goal was to update this list every year, I don't think the community can absorb that. I would encourage more of a three to five year time table, because the thought that somebody

would have to revisit this process, revisit their training every year, I think that would be just -- I don't know that you could do it, but I don't know that anybody would be happy to do it.

MR. CONNOR: Well, as I mentioned, you know, we haven't done this in three years, so that we do have very large lists. We don't foresee that unless you guys keep approving new drugs all the time. Actually, the drug approvals the past few years have been higher than they have in the past, so we had a double whammy.

We got more drugs and we had more years that we had to look at. But I think -- I understand the question about -- you talked about how you deal with this on a practical basis. We get many calls every -- almost daily on specific issues on how to handle this. A lot of them deal with how do we dispose of the waste materials.

I'd be interested in any of the lists that you have that we could look at. We have tried to be conservative. As I mentioned, some of these -- some of the drugs on this list may not

stay on the list.

We are not changing what we have done since the Alert was first published, we're just adding -- updating the list. And I really think -- I personally think that's a good thing. A very toxic drug comes out, should we wait three years to tell people that they have to handle this on a -- using proper precautions? So I know it's difficult for you guys, and the whole issue of RECRA lists versus, you know, hazardous drug list, is a very complicated issue to deal with. Thank you.

MR. REED: Thanks. I would just reiterate a point that Tom said, that if you have information on additional lists that we haven't considered, please send those. It's best I think to send it to the formal docket. Thanks. Any other questions?

MR. SIGLER: Hi, I'm Joel Sigler with Kaiser- Permanente. In my organization, one of the drugs that we're struggling with trying to figure out engineering controls based on your

list, it's created a lot of discussion in our organization, is BCG, and there are those that are in favor of significant engineering controls and others that think that's too conservative. I'm just wondering if you'd give any insight to the discussion that may have occurred when BCG was originally put on the list? That might give us some guidance.

MR. CONNOR: Initially it was on the list, and this is one we do get questions on. It was on the list because it was on those lists that we adopted for the first go around. Lucy Powell was scheduled to be here, most of you know Lucy.

Her recommendation is that BCG should not be on the list of hazardous drugs the way it is, because it should be handled separately from other drugs so you do not get cross contamination of those drug products, which have been shown in the past, there is evidence to document that, that the BCG should be handled in a separate containment isolator biological safety cabinet from IV drugs. And she and I have had quite a few

discussions on this, about whether it should be on that list, whether we should identify it differently somehow with a footnote or something, so that's something that we need to take into consideration. Did I answer your question?

MR. SIGLER: Yeah; and I'm sorry, I don't want to get too specific about this, but it sounds like you're saying that it may or may not end up on the list, but you would still recommend some kind of barrier isolator or other engineering controls?

MR. CONNOR: Yes; I think that's what Lucy -- I think if you look in the package inserts, the recommendations by the manufacturer, I think that --

MR. SIGLER: Yeah; I'm just wondering, any other insight to discussion of whether even that was necessary? Because some of our people in our organization think that it's not really an airborne hazard and it's more of a, you know, a needle stick hazard. I don't necessarily feel that way, I'm just wondering if there was any

other discussion that you might be able to share.

MR. CONNOR: I don't know if I've seen data on that, I'm sorry.

MR. SIGLER: Okay, thank you.

MR. CONNOR: Okay.

MR. REED: Thanks, Joel. Any other questions or comments?

MR. SCHATZ: Tony Schatz, Shering-Plough. Did I hear you correctly when you said that you were not going back to the original list to update that, you were just adding or subtracting from it? Because I mean they were based on different criteria than what you're basing the updates on.

MR. CONNOR: That is correct. Right now we are not looking at the appendix A, that is in the Alert, we're not making any changes to that. BCG might be an exception because it does not really fit in the hazardous drug list, it should be a separate category.

What we did, which I did not mention, we, at NIOSH, took that original list, appendix A,

and applied NIOSH criteria from the definition to that list in retrospect, and those drugs that we have on there fit that definition.

MR. SCHATZ: So the current definition you're using the drugs on appendix A fit that?

MR. CONNOR: I'm sorry, say that again.

MR. SCHATZ: The definition you showed --

MR. CONNOR: Yes.

MR. SCHATZ: -- with the three source of information, they meet that?

MR. CONNOR: Yes.

MR. SCHATZ: The ones that are on the list?

MR. CONNOR: So we went, again, in retrospect, after we had that list, and we applied those criteria to that list.

MR. SCHATZ: Okay. And the discussion about dose response and exposure and clinical dose was mentioned, and whether that's relevant to occupational exposure, you know, is the question. But is there going to be, at maybe an outcome of

this, more guidance put in the Alert for risk assessments as opposed to you need to do a risk assessment? Will there be any kind of guidance put in there on dose response or physical form or certain things that people need to consider for risk assessment?

MR. CONNOR: I think it would depend on the feedback that we get from you guys. If you feel strongly about those issues, please send that information to us by way of the docket.

MR. REED: Yeah; Tony, I would agree with Tom, that we would certainly consider that information. And if we think there's a sufficient need for guidance in this area, dose response will certainly address it.

MR. CONNOR: This is an ongoing process, we are developing it, we hope to keep refining it as much as possible.

MR. McGRATH: Good morning. Bill McGrath, Bristol- Myers Squib. Just a general comment about the two lists that we have here. I'm looking at the original appendix A, which only

has the generic name, the source, how it got on the list in the first place, and the therapeutic application of the drug, and the new list which has a lot more information, justifying whether or not it would be on the list. I would suggest, you said you don't intend to modify the appendix A right now, but I think in order to make it a more helpful document, since we do talk about dosage form earlier in the guidance, that we at least add the house applied column to the overall list when it gets updated. I think this kind of information, if I were a person that was working with the compound, I'd be -- and there were many dosage forms for a particular compound, there might be an injectable version, there might be a solid dosage tablet and capsule like cytoxin, for example.

I think in helping make decisions about risk, it would be very helpful to know how the drug could be supplied in the health care facility. So I think any more information, creating more of a table with additional

information, I think that's going to improve the value of the list itself rather than just whether or not an individual compound is on the list or not.

MR. REED: That makes sense, thank you.

MR. CONNOR: Come on, Alan.

MR. REED: Come on, bring it on.

MR. ADER: Okay. Alan Ader from Safe Bridge Consultants. I wanted to reiterate a couple of points made by some of the folks and then add a few comments in general. We took a look at the list and there are at least 15 to 20 compounds that should not be on the list because they haven't had a quantitative risk assessment done. As Chuck said, the dose makes the poison, and I think it's critical to understand that in the nature of this process. The second point I wanted to make was, the nature of the testing approaches for FDA approvals versus to deal with these types of compounds, FDA follows OECD guidelines and other guidelines, testing guidelines, that requires for reproductive and

developmental tox, that a toxic dose be achieved so that to cause maternal toxicity in some of these tests. At some point there is a dose limiting -- a dose, but many of these compounds have maternal toxicity at very high doses, and I think we're placed in that list because they did show that, but they're not occupationally relevant because they are at such high doses.

So the nature of the testing should be evaluated as part of this overall quantitative risk assessment. And significant scientific rigor should be applied so that you can actually have appropriate designations. If you have a compound on your list that shouldn't be handled like others, it may dilute the overall impact of the listings.

Lastly, the point that has not been made, which I think is important, is for a group of these compounds that are not absorbed occupationally, in other words, they're higher molecular weight compounds that are not absorbed by inhalation, which is the primary route, and by

dermal routes, because they're large molecular weight materials, and that should be taken into account.

There are probably five to ten of those compounds on the list for which rigor, in evaluating whether they should be on the list, should be applied. They're only given by IV injection because of that reason. And many companies do not consider them to be hazardous drugs, although they need to, like all pharmaceuticals, need some rigor in their handling. So those are my points. I guess -- I had one question. In the current system that you have for submitting comments, you don't really have a section on general comments? You'll accept those, I assume, but do we need to go to some other page and submit general comments in addition to the specific comments drug by drug?

MR. REED: No, I'd like to keep it simple. Barb, if you're okay with it, just to go to one -- to the one web site for both general and specific comments, is that --

MS. McKENZIE: Yeah; there's an address on the comment --

MR. ADER: Okay. Because right now I just saw -- all I saw is yes, no, maybe, or --

MS. McKENZIE: Right; at the top of the comment, on the right hand side, there's an email -- send your comments to that address.

MR. ADER: Okay.

MS. McKENZIE: And I'll put those up on the -- on the break.

MR. REED: Okay. Thanks, Alan. Just to clarify in my mind, you said the 15 to 20 drugs that were on the list you don't think should be on the list, and that's the new list, correct?

MR. ADER: Yeah; not the past list, the current list, the 62.

MR. REED: Okay.

MR. ADER: There's probably at least 15 to 20.

MR. REED: Okay.

MR. CONNOR: I just wanted to mention, we are very concerned about diluting the list with

drugs that should not be on the list. We think that's certainly counter productive if we do that. But suppose you have, I'll throw out a question to you guys, a high molecular weight drug that's probably not going to be absorbed -- or inhaled, but it's super toxic, really toxic, very low doses; now, would you make an exception for that? Suppose it's therapeutic, you know.

MR. ADER: The general answer is, it depends.

MR. CONNOR: I think -- why don't we take -- how long are we scheduled for a break?

MR. REED: I would suggest that we take a break. I think we're going to finish early, but I want to make sure that there's ample time for comments and questions. So I would suggest that we take a break now. I have 10:30, if we could be back by 10:45, we can talk, you know, do whatever, and then come back with additional questions with a fresh mind. So 10:45, please.

(Recess)

MR. REED: Okay, thank you. We'll

regroup here. Barb is going to give us a primer on the web site addresses here for comment.

MS. McKENZIE: The hazardous drugs web site is www.cdc.gov/NIOSH/topics/hazardousdrugs. And another easy way to get to it is if you just go to the NIOSH web site, which is www.cdc.gov/NIOSH, click on H in the alphabet up at the top, and you'll get to the H list, and hazardous drugs is there under health care, you can just click on that.

At the very top of that page, there's a box about this public meeting, and there's a link to the Federal Register notice and a link to the page that has the fit list, the not fit list, and the comment grid. And the comment grid gets mailed back to the docket office, which is NIOCIN.docket@cdc.gov, and that is at the top of the right hand -- on the right hand side of the comment grid, mail to.

And if you just put hazardous drugs in the subject line, it will get to the right mailbox. And you can also send general comments

to that email address also, not just the comment grid, and questions or, you know, anything that you have. Tom and I both will view that mailbox on a regular basis to see what comes into it.

MR. REED: Thanks, Barb. Any questions on the docket information? Again, September 20th is the deadline for comments formally submitted. Tom and I had a short discussion at the break, and there was a question, I forget who it was who raised the question about the original list, and this particular meeting is principally for -- to comment on the updated list of hazardous drugs, the new proposed additions to the list. We would also consider comments on the original list itself. So, again, it would be best if you could send those to the docket with specific comments.

So we have a chance after the break now to get back into questions and comments. Again, we're looking for both comments on the actual definition itself, the process, and if you have comments on the specific drugs themselves, if there's sufficient time, we would be happy to hear

those, as well. So any additional questions from the public?

MR. NAUMANN: Bruce Naumann from Merck. I just had a question to help get us, you know, back on track and thinking about what we're really trying to accomplish here, because obviously we're all -- we all have the same goal, we're trying to protect health care workers.

And I wanted to ask Tom a question. He's done a lot of work over the years monitoring levels of hazardous drugs and various health care settings and published a review article I think earlier this year on the subject. I'm wondering if you can just help us understand in general what you've seen over the years in terms of levels outside of biological safety cabinets on the floor, et cetera, and try to relate it back to what the -- kind of the overall philosophy of the Alert is, trying to increase awareness, making sure people are using proper precautions. And if you have anymore recent data after the Alert has -- now that the Alert is out a few years, to see

if things are actually improving or ultimately, you know, considering there are safe levels for hazardous drugs, how much of a margin of safety there might be and how much more work we have to do to get to what our goal is in terms of -- I mean obviously the best level would be zero, we'd like to see no measurable -- and reality is, you are measuring some, and I'm wondering, you know, order of magnitude -- per square centimeter, et cetera, and if you have a goal in mind as to what you're really trying to accomplish.

MR. CONNOR: Thank you, Bruce. Basically, I think -- starting off when we had our initial discussion about the Alert was to make people aware of the issue. Back in the 1980's, there were studies done that showed the use of biological safety cabinets had reduced exposure, and the methods then were quite crude. They were looking at chemical mutogens being excreted in the urine and measuring those and the study that was done by Roger Anderson, who was the Director of Pharmacy at M.D. Anderson Cancer Center for many

years.

It showed that when you stopped using the horizontal flow, which obviously blew all the drugs towards the worker, that the amount of mitogenic drugs being excreted in the urine went down considerably. So, you know, at that time, everyone said we'll get a class 2 biological safety cabinet and we're okay, we don't have to worry about technique, we don't have to worry about anything else. And then studies started coming out of Europe. Paul Sessinc in the Netherlands and some other researchers in Italy and Germany started doing environmental studies, and people were using biological safety cabinets and so forth, and they were still showing contamination in the pharmacy, in the patient treatment areas, basically doing wipe samples, measuring the amount of drugs that were on work surfaces and floors and so forth.

So a number of us realized that we probably have the same problem in the United States. So with Melissa's help and Larry's help,

we initiated the NIOSH working group. And we developed the Alert, basically at that time just to raise awareness.

And I think we have, we've gone, you know, we have strong associations with Oncology Nursing Society, ASHP, some -- also with ANA, and pharmaceutical manufacturing groups, and I think we've gotten the word out to a lot of people in the United States and around the world.

We get questions on almost a daily basis on specific handling issues, either by email, by telephone, from U.S. -- all around the world, and there's certainly an awareness of this issue, and I think that was our major goal. As far as the levels are found, you know, we usually measure nanograms per square centimeter, two or three or four of the more common drugs, and they're good methods available for sampling, environmental sampling and measurement of sycoflocimid, (?) iflocimid, (?) fluorouracil, methotrexate, -- and a few others. So they've typically been used as markers.

But as I mentioned, there's about 100 antineoplastic drugs out there and 120 drugs that we consider hazardous, so we don't know, you know, some of the drugs could be much higher levels than the ones that we're looking at, we really don't know that. But we use these as markers, as some indication of exposure.

And we have not really done longitudinal studies. We're analyzing some data now that will give us a feel for changes that have taken place in the U.S. There's really not that many studies that have come out of the U.S. looking at this. There's been a few, the one published by WIK a few years ago, but really not a whole lot.

We've seen levels from, you know, down to our limited detection, which is a couple of nanograms usually per square centimeter up to, you know, several hundred, even up into thousands of nanograms per square centimeter.

So, you know, that's not much, but when you multiply that by, you know, 100 square centimeters, which is sometimes used for

calculation for germal exposure, that could be a considerable amount of that one drug, and we don't know what's going on with the other drugs. So it's been about -- in that range. We would obviously -- we know we can't get it down to zero. We would like to, you know, reduce the exposure as much as possible using engineering controls and then backed up by proper use of technique and personal protective equipment. Melissa, do you want to add anything to that on an overall philosophy since you were so instrumental in a lot of this?

MS. McDIARMID: Well, in terms of whether there's the efficacy question, which I think maybe Bruce is wondering why -- was it worth it or what did we do, I guess even before we say was the effort regarding many of our people -- activities regarding the Alert, I think it was, but there's only sort of semi- quantitative information kind of -- a nurse that had been in our group at Maryland did a -- I don't know if some of you remember, we were in San Antonio at

the Rollout, we were doing an onsite questionnaire, and it was to try to see -- we got permission for anybody who signed up for that to be able to call them back in six months to find out whether there was any change in handling or level of visibility in their hospitals.

We wanted to kind of see whether this was going to just be, you know, like a one shot wonder or whether they were going to actually do something. And I don't recall the detail, except that I think a majority of the folks did have a working group put together or something like that as a result of coming to the meeting. Of course, some places are more ready to hear the gospel than others, as we know, right, so -- and they may have already, you know, this maybe -- first of all, the fact they even came to the meeting in San Antonio meant that they were sort of thinking about this or we had, you know, so maybe they were the worry well, we might say.

But like Tom, I probably get at least two or three calls a month about it, and typically

they're in the area that a doc does, which is like surveillance, alternative duties, stuff like that. And unfortunately, I think we needed to remind people.

But as somebody who used to be at OSHA, and I was very instrumental in writing the 1995 guidance, it kind of griped me that we even needed to do this again, because you would think people would get it, and I can't think of another industry that has, you know, such common use of just no holds barred toxicons.

And I know you guys in Pharma don't understand the way that -- what goes on in hospitals, but it would make you crazy. I mean you'd be taking aspirin every day if you were in charge of the safety and health, because it's just a totally different deal than what you're used to seeing in your places, which are, you know, very well controlled, and your companies invest in safety and health. That's not happening in health care, it is still not happening in health care, not just with these toxicons, but with anything.

I mean they're just now getting to blood borne, I did you not, and TB, and respirators don't make me, don't make me, and do we really have to fit test. I mean it's all this get out of jail free card stuff because we wear the white hats and we don't have enough money, and yet, as some of you have heard me say, nobody told paracelses (?) to call off the rules of toxicology because they're entering a hospital, you know, that's not the deal.

And unfortunately we are just now getting them kicking and screaming to deal with not just this hazard, but all kinds of them. But I think that the hook we have, in a way, for hazardous drugs is, even me, who has practiced in health care my whole career would say, some of these agents are at the top of the hit parade in terms of hazard.

You know, a lot of our colleagues never work in an industry where group one carcinogens are still handled on a regular basis, let alone with complete disregard for safe handling,

complete. And explanations vary from I didn't know to I'm in a hurry to don't make me or the training or HAZCOM doesn't cover it, which, of course, is not true.

You know, this pull down menu of excuses would just make us crazy if we were in another industry, but in health care, it's just ubiguidous (?). But I think what's finally getting peoples attention, and I'm getting back to the original question that Tom said was, I think that the resurgence of interest and concern that the Alert generated did allow another generation, if you will, of maybe younger health care workers or younger safety and health people who had to sort of do training or get religion or whatever, I do think that it's ultimately helped.

But, you know, as I said to Tom yesterday, you know, there is change at a glacial speed, that's true in federal agencies and it's way true in health care institutions.

And it's just a really tough issue because they -- some of my colleagues in other

areas of occupational health have said that, you know, to all the excuses, we hear probably some of you from your own companies about doing the right thing, to all those excuses, add this notion of, in health care, you're sort of, you know, our business, our mission is care of the sick, and so, you know, we're supposed to sacrifice ourselves.

And a number of us have actually even written papers on why health care doesn't get it, and I think part of that sacrificing yourself is the expectation, you know, that we inherit from Florence Nightingale, who, you know, kept the hot stovepipe from falling on a patient by exposing her own arms to it, and we're still doing that every day and accepting explanations for hurrying to do the work, or cutting corners because a patient needs the drug, or we can't afford the right thing to do, so we'll muddle through.

But it's just these toxicons are so unforgiving that, you know, the rules of risk don't get called off because of our wholly mission, and that's just been a really tough thing

to sell, especially in this time of, you know, this huge financial crisis in health care. So all by way of saying, yes, I think the intervention has helped, and I think, you know, these updates have helped.

But it's incredibly frustrating, from a safety and health point of view, because this kind of recalcitrance just wouldn't be accepted in another industry, but it is in health care because of this psychosocial notion of us, you know, sacrificing ourselves and not spending the little bit of money there is on health care protection.

But this will be the last thing I say. For anybody that has to, you know, kind of sell this, I remind folks, besides the paracelses comment that I made, that, you know, in the same way that, when you get on an airplane and they always tell you, if the oxygen mask appears and you're with a child, they tell the adult to put the mask on first, even though that might seem, you know, momentarily inappropriate, you do that so that you don't fall out and so that you can

still take care of your child, and I think that's the same thing, and I've used that example giving talks in health care, that we have to protect health care workers, as well, because otherwise, we're not going to be able to care for our patients, or certainly in the example of -- or a pandemic flu, if we, you know, if we're namby (?) about wearing respiratory protection and having those standard rules at our emergency room door, we're going to have to close the institution, because we're going to contaminate it from the inside and the outside, and then where will the mission be. And this is just really hard for our community to get. But I think that they do get the airline thing and that sort of makes sense to people. So that's kind of, you know, one of the things that I bring up when I'm talking to leadership in health care, to help them kind of get it. Anyway --

MR. CONNOR: Thank you.

MS. McDIARMID: You're welcome.

MR. CONNOR: Bruce, does that answer

your question?

MR. NAUMANN: Well, actually --

MR. CONNOR: Go ahead.

MR. NAUMANN: -- now that we've got the discussion going, I hope I didn't, you know, send the message that I didn't think it was worth it.

MR. CONNOR: Oh, no.

MR. NAUMANN: I'm a busy guy and I wouldn't be spending my time doing this unless I thought it was worth it. What I was really trying to do was, focus -- because we were getting there with the earlier comments, more in the concept of how do we make the process as efficient and science-based as possible so that we will have greater, you know, compliance at the hospitals? How do you, you know, avoid the delusion effect? And so as we go through the, you know, the process of trying to evaluate each of the proposed new listings, and actually, some of the ones that are proposed not to be on the list are possible candidates, too, after looking through them, some are borderline, that's the question. Where do we

draw the line? What are we really trying to accomplish?

Which subset of compounds do we want to single out to say, you know, hospitals or whatever, you really need to focus on these compounds, forget about these others ones that are just kind of borderline.

If you look -- if you do any kind of a risk assessment, you realize you're, you know, orders are magnitude away from a problem. Which are the ones that we really -- do you really need to focus on to make sure that you're protecting your workers?

MR. REED: Thanks, Bruce. As the next speaker comes up, I just want to mention as an -- it's more of an anecdotal aside. From Melissa's presentation, you can see how passionate and intellectually, sort of the focus she's brought this topic to our attention. From where I sat seven years ago now almost, she single handedly sort of stimulated the NIOSH involvement that got this off the ground.

And one last sort of tangentuous side to what Tom mentioned earlier, we do have some additional documents that are being spun off from the Alert, to provide additional recommendations in the areas that we thought were important, that we didn't cover as thoroughly and deeply in the Alert as we would want to have done at the time, and also, the additional information has come to our -- that we want to expand upon. For example, medical surveillance, there's a work by solutions document that's been finalized.

We had one in the draft stages as being peer reviewed on protective equipment, one in its very early stages on engineering controls, and lastly, we have a fourth topic that probably won't be a work by solutions, it'll be some other type of technical policy document on alternative duty. So we have additional work in this area that we hope to help in this transformation process.

MS. BROWN: Can everyone hear me? I usually don't have any problem carrying my voice either. I'm actually the weird person in this

group.

MS. REED: Excuse me, could you identify yourself, please?

MS. BROWN: Oh, I'm Dianne Brown, I work for AFSCME, which is the American Federation State County Municiple Employees.

I'm not a doctor, I'm not a nurse, I'm not a scientist, I am a health and safety rep for a union. And I am the voice of the housekeeper and the custodian and the pharmacy tech. And for the folks in this room, I want you to remember, especially public employees, public hospitals that really have no money, they are not using the engineering controls that you think they're using. The technique out there would make you cry, okay. I don't even do this stuff for a living and I can look at the technique and it makes me cry, okay. Just from working with this great group, I'm working with a lot of public hospitals now, and the reason I am is because of the Alert, because some of the pharmacists who I don't represent read the Alert and started raising some questions, and

then the pharmacy technicians got brave enough to start asking the questions, too, who are, in some cases, actually showing symptoms of over exposure.

I think that the medical surveillance work place solution is very important because I actually have a hospital who's actually considering putting it in place for the pharmacy techs because of that document.

So when we look into increasing the list or adding to the list, I want you to remember that all scientific studies that you do in your perfect world, that gets all thrown out the window when you talk about who's mixing this stuff, especially in some of these public hospitals. Even the teaching hospitals are not as pristine as we would like to think they are.

I saw stuff being mixed in a basement, in a -- I'm serious, it was a converted janitor's closet that they were mixing these drugs in, and there were shelves of all kinds of stuff all around them, stuff that shouldn't have even been there, and they're mixing in this tiny place and

practically running into each other. And they wouldn't allow me to bring a camera in, but I wish I could have taken pictures and shown them to you, because that's the world that I'm living in. And I do think that these updates are very important. I'll be really interested to see the other documents that come out, because I can use those to start these conversations and to get with these hospital administrators about, I know you have this amount of money to work with, but we really need to control these because you may be contaminating your patients, you know, other places in the hospital, you might be contaminating visitors, not to mention your workers, and in particular, the housekeeping staff who really get no training at all.

And don't forget that, you know, over half the states have no OSHA protections at all, at least not currently, and so there's nobody going to go in and smack them around, nobody is going to get a fine, nobody is going to get inspected.

So what our folks depend on are the type of documents you have that NIOSH puts out, because they don't even want to hear the word OSHA, they don't even look at the standards, they could care less -- technical documents as recommendations as how I push these changes in these work places. Thanks for the time.

MR. CONNOR: Thanks.

MR. REED: Thank you, Dianne. Any other comments or questions?

MR. JOHNSTON: Jim Johnston from WYETH. You mentioned engineering controls, and I wondered, in terms of quantitative evaluation, whether or not you had considered surrogate testing, typical drug preparation steps to look at exposure risk potentials?

MR. CONNOR: We haven't really discussed that. I don't see -- I think it's the standard practice that's used, I think it addresses a bit more. But certainly using surrogates, I did one study using fluorescein dye, you know, florosi (?) dye they use for training for pharmacists and

nurses to look at the technique.

I think if you have a suitable surrogate, if you're testing in engineering control, it's a lot safer than using the agent. There may be some drawbacks to that because of the physical characteristics. I think maybe Alan could address that a bit more.

MR. JOHNSTON: Yeah.

MR. CONNOR: Just a follow-on for Alan is that, there are typical different types of drug preparation steps, and typical ways they're handling, depending on the form and so forth, and to make evaluations on a particular way in which a drug is formulated and so forth might be helpful to evaluate this particular methodology versus another one and do that in a quantitative way.

But perhaps Alan wants to talk to that.

MR. ADER: Alan Ader from Safe Bridge Consultants. We do a lot of work for pharmaceutical companies and we've done some work in the drug delivery and hospital pharmacy type of -- and compounding pharmacy to look at worker

exposure under different conditions, different compounds, using both surrogates and the actual -- what we call the active pharmaceutical ingredient, and we would always urge both -- and I think that this is an important aspect, that the quantitative exposure assessment needs to be performed for your facility, for your particular use.

Whether you have the resources or not to do that is another question, because certainly a public hospital may not have the funds to do quantitative industrial hygiene assessment. But as you already have pointed out, you could qualitatively assess that and say it doesn't look right based on some criteria which has been established by the NIOSH hazard alert.

So you could do both a qualitative risk assessment and a quantitative. As an industrial hygienist and toxicologist, I always learned to take your pumps with you and try to do that. But it doesn't seem to be the norm as it was 20 -- 25 years ago when I was an industrial hygienist to go out and actually measure exposure, but you need to

do that.

And I think the hazard alert does say you should consider that in addition to a qualitative assessment. But I would urge NIOSH, in their engineering aspect of, I think you called it, Larry, you said something that there's going to be an engineering document to support the recommendations that you do quantitative assessment of biological safety cabinets, lamorative flow hoods, what do we call those devices that are engineered solutions that go on top of the, I'm not sure what you called it --

MR. CONNOR: Closed system transfer device?

MR. ADER: Closed system transfer, and any other devices that people have, ventilated enclosures, and so forth, that there be quantitative data to support, why are we using this control. That's what's done in the pharmaceutical industry.

We come up with quantitative data to show, hey, this is why we're using this control

for this type of compound. And I would urge NIOSH to consider developing some of the base data for that for use in health care type of applications.

MR. CONNOR: Thank you, Alan. One quick question, do you find that surrogates really represent the drugs? I mean you've got --

MR. ADER: Yeah; as far as surrogates go, the type of surrogates that are out there are both, I would call them non- hazardous sugars, like mannitol and lactose are used as indicators of exposure. And then there are existing low toxicity material such as naproxisodium and acetaminophen are used.

I'm a favorite of using active pharmaceutical ingredients, because I think they behave a little bit more like the other types of active pharmaceutical ingredients that you're trying to mimic. But we tell our clients who do surrogate tests to choose a surrogate which behaves something like your active ingredients. So the particle size and bulk density, these are terminologies for pharmaceuticals, should be

similar. And if you're handling solutions, they should have the same flowability characteristics as your active pharmaceutical ingredient that you're concerned about. If you have lyophilize power, the lyophilize powder should be similar to what you might handle with the active ingredient that might be hazardous or toxic.

So we would recommend that you test using a surrogate, but that you follow it up with the actual compound that you might be interested in evaluating. So test your unit or device or control with naproxisodium or acetaminophen and then follow that up with the active ingredient that you're most concerned about, so that you show a consistency between the results.

MR. CONNOR: Thank you. It's more than I wanted, but that's all right.

MR. REED: Did that answer your question, Jim?

MR. JOHNSTON: Yes.

MR. REED: Any other comments or questions?

MR. RALE: Hank Rale, Containment Technologies Group, and kind of as a person with a foot in both camps, almost 30 years in pharmaceutical, and we build isolators for hospital pharmacy, as well. That was -- the idea of testing was primary before we ever released a product. We actually worked with Lucy Powell and developed procedures, techniques, and also worked with Safe Bridge Consultants to do significant testings so we understood what the exposure limits would be, handling 100 to 150 doses in an eight hour period, and doing air sampling and surface sampling. And we have all those protocols and would be happy to share them if you'd like to take a look at them.

MR. CONNOR: Okay, thank you.

MR. REED: Thanks, Hank.

MS. REILLY: Hi, Cindy Reilly again. Two comments, and the first was actually more of a question. Has any consideration been given to the characteristics of the worker? Like, for instance, we know the demographics of the work

force are changing, particularly in pharmacy, and I can't speak necessarily to other groups, but in pharmacy, it's increasingly becoming a female field, and so you're looking at different workers who are handling these agents at different lengths of exposure.

If you look at some of the agents that are proposed on the list, there are some that you might consider are toxic only to certain sub populations that are working with them, like a pregnant woman or someone of child bearing age versus a man with fertility, and then also some immunocompromised agent, so that if the worker was not immunocompromised, the toxicity might be less.

So has there been any discussion of that or -- work characteristics at all?

MR. CONNOR: No; I don't think we have taken that into consideration. We are aware that pharmacy is getting to be more and more women, and obviously, most of the nurses are women. We were talking in the break, one of the questions we get all of the time is about oxytocin, which is

obviously, in the third trimester, it could be a concern for occupation exposure. So, you know, that is one example where you would have a certain population that would be susceptible to that.

And I don't know if we should somehow in the Alert identify that it's only that population, because I get probably a call every week about oxytocin, why is it listed as a hazardous drug. So we really haven't looked to that issue. It's maybe something we need to consider.

MS. REILLY: Well, I think, just as -- that the demographics of what is toxic and for how it will change, in fact, it will increase when you start to look at the changes in the work force. And your comment about oxytocin kind of leads to my next comment. We get calls about that, as well, and as we posted our comments, several members called us and said, are they going to look at the old list, you know, this is what we feel about this.

And then we also got some comments from individuals that felt that some of the drugs

should be on the old list that aren't. OKT3 (?) was suggested as something that should be considered. And then there was, you know, just some question as to why some drugs were considered, but not others. Protuximad is being considered, but not Implixomad, and I'm not sure -- I'm assuming that this was based on an assessment of the labeling. But there was -- I think the members were looking for some consistency, and I think that this is what makes it difficult for them to implement, because they see one agent on the list, whereas they see something with a similar mechanism and that's not included.

MR. CONNOR: Actually, this came up in the break, too. We did not include all monoclonalantibodies(?). We looked at each one individually and determined if it should be on the list. That's another question we get, you know, are monoclonalantibodies on the list of hazardous drugs, and we tell them certain ones based on the criteria. So we did it on a drug by drug basis

rather than on a class of drugs. And again, we want consistency.

Like Bruce said, you know, we would like to have a very concise list that people can look at and not have questions about, but we still have all these drugs that fall in that gray area around that list, and those are the ones that really give us the problem, and that's why we're trying to get feedback on those that are in the gray area.

MS. REILLY: Okay. Thank you.

MR. CONNOR: Thank you. Excuse me, if you have -- you said there were a number of drugs on the list that you -- were not on the list; if you could -- okay, let me know. And also, I think Larry wanted to bring up the existing list.

MR. REED: Go ahead.

MR. CONNOR: This would be a good time. We've mentioned BCG today, we mentioned oxytocin, they're kind of a little bit of -- not really -- maybe -- and somehow we should handle them a little bit differently than the list of hazardous drugs. If there are other drugs on that list that

you feel strongly should not be on there, I think we would like some feedback on that also.

Again, we took that list from four institutions and one that Bruce developed for us also, but there may be some that may not quite fit on that list, and so if you have strong feelings about that, we would appreciate feedback. And also, again, the list that we -- the ones we determined do not fit on this list, this time, if you have -- think some of those should be on the list, we would like feedback on that, too.

MR. NAUMANN: Bruce Naumann, Merck. Just as a follow- up to Cindy's comment, you know, the Alert itself is not, you know, a stand alone document. Obviously, it drives a lot of procedure, practices, and so forth, good handling practices, hospitals, et cetera, but it's really not the only resource.

And the Alert does a good job of directing people toward the safety data sheets that are generated by the manufacturers, and that's a very good source of information on what

the hazards are and what, you know, the critical effects are that ultimately led to the occupational exposure limits, which are required to be included in section A in the safety data sheet by OSHA. So typically, when the occupational exposure limits are established, you know, you're looking at the entire range of data, all of the potential susceptible sub populations, including the unborn. So the limits that are established are designed to protect all individuals, males, females, pregnant females, both sexes intending to have a family, and the unborn.

And so, you know, typically we don't -- I mean the internal documents that we have highlight what the critical end point was that we were thinking about in the margin of safety that's built in to protect that susceptible sub population.

Safety data sheets don't get into that kind of detail, like the OEL is based on this particular effect and it's got a safety factor of

100 built into it, but it certainly discusses all of the potential effects, and if they're written very well, get into giving you some idea of where the no effect levels were, et cetera, so you can infer from that typically what the main concern was with the compound.

Certainly some of the earlier sections of the sheet, I guess section 3 is becoming section 2 under the GHS system, and that's designed to provide an opportunity for the reader to see what the primary hazards, the most important adverse health effects that are associated with the compound, and I would assume that any driver for an occupational exposure limit would be reflected somehow in that label text that appears up front.

MR. REED: Thank you, Bruce. Any additional comments or questions?

MR. SCHATZ: Tony Schatz again, Shering. This is to follow up on what Bruce said about the MSDS and the Alert not being a stand alone document. I guess the question I have would be,

and one of the concerns I have is, the Alert allows for people to put things on the list at their facility based on the definition in the Alert, et cetera.

Obviously, that's going to lead to inconsistencies of drugs being on different lists and different facilities. And I know that you're trying to come up with an expert list, so to speak, and it's a recommendation, there's no regulatory arm behind it, but it's -- are there any plans or any text in the Alert moving forward or anything that would kind of give people an idea of the expertise that's involved and required to put something on a list?

Because there are a lot of people out there that are just aren't qualified, frankly, to make that determination and put something on the list. Is there anything going forward to, maybe in the text portion, to explain what the expertise is that's required and how the list has come together from NIOSH so that maybe people would refer to that more than doing their own thing, so

to speak, or just some comments on that.

MR. CONNOR: This is -- actually, we addressed this early on, because we developed -- we took lists that had already been developed, and we were aware that these were the drugs that were used in that facility, and they may not use all the drugs that were considered hazardous, so that's why we -- we actually had a number of other lists that we did not include when we developed the first one, because some institutions would just list the antineoplastics as hazardous drugs, and I would say the majority of them were doing that, the other list that we found.

These lists were fairly comprehensive. The NIH list was the most comprehensive because they do handle so many different drugs. The one that Bruce developed for Pharma was quite comprehensive. But we were afraid that we may be missing some because they were not being used at those institutions.

The other part of that is, people have been and are doing -- generating their own lists.

And we developed the NIOSH Alert so they could look to this list for guidance. We also have some wording in the appendix A about how to generate your own list, what type of information to put together. There are some -- not a lot of detail.

But a number of institutions, like NIH is obviously a good example. They have a small committee that reviews the new drugs that they start to use and whether it should be handled as a hazardous drug. Other health and safety committees in hospitals and other institutions also do this to some extent, but they may not have the expertise to do it, as you mentioned. So, I don't know, we could include some more guidance about how to do this, that's something we could look into.

MR. REED: Tony, do you think that the guidance that's in the Alert now needs to be expanded?

MR. SCHATZ: I think it could be a little bit, you know, I can't get into the details at the moment -- but if you look at a definition

of what a carcinogen is or -- things that we discussed about -- those kinds of decisions that are very -- that someone -- trained to do that --

MR. REED: I'm sorry, could you speak here?

MR. SCHATZ: My voice doesn't carry. As far as the details right now, I can't, without looking through the Alert again and looking at the specific language, give you an idea of what should be updated, if anything.

But some of the concern of what's come up today about tumors in one species of mice, or you know, in female mice, but not in rats, et cetera, and some of the weight of evidence determinations that we make as experts in the field of toxicology or whatever, you know, maybe we need to expand on some of that, I don't know.

But dose response certainly is important, and we talked about that today, so I guess when you look at a definition, if you don't know this as a background, if you're not trained in this, you look at carcinogen, you look at

repro, you look at developmental tratagen(?), and you may not get all those nuances and all those important weight of evidence and dose factors that you need to put into making a decision, and maybe we need to expand that, maybe we don't, I'd have to look at the document a little closer.

MR. REED: Okay. Thank you.

MR. NAUMANN: Bruce Naumann, Merck again. Just going back to the original activity on the list, it's not my list, I was actually in Chuck's role last time, you know, so I was representing Pharma, and you know, one of the things that we actually suggested the first time around was, we were expressing concerns about having a list, you know, all the things that you have mentioned, you know, lists are outdated, you know, the minute they're published and so forth, what about all the old compounds that didn't quite make the list the first time.

And I think our suggestion was that what we ought to really do is, try to identify those types of drugs that tend to, you know, find

themselves on the list. And we pointed to the American Hospital Formulary Service therapeutic classification criteria, which actually does -- was reflected in the list, and that, you know, gives the users some additional information to help them understand the types of compounds.

So I suspect we'll probably never -- we'll have to think about it I guess as we go through it, and maybe next time, you know, is having a list really the best approach or giving more general guidance, telling them to look up the classification, if it's in one of those categories, it's in, if maybe it satisfies certain dose criteria. I think the other Pharma comment last time was to try to capture this concept of dose response, not purely hazard, but hazard plus potency in terms of the dose cut-off.

So the ten milligrams per day clinical dose and the, you know, the animal dose of a milligram per kilogram per day were recommended as really being hard wired to the definition and not, don't take this the wrong way, you know, buried in

the fine print in a footnote.

And I think, you know, the people that are qualified -- there are people qualified, there are people running pharmacies that have, you know, Ph.D.'s in pharmacology and certainly capable of evaluating dose response.

So if you have the right people involved, it's very easy to apply some very straight forward criteria, and that's the thing, we have to keep it simple and direct at achieving, you know, what it is we're trying to accomplish in terms of the types of compounds, including the potency of those compounds, so hopefully we'll get there.

MR. CONNOR: Thanks. I'll tell you, we've got a lot of feedback from individuals like out in the middle of North Dakota somewhere, and you know, I'm not -- I'm just using that as an example, but they really appreciate having the list with some guidance. I mean they really need it. They don't have the expertise to do it. As I mentioned, some facilities have put together a

committee, they may have a pharmacologist or a toxicologist on their committee, and so they do have some of the expertise. But a lot of places don't do that, they have not been able to generate their own list. So it has been helpful to them to have some type of guidance.

MR. REED: And I would add to what Tom said that we had this internal discussion certainly within NIOSH about the need for a list, and I think we felt that it was very important to have such a list. Doctor Howard, the Director of the Agency, was at least as adamantly supportive of the list, if it were a living list, and, hence, this meeting and the process for updating it on a periodic basis. Are there any other questions or comments?

Okay. Not seeing any questions, I think we'll -- I'll just have some closing comments. And I'm not sure, Anita, we don't want to put you on the spot if you want to say anything, or Tom. But on behalf of NIOSH, and I guess originally on behalf of the entire working group that helped get

this all -- effort off the ground with the Alert, and on behalf of NIOSH itself and the hazardous drug group that will -- that has done so much work so far, and then most importantly, I think engaging the expert panel, thanking them in advance for their hard work in helping assess this information for the final NIOSH decision on the update is very important, so I want to thank you for that. Barb has something additional to say here. Barb is reminding me, I guess I thought I had done that, but just to be perfectly clear, if there are comments on the specific drugs themselves, you know, assuming that we have the time, we can do that now.

There's also the mechanism for that through the docket, as well, where you can provide that information up until September 20th. So if you have comments, thanks for that reminder, Barb, if you have comments on the specific drugs themselves, we have time to do that now if you're ready to do so. So anything I think is fair game basically is what we're saying, the process, the

definition, and the specific drugs themselves.

MR. SCHWARTZ: Chuck Schwartz from Pfizer. Not wanting to go to specific comments, but getting a little closer there, the -- one of the things that I wonder about is, should we be really concerned and calling out specific doses that define -- specific doses in terms of a clinical dose or animal toxicology studies or such that appear to be black and white lines, or does the whole thing boil down to it all depends.

And one of the things that I'm thinking about here is that many times the therapeutic does of the drugs are based on very, very specific and fine detailed pharmacologic end points. Some of them have no relevance in a healthy population, and they only effect patients who have a disease. So if we start to look at just the dose of less than X milligrams per day, we start to get tangled up in wasting resources, and very sensitive to what was said before about focusing our resources on the drugs that really are hazardous. And there are some out there that really -- this is a great

tool to use.

There are some that really belong here, and you know, the overall effort is tremendous. But we've got to be careful that we don't use bright lines of X milligrams per kilogram in a toxicology study, an OEL of less than however many micrograms per cubic meter, a dose of so many milligrams per day. I mean serious organ toxicity, carcinogenesis, developmental reprotoxicology, that's what we're after, that's what we've got to focus on, not fine pharmacology.

MR. CONNOR: I think Bruce mentioned that we buried the footnote. We did not want to be wedded to a specific number. And in that footnote we say that it is used in some instances to make these determinations. But we did not want to have a really, you know, a black and white cut-off line as you mentioned, realizing that there are -- there will be exceptions. And that's why we kept the footnote the way it was.

And the other part of that, there are certainly some targeted therapies now that will

only bind to certain receptors. If you don't have that -- it's not going to bind to those receptors. So, you know, we're aware of that, we're trying to take that into consideration. Again, it's the gray area that's really difficult. The black and white ones are fairly straight forward, but we're asking your help on the ones in the gray area.

MR. REED: Are there any additional comments or questions? And Barb's reminder, do you have any comments, for example, on the specific drugs themselves that we proposed adding, or those that may be missing from the list that you think should be added?

MR. CONNOR: If we do adjourn, it sounds like we may be, do we want to keep the individuals on the panel here for further discussion?

MR. REED: Yeah, I was just going to mention that the panel of experts, for those who are here, and John, I know that you may be filling in for Caroline from Federal OSHA, we would like to spend a few minutes just to talk about the process from here, the fall meeting, in

preparation for the fall meeting, where we assess all of the information that has been put into the public domain. So I guess one last opportunity for questions and comments. Okay.

MS. McCONNELL-MEACHEN: Mary McConnell-Meachen from Boehringer Ingelheim. We had a little discussion earlier about list versus no list, and while my personal preference is a process as opposed to a list, I think if we're going to have a list and we really want it to be a well defined list, then we need a process to go back and look at the things that were left off and not just wait for people to make suggestions, but an organized approach to look at older drugs that might have been missed.

MR. REED: From the original list?

MS. McCONNELL-MEACHEN: From the original list, yes.

MR. REED: Okay, thanks.

MR. CONNOR: Bruce, was it you and Chuck that helped develop the Pharma list?

MR. NAUMANN: Chuck is representing

Pharma this time --

MR. CONNOR: Okay.

MR. NAUMANN: -- as I was last time, and basically there's like this network --

MR. CONNOR: Okay. So that was fairly comprehensive, the evaluation that you guys did at that time, was it not?

MR. SCHWARTZ: Just for the record, I was not part of that process.

MR. CONNOR: Okay, all right.

MR. SCHWARTZ: That's Bruce's fault.

MR. NAUMANN: That's right. As I mentioned before, we looked at the proposed list, which came from the various institutions, NIH being the most comprehensive, and we kind of got a sense for the type of compounds that were included on these existing lists and took a step back, looking at the definition and tried to understand, you know, what sorts of compounds were we really concerned about outside of the antineoplastics, and that's why we got into the ASHP AFHS, you know, classifications scheme. And so we did, we

did a very comprehensive review of compounds. I guess looking back, I think we extended it beyond -- obviously we extended it beyond the compounds that were already on the list, because -- actually I think about -- I was tallying them up on the airplane, and we actually proposed about 20 percent more compounds be listed, I guess.

So how many are on there, 132? I think we had about 20 or 30 compounds that we added to the list as part of that process based on looking at other therapeutic classes that had mostly reproductive and developmental toxicity concerns that were not included in the original list. So, yeah, I would say it was pretty comprehensive last time.

And we had a dialogue about getting into some of these gray areas and trying to incorporate or factor in dose response to the extent we could, and I think we were probably more inclusive than less inclusive kind of on purpose because of the goals of what we're trying, you know, I think what you're trying to accomplish here, knowing that

maybe in some areas they're not paying attention.

So -- and then we get into this philosophical problem of having too many compounds and diluting it. So it's a tough line to walk, but I think it was pretty comprehensive the first time around. And that's why, as you indicated, when you did your retrospective review, it came in pretty close, right, relative to the definition that --

MR. CONNOR: Yes.

MR. NAUMANN: -- we have working with right now.

MR. CONNOR: So when you went back and looked at it, you would look at like all antineoplastic drugs on the -- list?

MR. NAUMANN: We looked --

MR. CONNOR: You would look at all neoplastics?

MR. NAUMANN: -- we looked at the monographs in the specific categories that we had identified that seemed to be consistent with the NIOSH definition.

MR. CONNOR: Okay.

MR. NAUMANN: And there were maybe about eight or nine different sub categories outside of the antineoplastic. It went through, you know, the compounds that were at least included in that -- the information monographs that were available at the time.

MR. CONNOR: I'm just getting at, would we have missed drugs in those categories?

MR. NAUMANN: That document doesn't include all drugs.

MR. CONNOR: All right.

MR. NAUMANN: So there may be some internationally. Even the PDR I think reflects mostly drugs that are sold in the United States primarily.

MR. CONNOR: Okay. So that gets back to Mary's question, okay. Thank you.

MR. NAUMANN: Yeah; so there may be some older drugs out there that should be listed and there probably should be some formal mechanism to go back and get caught up if, in deed, and it

sounds like we do want to stay with a, you know, a list of some sort even though we'll probably continue to call it an example list, but we don't want to leave obvious ones off the list and mislead people.

MR. REED: Great; thanks, Bruce. Any other questions or comments? Okay. Again, I guess this -- Tom mentioned earlier, we would like the panel to stay on, all who are here. And also, the two members -- additional members of the NIOSH working group, if you can, that would be Jim O'Callaghan and Doug Trout, just to chat about the process from here on out.

And so, again, I guess I want to thank you all. This is a great meeting for NIOSH in terms of assessing the public information about this list. And I guess I would just lastly say that it's -- as the working group effort was years ago, this effort is great because it focuses on sort of commonalities in a diverse group of people, the commonality being worker health. So with that, thank you very much for your comments.

(Whereupon, at 11:46 a.m., the PROCEEDINGS were adjourned.)

* * * * *

CERTIFICATE OF NOTARY PUBLIC

I, CARLETON J. ANDERSON, III, notary public, do hereby certify that the foregoing PROCEEDING was duly recorded by a court reporter under my control and thereafter reduced to print under my direction; that said transcript is a true record of the testimony given by witnesses; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this proceeding was called; and, furthermore, that I am not a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

CARLETON J. ANDERSON
Notary Public, District of Columbia
My Commission Expires October 31, 2011

C. J. Anderson

Carleton J. Anderson, III,
Notary Public for the District of Columbia
My commision expires October 31, 2011