

FOOD AND DRUG ADMINISTRATION  
INSTITUTE FOR SAFE MEDICATION  
PRACTICES

AND

U.S. PHARMACOPEIA

PUBLIC WORKSHOP

IMPROVING PATIENT SAFETY BY ENHANCING THE CONTAINER  
LABELING FOR PARENTAL INFUSION DRUG PRODUCTS

Thursday, January 11, 2007

The workshop came to order at 8:00 a.m. in the Lister Hill Auditorium of the National Library of Medicine, Building 38A of the National Institutes of Health Main Campus, Bethesda, MD. Dr. Gerald Dal Pan, director of the Office of Surveillance and Epidemiology, presiding.

PRESENT:

GERALD DAL PAN, MD, MHS, FDA  
ERIC DUFFY, PHD, FDA  
CAROL HOLQUIST, RPH, FDA  
SHAWN C BECKER, MS, BSN, RN, USP  
DIANE D. COUSINS, RPH, USP  
JAMES W. KELLY, MS, PHD, RPH, USP  
MIKE COHEN, RPH, MS, SCD  
INSTITUTE FOR SAFE MEDICATION PRACTICES  
ALLEN VAIDA, PHARMD  
INSTITUTE FOR SAFE MEDICATION PRACTICES  
DEBORA SIMMONS, RN, MSN  
UNIVERSITY OF TEXAS  
TIMOTHY LESAR, PHARMD  
ALBANY MEDICAL CENTER  
VICKI DREWS  
BAXTER INTERNATIONAL  
SUSAN OLINGER  
B. BRAUN MEDICAL, INC  
MARY BAKER, PHARMD, HOSPIRA, INC  
TOM WILLER, PHD, HOSPIRA, INC

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

## A-G-E-N-D-A

Welcome . . . . .	4
<i>Gerald Dal Pan, FDA</i>	
Scope of Medication Errors . . . . .	6
<i>Mike Cohen, ISMP</i>	
Historical Perspective . . . . .	28
<i>Diane Cousins, USP</i>	
<u>Session I: Container Label Information Requirements</u>	
Moderator Introduction . . . . .	39
<i>Allen Vaida, ISMP</i>	
Overview of USP Requirements . . . . .	40
<i>James W. Kelly, USP</i>	
Overview of FDA Requirements . . . . .	47
<i>Eric Duffy, FDA</i>	
Small-Volume Parenterals - Manufacturer Presentation on the Challenges from the Industry Perspective	55
<i>Vicki Drews, Baxter International</i>	
Large-Volume Parenterals - Manufacturer Presentation on the Challenges from the Industry Perspective	
<i>Mary Baker, Hospira . . . . . 75</i>	
<i>Tom Willer, Hospira . . . . . 80</i>	
Panel Discussion and Questions from the Audience	89
<u>Session II: Minimizing Confusion Among Product Labels</u>	
Moderator Introduction . . . . .	130
<i>Shawn C. Becker, USP</i>	
Nursing Perspective . . . . .	132
<i>Debora Simmons, University of Texas MD Anderson Cancer Center</i>	
Pharmacy Perspective . . . . .	156
<i>Timothy Lesar, Albany Medical Center</i>	
Manufacturer Presentation on Industry Solutions and Proposals . . . . .	186
<i>Susan Olinger, B Braun Medical, Inc.</i>	

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

Panel Discussion and Questions from the Audience 195

Moderator Wrap-Up of Session II; Instructions for  
the Open Public Hearing . . . . . 223

Open Public Hearing

Gerhard Maher, Schreiner MediPharm . . . . . 224

Bona Benjamin, American Society of Health System  
Pharmacists . . . . . 228

Jerry Phillips, Drug Safety Institute . . . . . 233

Miriam Klein, Woodhull Medical and Mental  
Health Center . . . . . 240

Dennis Tribble, ForHealth Technologies, Inc. . . 246

Meeting Summary and Closing Remarks

Meeting Summary . . . . . 253  
*Carol Holquist, FDA*

Closing Remarks . . . . . 256  
*Gerald Dal Pan, FDA*

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

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

8:05 a.m.

DR. DAL PAN: My name is Gerald Dal Pan.

I'd like to welcome you today. I'm the Director of FDA's Office of Surveillance and Epidemiology within the Center for Drug Evaluation and Research. And within our office we have a Division of Medication Errors which concerns itself largely with the identification and prevention of medication errors.

And we're pleased to welcome you today to this one-day public workshop cosponsored by the FDA, the U.S. Pharmacopeia and the Institute for Safe Medication Practices on the topic of How to Improve the Labels on Intravenous Drug Products to Minimize Medication Errors. So today we have a unique opportunity to hear from all the different stakeholders to get a better understanding of the medication error issues they face and the challenges they have in making changes to improve patient safety.

We'll hear today from the FDA and from the USP which are the two groups that set forth the requirements for labeling, and we'll also hear from the Institute for Safe Medication Practices, healthcare practitioners, manufacturers and the public. Today's meeting is very timely in that it

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

(202) 234-4433

[www.nealrgross.com](http://www.nealrgross.com)

1 follows the July 2006 Institute of Medicine report  
2 on minimizing medication errors which recommended,  
3 amongst other things, that FDA work with other  
4 stakeholders to improve product labeling. This  
5 meeting though will not cover all aspects of product  
6 labeling, but will instead focus on improving the  
7 labeling for small-volume and large-volume  
8 parenteral infusion products. And we'll take the  
9 information we gain from today's workshop into  
10 consideration when we get involved in future  
11 decision-making on labeling requirements or other  
12 regulations concerning these products.

13 We'll begin the workshop with two  
14 overview presentations, one on the scope of  
15 medication errors that are seen with these products  
16 and the other will give us a historical perspective  
17 on the topic we're addressing today. Then we'll  
18 begin with Session 1 which includes presentations  
19 and a panel discussion on container label  
20 information requirements. After the lunch break  
21 we'll continue with presentations and a panel  
22 discussion on how to minimize confusion among  
23 product labels. During both the morning and  
24 afternoon panel discussions we encourage audience  
25 participation so please use the microphones if you

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 have any questions for the panelists or if you want  
2 to make any other comments. Our final session which  
3 will be immediately following the afternoon break  
4 will be a one-hour open public session where we will  
5 hear from those who signed up to speak through the  
6 Federal Register notice. Let me add here that we  
7 have a very packed agenda today. We have lots of  
8 speakers, and we are aiming to finish on time. So  
9 I'll ask each of the session chairs to ensure that  
10 your session and the speakers within it keep to the  
11 schedule we've outlined. So by the end of this  
12 meeting we hope to have a better understanding of  
13 the experience and perspective of each of the  
14 stakeholder groups as well as ideas and  
15 recommendations on how to improve the labels on  
16 intravenous drug products to minimize medication  
17 errors. So we have a full program and let's get  
18 started.

19 Our first speaker today is Dr. Michael  
20 Cohen who is President of the Institute of Safe  
21 Medication Practices, a non-profit organization  
22 devoted entirely to medication error prevention and  
23 safe medication use. Dr. Cohen's presentation will  
24 be on the scope of medication errors. So Dr. Cohen?

25 DR. COHEN: Thank you. Well, good

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 morning everybody. Thank you, Dr. Dal Pan. Let's  
2 see, my slides. This will take me a second here.  
3 Do not start the countdown until my first slide is -  
4 we only have, you know, everybody's squeezing in  
5 their 15 minutes or whatever. There we go. Okay.  
6 Well first of all, I'm probably one of the few  
7 people in the room that goes back to the days when  
8 we were making our own IV solutions, believe it or  
9 not, and sterilizing them. When I first started in  
10 hospital pharmacy that was still going on in some  
11 hospitals around the country. And through the years  
12 certainly a lot of improvements have been made. I  
13 think personally one of the most important areas of  
14 all has been the adoption nationwide and really  
15 internationally of pre-mixed solutions of drugs in  
16 large-volume parenteral containers, or containers  
17 from 25ml on up, especially those that contain high-  
18 alert drugs, ones that we previously mixed and  
19 unfortunately sometimes caused some very, very  
20 serious medication errors. I think the labeling in  
21 general has improved as well, but certainly there is  
22 still room for improvement.

23 And just in the way of background, I  
24 just wanted to tell you at least from my memory of  
25 kind of how we got together to have this meeting.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 We actually had several incidents that involved  
2 inadvertent direct injection of sterile water for  
3 injection. And these were accidentally given  
4 because they were mixed up with other containers or  
5 in some cases sterile water was actually used  
6 intravenously in patients where it was intended  
7 actually to be used for - a different solution was  
8 supposed to be used for plasmapheresis. But  
9 unfortunately the way that the drug information  
10 appeared, it looked like sterile water for injection  
11 could be given and it was actually used in the  
12 pharmacy to compound some of these solutions in  
13 error and unfortunately patients died. There were  
14 several fatalities that occurred. And so we had  
15 heard of this happening in the past where sterile  
16 water was confused with other products. As a matter  
17 of fact, at one time one of the manufacturers  
18 actually used the abbreviation "DW" on their label  
19 for distilled water and it was mistaken as 5 percent  
20 dextrose water and was actually accidentally  
21 infused. At any rate, in looking at the containers  
22 it certainly looked like there was room for  
23 improvement as far as the warning systems and you  
24 can certainly see how people could possibly confuse  
25 this and how the warnings were rather weak on the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 container. I know some of the manufacturers  
2 actually, in response to a series of these incidents  
3 that happened - it was about six or seven years ago  
4 - did in fact change their labeling. But anyway -  
5 and improved their warning.

6 In the discussions that we had with some  
7 of the companies, we had people visit us from Baxter  
8 and also Hospira. I guess it was Abbott at the  
9 time. And we also interacted with B. Braun. It  
10 just seemed like everyone in the industry was  
11 interested in taking a look at the parenteral bag  
12 labeling, the infusion bag labeling, the infusion  
13 bottle labeling, and we recognized, for example,  
14 there was a lot of rather unnecessary information on  
15 some of the labeling that was basically covered up  
16 anyway with pharmacy labels and just all thought it  
17 would be a good idea. So we began to interact with  
18 FDA, with Carol Holquist's group at the Division of  
19 Medication Error Technical Support, and Mary Gross  
20 was there at the time, and the idea came forth about  
21 having a public meeting which is what brought us  
22 here.

23 So what I wanted to do in the time that  
24 I have is kind of go over - now, I was asked to talk  
25 about the scope of medication errors, and I'll kind

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 of touch on that, but it's a little difficult to do  
2 because even one incident that's serious could take  
3 quite a bit of time to actually describe. So what I  
4 tried to do was I went back into the medication  
5 error reports, the newsletter articles that we've  
6 done at ISMP and kind of tried to pull out the major  
7 areas that I think need improvement with parenteral  
8 labeling. So we'll go over that and I'll talk about  
9 some recommendations along the way. Dr. Dal Pan  
10 mentioned the Preventing Medication Errors Report  
11 which was published this past July, and right there  
12 in Recommendation Number 4 there's a license for us  
13 to even have this meeting, the beginning of perhaps  
14 guidance statements from the Food and Drug  
15 Administration to help internally and also with the  
16 industry to improve this labeling. And so this is  
17 kind of a first step in maybe even addressing this  
18 particular recommendation is getting all of us  
19 together in one room and starting to hash out some  
20 of these problems.

21 I think the first issue is the kind of  
22 label clutter that we see. I can tell you both as a  
23 practitioner for 28 years and also interacting with  
24 nurses, pharmacists and physicians around the  
25 country that really you can pretty much bet that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 people are not reading the text on the IV bags. And  
2 it's often, as I mentioned a little bit earlier,  
3 covered up. We have bar codes on these bags now.  
4 They're not as readable as they should be. We're  
5 certainly hearing that, or getting that kind of  
6 feedback from organizations that have adopted bar  
7 code systems. And one of the main reasons even for  
8 pulling this together as I said was to examine this,  
9 do we need this type of text which really doesn't  
10 advise you of potentially harmful situations that  
11 could be better presented with a larger warning, for  
12 example, in some situations. So we'll examine some  
13 of those as we go along. So that would be one  
14 objective, to take a look at the readability of  
15 these labels. And even the positioning of the  
16 concentration information. There's a lot of  
17 inconsistency here. Sometimes you'll see the dosing  
18 above the name of the solution, sometimes you'll see  
19 it below, sometimes you'll see a concentration  
20 expressed, sometimes you'll see milligrams or  
21 milliequivalents expressed for the same product by  
22 another manufacturer. And this is something that  
23 actually I believe leads to medication errors when  
24 nurses are confused, when they see a product that  
25 they're not used to for example expressed in one way

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 and then other products in other ways. And I'll  
2 show you some good examples of that.

3 Tim Vanderveen from ALARIS has been good  
4 enough to share this slide with several of us.  
5 You're probably going to see a couple of others  
6 using this slide today as well, and I know we have  
7 people here that are front line practitioners  
8 that'll probably even expand on this. And this is  
9 the actual, how these solutions are actually used.  
10 And sometimes in critical care you have a number of  
11 these solutions that are actually hanging facing  
12 you, not facing you, some with pharmacy labels, some  
13 not with pharmacy labels, some piggyback containers,  
14 some base solutions, et cetera. And obviously it  
15 becomes very, very difficult for nurses and those at  
16 the bedside, others at the bedside to even not make  
17 mistakes.

18 One area I think that we need to look at  
19 is expression of concentration and strength. So  
20 here's a good example of this inconsistency that I  
21 was just talking about. On the left you have a  
22 product where the milligrams is the expression used  
23 for nitroglycerin and 5 percent dextrose. Then in  
24 parentheses you may be able to see at the bottom  
25 here it listed as 400 micrograms per milliliter.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 This is the exact same solution, yet this  
2 manufacturer expresses it as micrograms per  
3 milliliter and then in parentheses 100 milligram per  
4 container. These have both been around for many  
5 years and I think we first pointed this out you know  
6 in our journal articles maybe about 20 years ago.  
7 But it's still the case today as far as I know, and  
8 I still think there's a real good possibility of  
9 confusion. I think you can see how easy it would be  
10 to confuse these. And there are other strengths as  
11 well of these solutions, other concentrations of the  
12 pre-mixed and so that is a particular problem. And  
13 I think it needs some consistency. So that would be  
14 one area I think we need to focus on today.

15 Another is the location of the  
16 concentration and strength. You can see the problem  
17 here. On the right you have a 70 percent dextrose  
18 solution. On the left you have a 10 percent  
19 dextrose solution and depending on the background  
20 and how the folds of the bag are, it's very easy to  
21 see how confusion could occur between the  
22 concentrations. Now, this slide was taken some time  
23 ago. I don't know of any regulations that would  
24 change this or any specific guidance that would  
25 change this. However, some of the manufacturers

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 have addressed this on their own, and I think you'll  
2 see some really good designs that would prevent this  
3 type of mix-up, but we have had to deal with this  
4 situation in the past.

5 Another, on the right 40 milligrams per  
6 milliliter for the magnesium sulfate bag on the left  
7 and 10 milligrams per milliliter for the magnesium  
8 sulfate bag on the right. Good background on the  
9 label, but again you know depending on how this bag  
10 is held in the pharmacy that might be missed. This  
11 is a product that I actually picked up from a very,  
12 very serious error that occurred outside the United  
13 States, and I think you can easily see the problem  
14 here as well with the D-5 versus D-50, just that  
15 slight turn in the label. So one of the things I  
16 think we could do a better job of is the positioning  
17 of the actual concentration for these high-  
18 concentration products. And not that - I'll show  
19 you this one. Not that this is adequate, but I've  
20 found this in my slides. On the left is a 50  
21 percent dextrose and you can see that the 50 percent  
22 designation is in both corners of the upper part of  
23 the label there. And I think that's the kind of  
24 thing that's helpful, although I don't think the  
25 text here, the font size, is large enough. I think

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 we could do a better job with that. And it also  
2 appears when you turn the bottle upside down. I  
3 think you know there's - it would be a good safe  
4 labeling practice to do this with the high  
5 concentration dextrose products and perhaps some  
6 other products to reduce confusion with similar-  
7 looking products.

8           Again, with some inconsistencies, and  
9 some of this might involve USP. 0.3 percent  
10 potassium chloride. I've never once in my entire  
11 career seen anyone order 0.30 percent potassium  
12 chloride. They've always ordered it in millimole or  
13 milliequivalents. And so you kind of wonder why do  
14 we need that type of expression of the concentration  
15 at all. And one of the problems is that could very  
16 possibly be confused with a concentration of another  
17 drug. As an example and not necessarily with  
18 potassium chloride, but as an example we've had mix-  
19 ups between 3 percent sodium chloride, a hypertonic  
20 solution, and 5 percent dextrose and 0.3 percent.

21           The strength here above the drug name.  
22 We love the idea of the use of tall man letterings,  
23 or mixed case lettering as some refer to it. And  
24 this was designed in this particular case to reduce  
25 confusion with another product that's frequently

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 mixed up, dobutamine, so we really appreciate this  
2 representation. However, I do have two comments  
3 about the use of tall man letterings. One is,  
4 again, there is a real inconsistency. Quite a few  
5 years ago we asked the FDA's Division of Generic  
6 Drugs to come up with a list of drugs. We  
7 recommended some, they added some of their own. And  
8 came up with not really standards, but  
9 recommendations for the industry on how to express  
10 drug names using tall man lettering. And this was  
11 done for about, I think it was about 17 or 18  
12 generic name pairs. However, since then quite a few  
13 of the companies have gone and on their own taken  
14 non-proprietary names and then used certain letter  
15 characters within that name on their own in an  
16 inconsistent way. One manufacturer doesn't  
17 necessarily do it the same as another. And there  
18 seems to be no - it's very haphazard. There seems  
19 to be no standard, and I think that's very important  
20 that even with the IV container label that we all do  
21 this the same way and that it goes through some  
22 approval process or a standards agency so that we  
23 all do these in the right way. I think sometimes  
24 I've actually seen these used in such a way that  
25 they actually look like brand names, the mixed-case

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 labeling, and it's kind of you know not exactly what  
2 USAN and USP intended with their non-proprietary  
3 names being used almost like a brand name. So I  
4 think that's very important.

5 I also want to point out here that with  
6 most product labeling you would see the name of the  
7 drug, the brand name sometimes and then the generic  
8 name in parentheses underneath and then it's  
9 followed by the strength. Here we have just the  
10 opposite with the strength on top. I think people's  
11 eyes focus on the drug name and it's not so  
12 difficult when you have similar-looking bags like  
13 this to mix up the strengths because they're not  
14 necessarily seen so easily, especially when people  
15 are so used to with other types of labeling seeing  
16 the strengths below the drug name. I'm sure  
17 there'll be some disagreement with that.

18 One thing I think that we need to state  
19 is that highly stylized labeling for the IV  
20 containers with you know a specific type of  
21 corporate dress can be very, very - can be a very  
22 unsafe practice. This is no longer the case, but at  
23 one time there were these rocket stripes which I  
24 think contributed not necessarily in this case  
25 because we have red labeling, but what you would see

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 depending on how the bottles were turned, you would  
2 see the rocket stripe and not the drug name and that  
3 led to some mix-ups.

4 The expression of the drug name. One of  
5 the manufacturers has gone to vertical labeling for  
6 several of their products. Others have not. I'm  
7 not sure that we wanted to see this type of  
8 inconsistency, but it's another area that we might  
9 want to focus on. With package design I think we've  
10 made some real mistakes out there. I think we do  
11 need to take into consideration human factors, that  
12 people don't always do what they're supposed to do.

13 In this particular case heparin is in an upper bag  
14 and just an infusion solution in the lower bag, yet  
15 the effluent can easily be attached to an IV set and  
16 administered to the patient and given without  
17 fracturing the separation here and thus the heparin  
18 actually remains in the bag. We had quite a few  
19 reports like that and unfortunately you know some of  
20 the patients got just pure water and not the drug  
21 when they needed it for you know patients with  
22 pulmonary embolism or deep vein thrombosis. This  
23 bag was around quite a few years and then it had -  
24 when the company came up with a way to stabilize the  
25 solutions of heparin and dextrose the bag was no

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 longer used, but there are other products that still  
2 use that separation, and we still sometimes have  
3 situations where only the plain solution is given  
4 and not the drug.

5 This also has been a longstanding  
6 problem where we're requiring nurses to pull the  
7 plug out of the vial which is inside the bag.  
8 There's a process for that. And then shake it up,  
9 dilute the drug, and consistently studies have shown  
10 in the area of 1 to 3 percent of these are not  
11 actually reaching the patient where the nurses  
12 actually forget to actually mix the drug. And  
13 again, the solution can come out the port at the  
14 bottom and patients can miss antibiotics that way.  
15 So we need to take these into consideration in  
16 designing these products. On the other hand I have  
17 to say that this type of product, and there's others  
18 like it, they're very worthwhile obviously. They've  
19 enabled us to have pre-mixed solutions in some  
20 situations where they wouldn't have been able to do  
21 that otherwise.

22 I think we also need to look at some of  
23 the carton labeling. This has been a real bone of  
24 contention with practitioners around the country,  
25 especially those in the pharmacy. The code numbers

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 are much larger than the drug name, and sometimes  
2 the lot numbers as you can see, and this is  
3 obviously a situation where you know the intention  
4 is the people in materials management that need to  
5 choose these solutions will probably go more by  
6 these code numbers than the drug name.

7 Unfortunately it makes the boxes look alike and  
8 occasionally it leads to a number of medication  
9 errors, even more than just one product being  
10 misused. So that's something else I think we have  
11 to take into consideration.

12 We have the problem with look-alike  
13 containers. That's another area. This is a pre-  
14 mixed drug, Ciprofloxacin, that was confused with  
15 dopamine. It's through the medication errors  
16 reporting program we learned of that. Sterile water  
17 with potassium chloride. I think you can see you  
18 know it would be great if everybody did what they  
19 were supposed to do and read labels, but  
20 unfortunately we sometimes set them up to make these  
21 mistakes by the appearance of these containers. And  
22 again, I think we could use some of the space in the  
23 label on the right to improve the warning system and  
24 come up with a standard warning that everyone could  
25 use. We've even had mix-ups between the cold

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 storage solution that's used for organ transplant or  
2 the organ preservation and intravenous solutions.  
3 We've had respiratory therapy drugs mixed up with  
4 intravenous drugs.

5 This is a good example of something that  
6 could be done to help differentiate product. I  
7 think they do a good job with this. This also, the  
8 triangle, the octagon for differentiating the high-  
9 concentration dextrose. I think that's very useful.

10 And then of course we had a public meeting right in  
11 this room in 2004 on the use of color and there's an  
12 awful lot to be learned. You can just type in  
13 "color coding" on fda.gov's website and all the  
14 papers that were presented that day, all the  
15 opinions that were expressed, but I haven't seen  
16 anything come back from FDA so far as to how they're  
17 addressing that particular issue. I don't know if  
18 anything is forthcoming or not, but I think a lot of  
19 learning occurred that day, and I hope something  
20 good comes from it. But basically most of us agree  
21 that the use of color coding was not something that  
22 would be considered a safe practice. Most of us  
23 believe that you could apply color to help to  
24 differentiate products. We talked about the  
25 different uses of color that day. And I think that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 does in fact also apply to IV containers. And so  
2 here's a manufacturer that had both a conventional  
3 concentration and a double strength and they used  
4 colors to differentiate this. I think this is an  
5 appropriate use of color and very, very helpful in  
6 preventing mix-ups with these products.

7 Label reminders and warnings. These are  
8 three versions of sterile water. The one on the  
9 left - I'm sorry, the one on the top right, you can  
10 see where it says "Warning: Hypotonic and hemolytic.

11 Do not inject until made approximately isotonic by  
12 addition of appropriate." I think it should say  
13 right on the front label panel, right underneath the  
14 drug name, "Warning: Do not give intravenously  
15 without further," well I don't know the exact  
16 wording that I would use. Without making it  
17 isotonic or something. But there should be a much  
18 stronger warning on this because it will kill people  
19 if it is done. I know one of the companies in  
20 particular has done something with this and that's  
21 very helpful. Except I'm not sure about the color  
22 because you know everything is red here, and I'm not  
23 sure how well our eye takes in the warning. But I  
24 think it's certainly much better, and I think it  
25 would be even larger if we didn't have to worry

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 about the text below that block.

2 Then the typography is another area. I  
3 think you know it's pretty clear what these  
4 solutions are, but if you really look carefully  
5 they're not the same. This is 0.2 percent, and this  
6 is 0.45 percent. That is mixed all the time. Now  
7 is it a critical error? Probably not for the vast  
8 majority of patients, but it would still certainly  
9 be considered a medication error and it is sodium,  
10 so for some patients that are sodium-restricted,  
11 that might in fact even play a role. I think we  
12 could do a better job with the labeling. And again,  
13 the inconsistency of having the milliequivalents  
14 above the drug name.

15 Good example of product differentiation.

16 I touched on this a little earlier. And then bar  
17 coding. High alert medications. I wonder if the  
18 time should come when we actually have some type of  
19 a symbol to identify what drugs are high alert. So  
20 that might be something that could be useful.

21 I want to point out that we have had  
22 some experience knowing that in a patient room at  
23 the bedside products may in fact not even be facing  
24 the practitioner and that we also have look-alike  
25 containers. There are a very limited number of

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 colors that can be used on these containers. We see  
2 black, blue, we see red. The manufacturers have to  
3 prove that it's safe to use these because the inks  
4 can migrate into the solution possibly so there's  
5 some work that has to be done to use a new color.  
6 But in any case, you see the lidocaine here, the way  
7 that it's labeled. We had a number of mix-ups  
8 between this drug, not this manufacturer's drug, but  
9 just lidocaine in general, and other products. Some  
10 of these were fatalities. And one of the  
11 manufacturers, this is a Hospira product right now,  
12 did something that I think is extremely useful and  
13 perhaps is something that should be done for that  
14 small cadre of drugs that we indicate are high  
15 alert, those that are much more likely to injure a  
16 patient if they're misused. I know there's some  
17 added expense to do something like this, but I just  
18 think it's a terrific idea because no matter how  
19 that bag is hung you can tell that there's lidocaine  
20 in it. Some of them have placed it on the over-  
21 wrap, but of course the bags are removed from the  
22 over-wrap and then you lose that safety feature once  
23 the products are hung.

24 There's still confusion about where the  
25 labels go. I'd love to have some decision-making on

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that, the pharmacy labels. So right now they're  
2 covering the text that you see there, but there are  
3 some pharmacists that put it on the front label  
4 panel and some that put it on the back of the bag.  
5 We tend to push the idea of putting it on the front  
6 label panel immediately below where the drug and the  
7 solution are actually listed. That way you would  
8 see both pieces of information. Others like to put  
9 it on the back or even do two-sided labeling, but in  
10 this case the company has done the two-sided  
11 labeling for us, and I think that's very, very  
12 useful. So the drug always appears no matter how  
13 it's hung.

14 And on the slides, and these will be  
15 publicly available, is our list of high alert drugs  
16 that we've updated this once through a survey  
17 process, a nationwide survey. We intend to  
18 continue. In fact, this year we have a whole series  
19 of articles planned in our newsletters on high alert  
20 drugs. And we plan to re-survey the country - we  
21 haven't done this since 2003 - to learn whether or  
22 not there are other drugs that people consider to be  
23 high alert.

24 One other thing I think that we have to  
25 build into the improvements that we'd like to see is

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the idea of companies having a proper response when  
2 a medication error is reported. That's a whole  
3 other area, but when Diane Cousins and I get letters  
4 like this from the manufacturer and that's basically  
5 their response. They never tell the practitioners  
6 or us for that matter what they really intend to do  
7 internally to address a serious problem that's been  
8 reported. That's disconcerting to us ,and it's  
9 frustrating to the practitioners who want to report  
10 to our program. They feel that nothing is being  
11 done. And so we'd like all of the folks in industry  
12 to recognize that a proper response would be -- not  
13 just thank you for telling us, we've entered it into  
14 our database, we'll continue to monitor it, but  
15 we're working on a solution and you know we'll get  
16 back to you. And then incorporate you know an  
17 appropriate procedure to actually do that.

18 We think you should have appropriate  
19 staff to whom the error should be reported. There  
20 should be specific contact number for reporting  
21 errors. Training and understanding of staff and  
22 system-based causes of medication errors. The  
23 appropriate response that I just talked about. And  
24 then adding medication safety information to the  
25 labeling. I would love to see that from FDA, some

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 requirement where you have drugs like some of the  
2 ones that I've been talking about that have  
3 constantly been involved with serious errors. Why  
4 not have a medication error statement in the  
5 labeling that would carry into the different drug  
6 information texts and databases so that people would  
7 be able to see this information and know immediately  
8 there's a specific problem that needs to be  
9 addressed. I think that would help to prevent  
10 medication errors.

11 And then finally the whole idea of  
12 failure analysis. We won't go into that right now.

13 I'm sure others will talk about it as well. But I  
14 think really it's incumbent upon you not just to  
15 have your internal staff look at a label or a  
16 package or a new product or consider what it might  
17 be confused with. I think the best way to do that  
18 is take it outside of your organization and have  
19 expert panels, practitioners that can actually place  
20 this in the environment in which the product will be  
21 used and then go through a standard process. You  
22 might learn a tremendous amount of information that  
23 not only will help you as a company to not have to  
24 change products down the road, but also I think will  
25 be very important to help all of our patients

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 prevent serious errors. Thank you.

2 (Applause)

3 DR. DAL PAN: Okay, well, thanks a lot,  
4 Dr. Cohen, for that presentation. Our next speaker  
5 is Ms. Diane Cousins who is the Vice President of  
6 the Department of Healthcare Quality and Information  
7 within the Standards Division of the U.S.  
8 Pharmacopeia. And she'll give us a historical  
9 perspective on labeling for parenteral infusion drug  
10 products.

11 MS. COUSINS: Good morning and thank  
12 you, Gerald. I'm not sure what it says in your  
13 career when you're invited to do a historical  
14 perspective on something, but I have to admit it's  
15 the first time I've been asked to do this. But you  
16 know when USP was invited to cosponsor this meeting  
17 we really jumped at the chance to call attention to  
18 this subject once again. And I say once again  
19 because for USP in a sense this is a back-to-the-  
20 future and I think the presentation today will show  
21 you why that's the case.

22 What I'll do for you this morning is  
23 just briefly to describe the work of two committees  
24 that were formed in the early '90s to examine  
25 medication errors with injections that were

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 beginning to become public. I'll tell you a bit  
2 about what those committees did, their  
3 recommendations for changes in the labels and  
4 labeling of injectables and how we USP and FDA moved  
5 to implement those changes.

6 If you are not familiar with USP we are  
7 the product non-profit organization that sets  
8 standards for drug products in the United States.  
9 We do this through authority created for us in the  
10 Food, Drug and Cosmetic Act such that the standards  
11 we set are enforceable by the Food and Drug  
12 Administration. USP also operates a couple  
13 reporting programs for many years and two of those  
14 currently are focused on medication errors. This  
15 gives USP the chance to hear from front line  
16 practitioners in the design of its standards to  
17 address errors that may be occurring to prevent  
18 their recurrence for the future.

19 In the early `90s fatal medication  
20 errors began to make the press and perhaps more  
21 frequently than ever before, and the public began to  
22 demand attention to this matter. And these are  
23 errors I know many of you are very familiar with,  
24 some of them unfortunately still occurring such as  
25 the administration of undiluted potassium chloride

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 injection, the administration of intrathecal  
2 vincristine and the administration of cancer drugs  
3 like cisplatin and methotrexate that were being  
4 administered as a single dose or regimen and not  
5 over time as it was intended. And so there was  
6 attention in particular to some fatal events that  
7 occurred in Washington State. And because of those  
8 events there was a bill introduced in the  
9 legislation that would require the color-coding of  
10 all ampules, vials and pre-filled syringes by  
11 pharmacological class prior to their sale in  
12 Washington State.

13 Well, as you can imagine there was quite  
14 a stir about this, not only by the pharmaceutical  
15 industry, but by healthcare practitioners alike.  
16 And there was in fact a compromise struck with the  
17 representative who had introduced that. In fact,  
18 the industry had pointed out to that representative  
19 that the ultimate responsibility for labeling design  
20 rested with the FDA and with USP and so  
21 Representative Grace Cole had agreed at that time to  
22 table the bill if realistic guidelines could be  
23 submitted to FDA and USP by a practitioner industry  
24 task force that would study the issue of errors with  
25 small-volume parenterals at that time, the focus of

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 this particular issue. The task force in fact was  
2 organized by the PMA, which was the Pharmaceutical  
3 Manufacturers Association, which of course now is  
4 the Pharmaceutical Research and Manufacturers  
5 Association or PhRMA. And FDA and USP engaged with  
6 this committee because they were also - we were also  
7 currently studying revisions to existing labeling  
8 laws and requirements that would address errors with  
9 injections. And in fact this committee included 17  
10 individuals from eight national organizations,  
11 practitioners, and 70 industry representatives.

12 At about the same time the Home and  
13 Hospital Parenterals Subcommittee of the USP's Drug  
14 Standards Division had concern about rising injuries  
15 being reported from the accidental misuse of  
16 injectables. And the committee had identified  
17 overcrowded labels as one possible cause and of  
18 course this overcrowding becomes more of an issue in  
19 emergent situations. And this is where we started  
20 to see errors occurring as well. And although  
21 certain of these product labeling issues could have  
22 been addressed by changes to the USP-NF, there were  
23 other requirements that were federally mandated and  
24 needed revising or deletion of federal laws or  
25 regulation. And as it turned out as these two

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 committees were moving in parallel it was the report  
2 of the PMA committee that would also provide support  
3 for many of the changes that came out of the joint  
4 USP and FDA committee.

5 The recommendations that were common to  
6 both reports are listed here. And the PMA committee  
7 had decided that all injectable labels certainly  
8 must be read, but also that they must be legible and  
9 they immediately eliminated color from their  
10 discussions and said only that color should be used  
11 as an enhancement in product labels. But beyond  
12 that the two reports were very similar, and I'll lay  
13 these out for you in a side-by-side comparison.

14 First on the issue of size of  
15 information on the label. The FDA and USP committee  
16 had recommended that the drug name and strength  
17 should be the most prominent information on a  
18 product label. PMA committee agreed, but they added  
19 that the drug name in that case could be either the  
20 proprietary name or the established name that would  
21 be most prominent. And so the "either" there gave  
22 the industry the ability to choose between one or  
23 the other, not necessarily both.

24 Also regarding size of information on  
25 the label, this particular recommendation addressed

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the relative sizes of information. The  
2 recommendation asked manufacturers to voluntarily  
3 select a type size for company-related information  
4 that would not upstage the name and the strength of  
5 the drug. Now there's little difference really in  
6 these recommendations except that the PMA encouraged  
7 discretion - I thought those were interesting words  
8 - in the size of company information on the label.

9 Now most information that was  
10 recommended for elimination was probably information  
11 that could be listed in the package inserts. So  
12 it's not that it would not be available, but it  
13 would be available elsewhere than on the immediate  
14 label of the container. It was felt that this  
15 elimination of the information from the label itself  
16 would not in any way compromise patient safety and  
17 so the items that were recommended for deletion to  
18 the right side of the slide are the words "sterile,"  
19 "non-pyrogenic," "pyrogen-free," the controlled  
20 substance warning, the legend warning, the "Caution:  
21 Federal law prohibits ..." warning, and non-specific  
22 dosing information which was always on labels, "For  
23 usual dosage, see accompanying package insert."  
24 Well obviously that was not critical. The FDA and  
25 USP committee did add information and that's to the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 left. Information that could be deleted might  
2 include container descriptions, storage requirements  
3 and the controlled substances designations. Now,  
4 the two items in black actually reflect FDA's formal  
5 response to the panel's recommendation when it was  
6 published for public comment and the FDA supported  
7 keeping storage instructions on the label so that  
8 healthcare practitioners wouldn't get familiar with  
9 not seeing it on the label because the majority of  
10 products that they would handle would not require  
11 storage statements then. So their fear was that  
12 when a storage statement did occur, it would not be  
13 seen or it would be easily overlooked by the  
14 practitioner. The FDA also formally opposed the  
15 removal of the schedule for controlled substances on  
16 the label because they believed it would cause  
17 confusion since many of the products that bear that  
18 designation could be stored or handled differently  
19 depending on their schedule. For example, Schedule  
20 II narcotics versus other drugs held under lock and  
21 key.

22 In the third area of the recommendations  
23 regarding abbreviations, the FDA and USP committee  
24 recommended that drug titles should not begin with  
25 the chemical symbol such as the Na for sodium, K for

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 potassium, that if injection is part of the  
2 established name then it should appear in full.  
3 However, on very small, and they actually use those  
4 words, very small labels it may appear as an  
5 abbreviation of INJ. So there's no solid  
6 recommendation about the size that would move it to  
7 that use of the abbreviation.

8           The PMA committee agreed with the joint  
9 committee except that it supported USP-type  
10 abbreviations like hydrochloride, HCL for  
11 hydrochloride, it supported the word "injection" to  
12 be used with the trade name as well as with the  
13 established name, and it also addressed punctuation  
14 marks, that punctuation marks like a period should  
15 not be used on the label and that the designation of  
16 USP should not be used where space is critical. And  
17 of course without that designation if there is a USP  
18 monograph the drug is still required to meet the USP  
19 standards or to state how it does not if it is not a  
20 USP standard. So there's an implication even though  
21 USP isn't on the label that it does meet the USP  
22 standards.

23           The final area, the area of the term  
24 "single-use" and "multi-use" was really the area  
25 that was most contentious. And while the FDA-USP

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 committee made several recommendations, there were  
2 some additions by the PMA committee and then there  
3 were several responses by the FDA either in  
4 agreement or in disagreement and I'll go through  
5 those as well. The items that were recommended of  
6 course by the committee were the preference to use  
7 "single-use" and "multiple-use" rather than "single-  
8 dose" and "multiple-dose" because there were  
9 products that had more than a single dose in a  
10 container and yet were intended for a single use.  
11 The expression of strength would be one where the  
12 total strength per total volume would be included on  
13 the label. Where the strength of certain drugs was  
14 expressed in percentages or in milliequivalents,  
15 that committee felt that that was acceptable. And  
16 they also recognized that there could be products  
17 that were available in dry powdered form where only  
18 the total strength of the dry powder and not the  
19 reconstituted product should be on the label.

20           And the PMA committee added a few to  
21 that. First, that the total strength per total  
22 volume where the total volume was 1 ml would  
23 eliminate the use of the 1 and that the only  
24 numerals would be used in immediately preceding the  
25 ml. That the statement of total volume that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 appeared anywhere else on the label could be  
2 eliminated and that the total strength, total volume  
3 as well as the strength per milliliter which happens  
4 to be a USP requirement as well should be in close  
5 proximity to one another so there was no  
6 misunderstanding of what was in the container.

7 Now the FDA responses here were a little  
8 bit more substantive. They disagreed with the  
9 single-use, single-dose - the use of "single-use"  
10 instead of "single-dose." They had a comment that  
11 the "single-use" would imply that there's no  
12 preservative in the product and unless reserved only  
13 for use with products not containing preservatives  
14 the FDA would not support it. Regarding single-dose  
15 less than 2ml, the FDA was comfortable with total  
16 strength per total volume. And where the size of  
17 the container would exceed 2mg, you see two  
18 expressions of the strength here that would be  
19 acceptable to the FDA. So you see the total mg per  
20 total mls, the milligrams per ml, and then total  
21 milliliters in the container. Regarding the  
22 multiple-dose products, the expression of the total  
23 content was of concern to the FDA because they felt  
24 that such a large number that would be routinely  
25 visible on the label could become so familiar to

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 someone that they might expect that this was an  
2 acceptable dose for the product, and that they might  
3 then administer that level of a dose which was a  
4 multiple-dose container and that would cause errors.

5 FDA did agree with the expression of the strength  
6 on dry powders to reflect the pre-reconstitution  
7 strength.

8 Now where are we today on these issues?

9 Well, we thought that this was sort of an important  
10 recount to give you because we thought it was  
11 important for you to see that standards and  
12 regulations actually were changed where they needed  
13 to be, particularly regarding the legend for  
14 example. That there were voluntary changes that  
15 were proposed like the proportionate size of the  
16 company information to the drug name and strength,  
17 but because they were voluntary they inconsistently  
18 appeared on product labels. You'll also hear about  
19 some changes in USP standards and requirements that  
20 are currently in process, and I might add to the end  
21 of that finally after all these years. And I would  
22 expect that today we'll have some refreshing new  
23 ideas that we'll think of that can address the  
24 problems that we're seeing today. And the only  
25 thing that I would say in closing that I would hope

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that what we do identify today doesn't take another  
2 15 years for us to address as some of these have  
3 taken for us today. Thank you.

4 (Applause)

5 DR. VAIDA: Thank you, Diane. I'm Alan  
6 Vaida, Executive Vice President of the Institute for  
7 Safe Medication Practices, and I'm going to be  
8 moderating the rest of this morning's session. We  
9 heard from Dr. Cohen about the scope of the problems  
10 and Ms. Cousins talking a little bit about the  
11 historical perspective and for the rest of this  
12 morning what we're going to hear is from  
13 representatives from the United States Pharmacopeia  
14 and the FDA talking about some of the requirements  
15 for labeling for large- and small-volume  
16 parenterals. Then we're going to have an  
17 opportunity to hear from two of the manufacturers on  
18 some of the challenges that they're facing with some  
19 of the labeling requirements and also trying to meet  
20 some of the safety requirements that their customers  
21 would like for them to meet. We're going to have a  
22 break in between and then we're going to end the  
23 session this morning with an opportunity for you to  
24 ask some questions of all this morning's speakers.

25 So our first speaker is Dr. James Kelly

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 from the United States Pharmacopeia. Dr. Kelly is  
2 Scientist, Department of Healthcare Quality and  
3 Information Standards Division. He currently works  
4 with the Compounding Pharmacy Expert Committee and  
5 formally with the Parenteral Products Industrial  
6 Expert Committee. He's the liaison for USP on that  
7 committee. So Dr. Kelly?

8 DR. KELLY: Thank you. Good morning  
9 everyone. I'm going to in a way continue a  
10 presentation that Diane Cousins had started. She  
11 had shown you the background of what was going on as  
12 part of a committee's trying to establish standards.

13 And what I have done with the Parenteral Products  
14 Industrial Committee is go ahead and incorporate  
15 standards that are now coming around to help us with  
16 these problems.

17 My objectives of this presentation would  
18 be mainly to give a background of the USP  
19 requirements for labeling on parenterals. The  
20 requirements will be mentioned in General Chapter  
21 Number 1, which is Injections, and new requirements  
22 for General Chapter 1 Injections will be talked  
23 about. The USP Compendia is recognized in the Food,  
24 Drug and Cosmetic Act of 1938 and is FDA-  
25 enforceable. The Compendia contains general

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 chapters, general notices and monographs. And I  
2 might mention that if the general chapters and  
3 general notices generally take precedent unless the  
4 monograph has a different labeling procedure. Then  
5 the monograph would take precedent.

6           And I just wanted to define how the USP  
7 defines the small-volume parenterals and the large-  
8 volume parenterals. Small-volume parenteral is any  
9 injection that is packaged in containers labeled as  
10 containing 100 milliliters or less, whereas the  
11 large-volume parenterals is a single-dose injection  
12 that is intended for IV use but packaged in  
13 containers labeled as containing more than 100ml.  
14 One of the requirements for labeling from General  
15 Chapter Number 1 for Injections is that in liquid  
16 preparations, the label should include the name of  
17 preparation, percent or amount of drug in a  
18 specified volume, ingredients added to adjust pH or  
19 make the solution isotonic are declared by name with  
20 a statement of their effect. Number 2, in dry  
21 preparations to which a diluent is to be added prior  
22 to use, the label should include the amount of  
23 active ingredient, the route of administration, the  
24 expiration date, name and place of business of  
25 manufacturer, packer, or distributor, and also an

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 identifying lot number. In addition to these, it  
2 would also have to have the composition of  
3 recommended diluents and we could have names only if  
4 the formula is present in the monograph. Amount of  
5 diluent to be used should also be on the label so  
6 that we know the final concentration and the final  
7 volume, a brief description of the physical  
8 appearance of the constituted solution, directions  
9 for proper storage and an expiration date that will  
10 give the time period the constituted solution will  
11 be of a certain potency and strength.

12 The USP medication error reporting  
13 programs, and there are basically two of them, gave  
14 rise to causing changes in the requirements, mainly  
15 because of all the reporting we got from different  
16 areas where they would talk about medication errors.

17 Potassium chloride for injection concentrate has  
18 been mentioned previously. There is a section in  
19 General Chapter 1, Injections, that lists the  
20 following text. And it essentially is saying that  
21 only a black closure system on the vial can be used  
22 on these products and it's prohibited except for the  
23 potassium chloride for injection concentrate. This  
24 goes back to color-coding. Color-coding is not very  
25 popular these days and I think Mike Cohen mentioned

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that earlier. It's not the best way of all times  
2 because manufacturers tend to change colors and that  
3 can cause confusion and errors.

4 Printing on Ferrules and Cap Overseals  
5 is a section that came about, and it was originally  
6 in Pharmacopeia Forum back in 2003. And we have  
7 only cautionary statements to be printed on the  
8 ferrules and cap overseals of vials. And the  
9 cautionary statement is basically one to prevent any  
10 life-threatening condition if the injectable drug is  
11 used inappropriately. And I give example of  
12 "Warning: Paralyzing Agent." Now, this is mandatory  
13 on all these paralyzing agents that are manufactured  
14 by industry. The committee had to come about with a  
15 notice of postponement, and the reason for the  
16 postponement was because there was a new revision  
17 that had extended the official date or effective  
18 date of this section. And it went from October of  
19 2005 to February of 2009.

20 Finally, this is the last - this is the  
21 final version we have that which I just mentioned we  
22 have a revised version mainly from comments in  
23 industry and the committee's decisions. It was  
24 voted on by Safe Medication Use Committee,  
25 Nomenclature Committee, and Parenteral Products

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Industrial Committee. Now the first part is similar  
2 to the last version with the exception that we say  
3 on the top circle surface. The reason for this is  
4 that a lot of companies will clutter the top of the  
5 - of either cap overseal or ferrule with a lot of  
6 information, logos, any other kind of information  
7 there, and it will just prevent, if there is a  
8 cautionary statement put anywhere else on the cap or  
9 ferrule, it'll detract from that cautionary  
10 statement. And it goes on, the other one had gone  
11 on, with the exception that the last, Number 3,  
12 identifying numbers or letters such as code numbers,  
13 lot numbers, et cetera, can appear on the side -  
14 they call it the skirt surface of the ferrule - on  
15 vials containing injectable products. This was  
16 brought about by industry to make quality assurance  
17 better and make sure that there is no mix-up in any  
18 vials. And we do have them all with either  
19 identification or some kind of lot number to be  
20 placed on the sides so that it eliminates any kind  
21 of problem in quality control.

22 And the second section, any anti-  
23 counterfeiting scheme must not detract from or  
24 interfere with cautionary statements. As you know,  
25 there's been a lot of discussion and controversy

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 today about counterfeiting of drugs and how to  
2 prevent counterfeiting. We have had groups in  
3 different industry talk to us and say, well, if we  
4 put a lot of information on there, won't that  
5 prevent counterfeiting. Yes, it could in some  
6 instances, but however we want to make the condition  
7 that if you have an anti-counterfeiting scheme such  
8 as RFID or any kind of bar code, it must not detract  
9 from or interfere with the cautionary statement.

10           The current requirements for labeling of  
11 strength and total volume for single- and multiple-  
12 dose injections is basically to have the amount or  
13 percentage of the drug stated in the specific volume  
14 such as this example I give here for diazepam. Now,  
15 there's a new requirement that will be going into  
16 Chapter 1 for Injections, and this one also will  
17 become official in February 1, 2009. What I mean  
18 "official," it will be going in official text, but  
19 it will become effective, it will become implemented  
20 at this date.

21           For single-dose, multiple-dose strength  
22 per total volume should be the primary expression  
23 followed by strength per milliliter enclosed in  
24 parentheses. And containers less than 1ml with  
25 strength per fraction of a ml should be the only

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 expression of strength. The following format is  
2 acceptable for contents greater than 1ml, total  
3 strength, total volume 500mg per 10 ml and followed  
4 by 50mg per ml, or if any other instance where you  
5 may have a biological product it would be total  
6 strength and total volume such as 25,000 units per  
7 5ml and the strength would be of course as follows.

8 The following format will be acceptable for content  
9 less than 1ml. You can have 12.5mg for 0.625ml as  
10 an example. And there are four exceptions to  
11 expressing strength per total volume. The first one  
12 is primary expression of drug content per container  
13 would not be any practical - would not suit a  
14 practical purpose in preventing errors if you had a  
15 vial of insulin. The use of lidocaine or other  
16 similar products ordered as - usually ordered and  
17 administered by percent. So that would be  
18 applicable and acceptable. And if you have a local  
19 anesthetic, say in combination with epinephrine  
20 expressed as a ratio 1 to 100,000, in such cases  
21 total strength should be used as 1 percent,  
22 parentheses, 100mg per 10ml. And in the following  
23 one it would be dry solids which need to be  
24 reconstituted should follow the same format with the  
25 exception that only total strength of the drug would

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 be listed. I'd like to thank you very much for this  
2 presentation.

3 (Applause)

4 DR. VAIDA: Thank you. Our next speaker  
5 is - let me just get this set up here for one  
6 minute. It's Dr. Eric Duffy from the FDA who's  
7 going to be speaking about FDA requirements for  
8 large- and small-volume parenterals. Dr. Duffy is  
9 Director, Division of Post-Marketing Drug  
10 Evaluation, Office of New Drug Quality Assessment,  
11 Center for Drug Evaluation and Research, as we all  
12 know as CDER, at the FDA. He's been there for over  
13 16 years and he now has oversight for changes to  
14 manufacture and controls for all marketed drugs.  
15 Dr. Duffy?

16 DR. DUFFY: Thank you. Well, good  
17 morning everyone. Can you hear me? All right. I'm  
18 actually very fortunate to follow the presentation  
19 from the USP representative because many of the  
20 requirements for parenteral products, infusion  
21 products, come from the USP General Chapter Number  
22 1. I will review the requirements and as I say,  
23 most - as you'll see, most of the requirements do  
24 indeed evolve from the USP. However, there are some  
25 regulatory requirements which I will briefly review

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 and they're derived from sections of the Federal  
2 Register - Code of Federal Regulations rather,  
3 principally 21 CFR Part 201. There are also  
4 additional requirements in the Food, Drug and  
5 Cosmetic Act.

6 Let me start by just commenting on what  
7 the minimum requirements really are. I think as the  
8 discussion proceeds here today we'll probably come  
9 back to the same type of comment frequently and that  
10 has to do with clutter. Oftentimes really  
11 difficulty in knowing what the product is and how  
12 it's to be used is obscured by a lot of information.

13 Useful information, yes, but oftentimes it's more  
14 information than is really needed. So the  
15 regulations provide for minimum requirements, those  
16 bare bones statements that are required on the  
17 label. And I'll review them for you here.

18 The first requirement, and this is for -  
19 it's really primarily intended for presentations  
20 that are very small, very small ampules or vials,  
21 and it's principally for SVPs. The proprietary name  
22 is required. The trade name is oftentimes used, but  
23 the proprietary name is indeed required and its  
24 prominence needs to be - relative to the trade name  
25 needs to be such that it is at least half the size

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 in terms of typeface. The established name needs to  
2 be expressed according to a certain pattern, and  
3 I'll review that in a moment. The lot number needs  
4 to be there for tracking purposes and for adverse  
5 event reporting. The name of the manufacturer or  
6 the re-packer and/or distributor is indeed required  
7 and a few other assorted requirements which I'll  
8 review in a moment.

9 In terms of nomenclature, there are  
10 indeed conventions. And here I'm going into the  
11 USP. I won't go into tremendous detail because we  
12 just had a very fine presentation on this, but the  
13 classes of drugs are expressed in specific ways.  
14 There's drug name and injection, a for-injection,  
15 something to be reconstituted, then there are  
16 different types of products such as emulsions,  
17 suspensions and injectable suspensions. These are  
18 all prepared in different ways and clearly  
19 instructions for preparation are necessary.  
20 Additional USP requirements would include the name  
21 of the preparation. And the next requirement is  
22 oftentimes confusing. It's how to express the  
23 concentration or the amount of drug present. It  
24 should be expressed in terms of percent content in a  
25 specified volume. Whether that's total volume or

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 some unit volume is oftentimes a matter for debate.

2 It's not entirely clear in my opinion in the USP  
3 Part 1.

4 The total amount of active ingredient  
5 for a dry preparation should be expressed. The  
6 route of administration, whether it be IV, SC or  
7 whatever should be expressed. A storage statement  
8 should be included and the expiration dating as  
9 well. Again, the name of the manufacturer and a lot  
10 number. Now, when you have a very small label, not  
11 all of this can go on the label so sometimes a  
12 matter of debate and it's a matter of opinion as to  
13 what is the bare bones essential requirement. What  
14 is a small label is also something that is  
15 oftentimes not entirely clear.

16 The label statement should designate the  
17 volume, for an LVP the concentration of each  
18 ingredient. For example, many products come in  
19 varying concentrations. I'm giving here an example  
20 of dextrose. It should be expressed in terms of its  
21 percent. Sodium chloride as well is another one  
22 commonly used.

23 There are some specific types of  
24 products for which there need to be some warnings,  
25 essentially. Irrigation solutions should be clearly

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 labeled as not to be used for infusion. That is  
2 oftentimes a source of a problem. For safe use of a  
3 product, an injectable product, one needs to inspect  
4 it prior to use for particulate, discoloration or  
5 whatever problems might be evident just on visual  
6 appearance. So the label should not obscure the  
7 product. One needs to be able to look at it, put it  
8 up to the light or whatever. So the label should be  
9 placed so that there is sufficient clear vision of  
10 the solution that the vial contains.

11 Another case where some essentially  
12 warnings need to be present would be for a pharmacy  
13 bulk pack. It needs to be clearly stated that it is  
14 indeed a pharmacy bulk pack for multiple - for  
15 pharmacy compounding in a typical pharmacy admixture  
16 program. Pharmacy bulk packs are indeed intended to  
17 be penetrated only once, and I believe that's a  
18 potential source of error. An expiration - a use  
19 period should also be expressed in the label.  
20 That's typically four hours. And pharmacy bulk  
21 packs are intended to be limited only to injections  
22 or for injections and injectable emulsions. As I  
23 say, it needs to be clearly indicated that a  
24 pharmacy bulk pack is really only for admixture  
25 programs, so a label statement such as "Pharmacy

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 bulk package. Not for direct infusion," should be  
2 very prominently expressed on the label. The  
3 intended admixture preparation procedures should be  
4 clearly expressed. Now, obviously a lot of this  
5 information is not going to be able to go on an  
6 immediate or carton container, but this would be on  
7 an insert label. And again, the expiry, the use  
8 period should be clearly expressed.

9           There are some special cases for  
10 particular types of products for safe use. One  
11 example is for total parenteral nutrition products  
12 there are concerns about leechable aluminum or  
13 aluminum present in excipients. And so we have a  
14 regulation that requires that the aluminum content  
15 be expressed. And that can be found in the CFR Part  
16 201.323. And the label - and this pertains to  
17 large-volume, small-volume and pharmacy bulk packs  
18 of TPN products. And there should be a clear  
19 expression of the aluminum content such as "Contains  
20 no more than a certain number of micrograms per  
21 liter of aluminum." This regulation, by the way,  
22 was a long time in coming.

23           Another special case for safety reasons  
24 is the labeling for sulfites. Certain people have  
25 allergic reactions to sulfites although there's some

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 debate as to the prevalence of sulfite allergy. It  
2 depends on who you talk to about this. I've heard  
3 some people say that there are only anecdotal  
4 reports numbering less than what you can count on  
5 one hand, and others say it's far more prevalent.  
6 However, just to be cautious there is a requirement  
7 at least that it be labeled whether it contains  
8 sulfites or not, and it need not necessarily appear  
9 on the immediate container or carton label.

10           There are some additional regulations  
11 for labeling which I've listed here and the first  
12 citation I have here, the CFR Part 201.15 states  
13 that the prominence of important components of a  
14 label are required. And this of course is always a  
15 very subjective sort of discussion one enters into,  
16 what's prominent. What should be more prominent  
17 than this? Are there other components of a label  
18 that draw one's attention from the statements that  
19 need to be most prominent? Are there fanciful logos  
20 or artwork that detract from one's ability to pick  
21 up on the most important components of a label?  
22 Oftentimes an interesting discussion that we have at  
23 FDA with the industry as they're proposing various  
24 types of labels.

25           Another requirement is for where the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 expiry appears, and that should be in a place where  
2 it's, again, easily found, prominent. Oftentimes  
3 this is a subject of debate. The identity of the  
4 product needs to be clear. That's pretty much  
5 obvious. The established name is required. And as  
6 was mentioned previously there needs to be clear  
7 indication when it's a controlled substance.

8           So essentially this is what we have for  
9 the bare bones requirements, much of it referring to  
10 the USP. But when it comes to establishing and  
11 approving a label, it's oftentimes subjective and we  
12 enter into conversation with our partners in  
13 industry to arrive at what we consider to be an  
14 appropriate label for safe use of the product. And  
15 for marketed products, which is what I'm responsible  
16 for, oftentimes companies go through a program to  
17 review their product line to see whether or not they  
18 feel that the product maintains its labeling in a  
19 way that continues to provide for safe use. And we  
20 encourage manufacturers to review on a periodic  
21 basis their entire product line to see whether or  
22 not they feel that the product maintains labeling  
23 which continues to provide for safe use. And we  
24 would encourage people to come to us and enter into  
25 a conversation about potential revisions or changes

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 to labeling to improve and continue to provide for  
2 safe use of their products.

3 So that's all I had. As I say, I'm  
4 fortunate to have followed the USP presentation  
5 because we do refer in large part to the USP  
6 requirements. So that's all I had and I'm looking  
7 forward to a good conversation throughout the day to  
8 see if we can come up with proposals and suggestions  
9 for how we can best continue to improve product  
10 labeling to ensure safe use. I wanted to make  
11 reference to one of my colleagues, a pharmacist Dr.  
12 David Lewis who assisted in preparation of this  
13 presentation. Thank you.

14 (Applause)

15 DR. VAIDA: Thank you, Dr. Duffy. Our  
16 next speaker is Vicki Drews. And Vicki is Associate  
17 Director, Global Regulatory Affairs for Baxter  
18 International. She has 18 years pharmaceutical  
19 industry experience and her primary role is in drug  
20 products packaged in flexible plastic containers.  
21 Vicki is going to focus on some of the challenges  
22 for small-volume parenterals faced by industry.

23 MS. DREWS: Can you see me? It's a  
24 common problem that I have. Well, while this is  
25 getting set up, I just wanted to thank the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 coordinating committee for this meeting, for giving  
2 me personally as well as Baxter an opportunity to  
3 share our experiences and thoughts around small-  
4 volume parenteral labeling. But I also wanted to  
5 thank everybody in the audience for taking time out  
6 of what I know are busy schedules these days. And I  
7 also wanted to in particular thank a few of my  
8 colleagues, some of whom are here in the audience  
9 today, for providing me with valuable information  
10 and most valuable graphical information for sharing  
11 with you today.

12           So with that I am going to be speaking  
13 about labeling challenges for small-volume  
14 parenterals. And I did make a few notes so pardon  
15 my shuffling of paper here, but I want to make sure  
16 that I get you the right information. A quick  
17 snapshot of the next 20 minutes. I'm going to focus  
18 in on the scope of my discussion a little bit just  
19 to make sure that you have a clear perspective on  
20 the information that I'm sharing, and then we'll  
21 jump right into the challenges. We'll talk a little  
22 bit about the current state of Baxter's labeling.  
23 We'll talk a little bit about the solutions that  
24 Baxter has implemented historically over the years  
25 and discuss a little bit about the barriers that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 we've seen in implementing those solutions as well  
2 as barriers to making those solutions effective.  
3 And then I'm going to give you some of my thoughts  
4 on what would be logical next steps.

5           So as my introduction explained, with  
6 insignificant exception the experience that I've had  
7 in the pharmaceutical industry has been limited to  
8 solutions in flexible plastic containers, both SVP  
9 as well as LVP. So what I'm going to be talking  
10 about today are flexible plastic containers with  
11 solution volumes from 25ml to 100ml. And I will be  
12 focusing primarily on the labeling on the immediate  
13 container although to a lesser extent I will bring  
14 up some factors of secondary packaging labeling, in  
15 particular the labeling on the over-wraps of our  
16 containers. And at Baxter, over-wraps take the form  
17 of either a transparent high-density polyethylene  
18 over-wrap or an opaque foil over-wrap. And it's  
19 important to note that these over-wraps are removed  
20 prior to use so their value as far as  
21 differentiating products is somewhat limited. That  
22 being said with regard to narrowing the scope I just  
23 want to make note that a lot of the challenges that  
24 I'm going to be talking about today apply equally to  
25 other types of small-volume parenterals, vials,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 ampules, syringes, some to a greater extent, some to  
2 a lesser extent, but I think that a lot of the  
3 challenges are shared across the product line in  
4 general.

5 I want to talk a little bit about  
6 Baxter's SVP product portfolio. It kind of falls  
7 into two big buckets: diluents, which are the 5  
8 percent dextrose solutions, normal, half-normal  
9 saline solutions, and then there's a bucket of pre-  
10 mixed drugs in many, many different therapeutic  
11 areas. And I wanted to give you this information  
12 for a couple of reasons. Number one, because I  
13 wanted to point out that for instance in the case of  
14 penicillins or cephalosporins, product mix-ups in  
15 this category could have significant health  
16 consequences if these products are administered to  
17 the wrong patient. And similarly, products in our  
18 critical care family such as our highly concentrated  
19 potassium chloride products could have significant  
20 health consequences if the right patient gets the  
21 wrong dose. So the challenges that we've heard this  
22 morning about or the problems that we've had in the  
23 area of medication errors are certainly relevant to  
24 this category of products.

25 So what are the challenges that we see?

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Well, most obviously there are challenges in space.  
2 And complicating those challenges we certainly have  
3 the required content which Dr. Kelly and Dr. Duffy  
4 so nicely went over in great detail before I got  
5 here. But the content really in my opinion falls  
6 into two different categories. We've got required  
7 content that is driven by regulatory requirements as  
8 we heard this morning, but we've also got required  
9 content that falls into a category called legal  
10 sensitivities. These are statements that companies  
11 are reluctant to really take off of their labeling  
12 because of liability concerns. And some of these  
13 statements are rooted in history. And I think that  
14 it does us justice to take a look at these  
15 statements as we move forward to see do these  
16 statements really have value as far as the safe use  
17 of the product is concerned today.

18 The second category of content that I  
19 want to speak to a little bit is the consistency of  
20 content. I think as a company Baxter believes that  
21 having consistency in your labeling is really value-  
22 added, that you know we're using the same statements  
23 to describe the same things, we're putting those  
24 statements in the same places on the label, but we  
25 find this to be a challenging job because when we

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 submit labels for review to FDA there's an element  
2 of reviewer preference and a lot of these comments  
3 are very valid comments, and we make those changes,  
4 and we would hope that we could make those changes  
5 across all of our products, but in the end we  
6 inevitably - it inevitably leads to inconsistency in  
7 our and I don't want to say content, but the  
8 presentation of the information.

9 Another one of the significant  
10 challenges I think that we have for SVP and this  
11 probably applies to LVPs as well is in the area of  
12 color. There was a little bit of discussion,  
13 actually there was a lot of discussion this morning  
14 about color-coding and the values, but I wanted to  
15 talk a little bit about some of the limitations we  
16 see. Number one, I think that there really is a  
17 finite number of colors that we can use on our bag.

18 And even though a printer might tell you there are  
19 500 or 5,000 different Pantone colors, the  
20 difference between a lot of those colors are really  
21 not very noticeable. And second to that, some  
22 colors are just better than others for printing on a  
23 flexible plastic container. I think that we need to  
24 be looking at the contrast nature of the inks to  
25 really determine whether these are suitable and

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 effective for differentiation.

2 And also along the lines of color we've  
3 got the cost impact. For every color that you put  
4 on a bag there is a separate print plate that needs  
5 to be developed and manufactured. And although  
6 these print plates aren't made of gold, they are  
7 used in substantial quantities in the manufacturing  
8 environment. So there is a cost of equipment there  
9 and there's also an added step to the manufacturing  
10 process when we add color, and this is additional  
11 colors to the labeling. So not only does it add  
12 cost in terms of equipment, it also adds cost in  
13 terms of time. Another element of cost, and this  
14 was alluded to earlier this morning is the  
15 qualification of the inks. As was mentioned, these  
16 inks when they're applied to the immediate container  
17 do have the potential to migrate into solutions so  
18 there is a very robust qualification activity that's  
19 associated with that, with getting these inks into  
20 production including biological testing, chemical  
21 testing and then most often there is a regulatory  
22 approval process that's associated with that. So  
23 all of this put together you know what we found is  
24 that these challenges have limited our ability to  
25 really make timely changes to labeling.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1           So just to kind of give you a graphic in  
2 terms of space constraints, you'll see these are the  
3 plastic containers. And I don't have a pointer, I  
4 apologize. But there's a 25ml, 50ml, 100ml bag.  
5 All of the bags are the same width. They range -  
6 they're 3 and a half inches wide and the length  
7 varies from 4 and a quarter inches on the small bag  
8 to about 6 inches on the large bag. Oh, thank you.

9       Ask and you shall receive. If I can figure out how  
10 to work it. Okay, well I'll figure it out when I  
11 need it. Apparently I'm just not pointing it in the  
12 right place. Okay. Can you see it? Oh, I see it's  
13 very faint there. Okay. It'll do. But what I did  
14 want to mention here thought that although the  
15 overall size of the container is quite constrained,  
16 the actual printable area of the container is  
17 substantially reduced. And this is due to  
18 manufacturing considerations, the seal area, et  
19 cetera, as well as the area that is reserved for the  
20 bar code. And I - this is probably - oh there.  
21 This area here really is the area that is reserved  
22 for the bar code. And these are not exact  
23 dimensions. I put them together myself.

24           With regard to labeling content, I'm not  
25 going to belabor this. I think that Dr. Kelly and

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Dr. Duffy did a great job this morning. We've got  
2 that regulatory-driven piece, but what I do want to  
3 mention here, and I think Dr. Duffy was the one who  
4 alluded to it, is that not only do we have the space  
5 constraint on the container, but we have this fairly  
6 large quantity of information that we are required  
7 to put on the container. And in the end we still  
8 have to have labeling that's sufficient to allow for  
9 the clinician to visually inspect the solution. So  
10 it does present problems as you might imagine. And  
11 then again as I mentioned before, there are  
12 statements that we've been adding which are not  
13 really driven by regulation and standards, but are  
14 really by reviewer preference and again these are  
15 value-added statements and we tend to drive them  
16 into as many labels as we can because we do believe  
17 they're value-added. The last bucket which I talked  
18 about earlier is this bucket of liability-driven  
19 statements.

20 So at Baxter today what we've found that  
21 we have is really a state of induced similarity.  
22 And the similarity is between different doses of the  
23 same drug as well as between different drugs. And  
24 in the end - and the similarity really is an end  
25 result of the space constraints, the consistency

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that we try to drive into our labeling and the color  
2 limitations that we have from a qualification  
3 perspective. And all of this really does impact  
4 consumer and patient safety.

5 So here, since a picture is worth a  
6 thousand words, is a graphical representation of two  
7 different doses of our highly concentrated potassium  
8 chloride product. And as you can see they look very  
9 much the same. This one is actually two different  
10 drugs. So despite the difference in names, the  
11 difference in quantity, dosing you know because of  
12 the font size that we're dealing with here and the  
13 limited space that we have available, the similarity  
14 in the colors, the two products do bear a  
15 resemblance. And it's worthwhile noting here, there  
16 it is, that this area on the left of all of this  
17 text, on both of these labels is the area that's  
18 reserved for the bar code.

19 So what has Baxter done in the past to  
20 try to address some of these challenges to enhance  
21 the safety of our labeling? Obviously our goals  
22 were to differentiate between different doses of the  
23 same drug as well as between different drugs, paying  
24 particular attention to those drugs that are used in  
25 the same therapeutic area. So we have gone into

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 using color differentiation as well as graphics to  
2 help enhance the difference between the products.  
3 And this has been used both on our over-wraps and  
4 most notably the foil over-wraps as well as on the  
5 immediate container. And I say on the foil over-  
6 wraps. The foil over-wraps are very nice for us  
7 because they have much larger printable space and we  
8 have a lot more flexibility in terms of colors to  
9 put on those over-wraps because the foil itself acts  
10 as a barrier to the inks permeating into the  
11 solution. So we do have a lot more flexibility and  
12 the timeframe to getting the ink to qualification  
13 status is much less.

14 And Baxter also has had some limited  
15 experience with standards. So I'll call them quasi-  
16 standards and I'll talk a little bit more about  
17 those later. So here's an example of some color  
18 differentiation and graphical differentiation that  
19 we've attempted on our foil over-wrap. In this case  
20 this is a fluconazole solution. But you'll see the  
21 color reversal is pretty obvious. And then in the  
22 right-hand side of the title block there's a  
23 graphic, the two circles for the 200ml code, four  
24 circles for the 400ml code. But again, it's  
25 important to note that these over-wraps as I

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 mentioned before are removed prior to use and  
2 therefore probably in most instances never make it  
3 to the patient bedside.

4 I think we saw this earlier today, but  
5 although these are technically LVPs, I think it's a  
6 great example of the use of color as well as  
7 graphics to differentiate between products. And I  
8 think it was Dr. Collin who showed a very similar  
9 graphic here, the difference between dobutamine and  
10 dopamine. Another example, color and graphics on  
11 the container. Again we're looking at fluconazole  
12 where we've taken the graphics that we used on the  
13 over-pouch and incorporated them into the label. So  
14 we've got the 2 for the 200, the 4 for the 400. And  
15 here it's even more noticeable, the space on the  
16 left-hand side of both labels that is consumed by  
17 the bar code.

18 So now I'll take you through some of the  
19 experiences that we've had with labeling standards.

20 And again, these are real limited standards so I  
21 don't even know if "standard" is the right word.  
22 But we have two experiences, one outside of the U.S.  
23 and in the LVP market, and that's in Canada. And  
24 this standard was developed in part based on  
25 feedback and discussions that we'd had with Dr.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Cohen and others from ISMP. And the concept of this  
2 standard was really the prominence of key product  
3 information and the consistent location of that  
4 information so that you really have a know-where-to-  
5 look type of label. The second experience that  
6 we've had is with our heavy dextrose solutions. And  
7 I think somebody actually flashed a picture of this  
8 earlier this morning as well. These heavy dextrose  
9 solutions are used in the pharmacy for compounding  
10 total parenteral nutrition solutions. And in this  
11 case it was a cooperative effort across  
12 manufacturers of these particular products with  
13 input from HIMA and FDA. And it involved enhanced  
14 graphics as well as the prominence of key product  
15 information. We also standardized color for these  
16 particular solutions across industry and there was  
17 an effort to eliminate text as well as to  
18 standardize what text we determined to be critical  
19 to the product.

20 So here is a graphic showing the  
21 Canadian LVP standard, a standard label on the  
22 right, the old label on the left. And you can see  
23 that the three pieces of key product information,  
24 the drug, the diluent and the dose are very  
25 prominently displayed in a kind of a matrix or

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 quadrant format in the middle of the label. And  
2 this is a picture of the heavy dextrose labels. So  
3 you can see that the concentrations, which were the  
4 factor in a lot of the medication errors are  
5 prominently displayed both by increasing font size  
6 as well as graphical representation, and the  
7 pharmacy bulk package warning prominently displayed  
8 as well on the center of the label.

9           So what have we seen at Baxter as far as  
10 barriers to effective solutions? As I mentioned  
11 before, the limitations of the over-wraps. Although  
12 it's very tempting to do some differentiating using  
13 over-wraps, we do recognize that the effect of  
14 differentiation is limited here. Manufacturer  
15 variability. You know, I think this one is key.  
16 You know, if Baxter decides they're going to label  
17 their dextrose products in blue and Hospira decides  
18 that they're going to do theirs in red, the effect  
19 of the differentiation is lost. So we really need  
20 as industry and as regulators and patient advocate  
21 groups, we really need to drive consistency in  
22 standards into this area.

23           There's also human factors that we need  
24 to consider. And you know what we've found over  
25 time is that although some of the enhancements that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 we've made to our products are really good and  
2 really effective, coming out of the gate there is an  
3 acclimatization to it. Customers get used to it and  
4 over time we see the ramp of product mix-ups kind of  
5 coming back to that previous state. Other factors  
6 include color-blindness, directly related to any  
7 decisions there might be around color-coding,  
8 language barriers that we're seeing in the hospital  
9 and other clinical environments as well as the  
10 unfamiliarity with scientific abbreviations. And  
11 this is particularly relevant for products that are  
12 used in multiple care environments, in acute care as  
13 well as in home care environments where the skill  
14 level of the end user may vary. And then you know  
15 certainly another barrier from an industry  
16 perspective is the cost of making changes. And it's  
17 not that we don't want to expend the dollars to make  
18 our labeling more effective, we just want to make  
19 sure that the solutions that we're implementing are  
20 the right solutions so that we're not facing the  
21 same problem two years down the road.

22           And I wanted to talk a little bit about  
23 SVPs in particular because that is the focus of this  
24 presentation and I did show you a lot of LVP shots.

25       What we found is that these historical standards,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 in particular the Canadian standard, really looks  
2 like an acceptable solution for LVPs. We've tried  
3 to apply it to our SVP products, and we find that  
4 the space challenges that I mentioned earlier really  
5 do inhibit our ability to apply this standard as it  
6 is today. The bar code space infringement is a  
7 significant factor as well as the quantity of the  
8 required text that we talked about earlier. So just  
9 to kind of again put you into perspective, I want to  
10 remind you that although the challenges that I was  
11 talking about really came from my experience with  
12 flexible SVP products, I do think that the  
13 challenges that I talked about do have relevance and  
14 applicability to other SVPs, in particular the space  
15 constraints which are probably more notable on other  
16 SVP products and content requirements apply across  
17 the board as well.

18 I also wanted to just talk briefly to  
19 the diluent SVPs because they do present a very  
20 unique challenge. Unlike the pre-mixed drug  
21 products which are single-dose pre-mixed products  
22 that are ready to administer, the diluent SVPs are  
23 used primarily for admixture. So the bar coding and  
24 other product labeling that's on that bag as it's  
25 printed at the manufacturer is not representative of

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the admix solution as it gets to the patient.

2           So what do I think should be the ideal  
3 state today? Well, I think we need to foster bar  
4 code technology. I think it was a good thing. I  
5 think it has a long ways to go. You know,  
6 manufacturers are there with regard to getting the  
7 bar codes on the bag, but I think there's some  
8 quality issues. I think somebody alluded to that  
9 earlier this morning with regard to the scanning,  
10 and I think that there are probably still instances  
11 where hospitals don't have the suitable equipment  
12 for scanning all types of bar codes that are printed  
13 on the parenteral products. And I think that we  
14 need to take a look at our labels. We need to  
15 implement labels that are based on practitioner  
16 input, that are focused on patient safety, but that  
17 are also realistic and feasible for industry to  
18 implement. Personally I think we need to rely less  
19 on aesthetic and variable differentiations such as  
20 color and graphics, and rely more on the prominence  
21 of the key product information. I think we really  
22 need to force a good, a true knowledge of the  
23 product before it's being used. And last but  
24 certainly not least I think that we need to  
25 standardize these things across the products, across

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 all product lines, LVPs, SVPs, vials, ampules,  
2 syringes as well as across the industry. So I think  
3 this kind of boils down to developing some sort of  
4 labeling standard.

5           So what do I see as being the next  
6 steps? As far as the standard is concerned what do  
7 I see I guess as being the key elements of the  
8 standard? First of all, I think it needs to be  
9 regulatory in nature. I think that's very  
10 important. I think it obviously needs to be focused  
11 on patient safety. I think it should be developed  
12 by a multi-organizational task force and certainly  
13 representatives from the very people who are here  
14 today. And I think that we do need, as I mentioned  
15 before, to minimize the impact of human factors.  
16 Reduced reliance on color and non-value added text  
17 and increased focus on key product information. And  
18 from an industry perspective it needs to be robust  
19 and enduring to the extent possible so that we can  
20 minimize the cost of reactive changes to customer  
21 feedback moving forward.

22           So how do we remove some of the barriers  
23 that we see with regard to the standards itself or  
24 some of the product information such as bar codes  
25 that we do see as good differentiating elements?

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Well, for manufacturing and for healthcare providers  
2 I think that we really need to give serious thought  
3 to investing in new bar coding technology, to reduce  
4 space requirements - and this doesn't have to be  
5 limited I suppose to bar coding technology. I mean,  
6 any kind of auto-identification technology. And  
7 there has to be an investment in the suitable bar  
8 code scanning equipment or systems so that the end  
9 user is getting the full benefit of those bar codes  
10 for maximum patient safety. And then for everyone I  
11 think that we really need to move in the direction  
12 of developing a regulatory standard. I think we  
13 need to drive consistency across all parenteral  
14 products. We need to reconsider the required  
15 elements for immediate containers for SVPs in  
16 particular, and I think this can be done by  
17 prioritizing information for smaller containers that  
18 have space limitations and provide flexibility to  
19 alternatively include product information on  
20 secondary packaging or package inserts.

21 So in wrapping things up you know what  
22 kind of benefits could we expect to see from a  
23 standard of this sort? Obviously we would be  
24 maximizing patient safety, but I think in addition  
25 to that we would realize benefits in the area of

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 efficiency. I think it would reduce the time for  
2 labeling development, and I don't know if Dr. Duffy  
3 would agree, but I think it may even reduce the  
4 regulatory review time. If there's a standard out  
5 there, we develop the label to meet the standard.  
6 If it meets the standard, I would think the label  
7 would be approvable. And certainly there are you  
8 know there is going to be unique situations where  
9 certain products are going to require different  
10 warning statements, et cetera, but I think that this  
11 would be a good goal. I think that we would also  
12 see reduced cost. The reduced cost in product  
13 development that gets directly to labeling  
14 development, reduced cost in the product lifecycle  
15 because we as industry would probably have a  
16 minimized instance of reactive changes to address  
17 customer feedback, and I would hope, although this  
18 certainly isn't my area of expertise, that by having  
19 labeling standards that meet everyone's requirements  
20 that it would streamline pharmacy operations and it  
21 would hopefully reduce the incidence of product mix-  
22 ups thereby reducing the cost of patient care. So  
23 that's all I had. Thank you.

24 (Applause)

25 DR. VAIDA: Thank you very much. We are

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 a little bit ahead of schedule so why don't we take  
2 a break, but try to reconvene back here at about 10  
3 after 10:00, and that way there's a cafeteria  
4 downstairs. Those of you, that way you have a  
5 chance to even finish a coffee or that because they  
6 don't want food or beverage back in the room. But  
7 we'll take a short break now and then convene back  
8 here about 10 after 10:00. Thank you.

9 (Whereupon, the foregoing matter went  
10 off the record at 9:50 a.m. and went back on the  
11 record at 10:14 a.m.)

12 DR. VAIDA: All right. We'll get  
13 started back. And our next presenters are from  
14 Hospira. We have Dr. Mary Baker who's Senior  
15 Medical Manager, Global Medical Affairs and Dr. Tom  
16 Willer who's also with Hospira and is Global  
17 Regulatory Affairs Director. Dr. Willer previously  
18 worked with Abbott Laboratories as Regulatory  
19 Affairs and Dr. Baker's responsibilities include  
20 directing clinical programs in parenteral nutrition,  
21 labeling and promotional review, drug compatibility,  
22 large- and small-volume injectables and medication  
23 error reduction. Their focus is going to be on  
24 challenges with large-volume parenterals.

25 DR. BAKER: Thank you, Allen. Can

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 everybody hear me? Great. Okay. Again, I'm Mary  
2 Baker from Hospira. I'm in Global Medical Affairs.

3 I work very closely with our regulatory group and  
4 Tom Willer, also our graphics group and our label  
5 control group. We've got hundreds I'll just say of  
6 large-volume parenterals and in terms of labeling  
7 changes when you include our large- and small-volume  
8 parenterals you're talking several thousand labeling  
9 changes every year. I'm going to give the basic  
10 overview of the challenges we face and then Tom will  
11 give more of a case study presentation. For those  
12 not familiar with Hospira we're a global specialty  
13 pharmaceutical and medication delivery company. If  
14 you want to find us we're about 30 miles north of  
15 Chicago in Lake Forest, Illinois.

16 Jim Kelly also previously mentioned the  
17 definition of large-volume parenterals as found in  
18 USP General Chapter 1. And the challenges we face  
19 at Hospira are certainly found in these main  
20 categories, but are not limited to these categories.

21 First of all, the limited amount of colors which  
22 Vicki previously mentioned, and I'll go a little bit  
23 more into that. Limited space. Even when you're  
24 dealing with something greater than 100ml, there's  
25 still a lot of information. Mike showed a slide of

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 a large-volume parenteral with a lot of information  
2 on there and that was a liter container. Printing  
3 technologies and government regulations.

4 As far as limited label space goes we  
5 deal with LVP plastics with basically two different  
6 types of material, polyvinyl chloride or PVC is the  
7 most common. It's been around probably since about  
8 '71 and polyolefin is a relatively newer material  
9 that we work with. Printing technologies, however,  
10 really haven't changed all that much. Hot-stamping  
11 is the most common. It's where you take a metal  
12 plate, a hot metal plate, and you apply it to an ink  
13 ribbon. And that's pretty much what most LVP  
14 labeling uses. Thermal transfer, a little bit newer  
15 process, but that results in slower line speeds,  
16 it's difficult to use with continuous motion and you  
17 have size limitations. You need certain amounts of  
18 space around the printing.

19 Here's an example of a hot stamp.  
20 Typically made of titanium or steel. It's a proven  
21 technology, again the current printing standard.  
22 Tons of validation work, years of validation work to  
23 rely on. And it's pretty durable. However, you  
24 have a limited ability to minimize the font size.  
25 Take a look at that LVP that Mike showed and it

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 would be really nice to minimize some of those  
2 letters in order to more prominently display the  
3 name of the drug, but with the printing technology  
4 the more you minimize the font, the greater chance  
5 that the letters will run into each other. Hot-  
6 stamping is a direction-dependent process and the  
7 colors are limited. In terms of qualifications,  
8 basically the inks that have been qualified are  
9 blue, black and red with white with the thermal  
10 transfer. Optimally you use two colors per label.  
11 That's for setting up the processes. You do need  
12 open space between the color blocks, at least a  
13 quarter inch because the plates vibrate.

14           And there are challenges with label  
15 content changes. Anytime we change a hot stamp  
16 plate it's time-intensive, labor-intensive,  
17 somebody's got to do it, and it's expensive. Now, a  
18 plate runs anywhere from \$800 to \$1,200 per plate  
19 and a line may take up to 16 plates. So that can,  
20 when you have hundreds of LVPs, that can get into  
21 quite an expensive process.

22           In terms of color-coding, both Tom  
23 Willer and I spoke at the FDA meeting in March of  
24 2005 where Hospira took a position against color-  
25 coding. The reason we did this was that there are a

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 lack of colors. A Pantone chart looks very nice,  
2 but subtle shades of green, subtle shades of blue,  
3 you can't pick them up. And again, you have to  
4 qualify each color for the immediate container.  
5 Color-blindness in certain practitioners. Hospitals  
6 have irregular lighting. It's not all what you see  
7 on TV. You have very nice lighting except when you  
8 go into a patient room it's dark, you don't want to  
9 wake up the patient so you have limited lighting.  
10 And we firmly believe that the drug name and the  
11 strength is the primary identifier. Government  
12 regulations which Vicki also mentioned. There are  
13 evolving standards for drug labeling, one being the  
14 prominence of the national drug code, bar code  
15 placement, putting a unique bar code on over-wraps  
16 and radio-frequency identification. We are missing  
17 a slide. Okay.

18           Hospira has an active label enhancement  
19 group that meets on a monthly basis. We have  
20 practitioners from medical, regulatory, graphics,  
21 label control and we review either entire product  
22 lines or we review classes of drugs or in many cases  
23 complaints that have come in from the outside. And  
24 each item is reviewed no matter if it comes from the  
25 customer or if it's an internal process and we do

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 make changes in our labeling. Now what I think some  
2 practitioners don't realize is that the time it  
3 takes to make the changes, that even if we do make a  
4 change, that the labeling has to be changed and then  
5 to get it into the manufacturing process, if a  
6 product is not made frequently, if it's made only  
7 once or twice a year the changes won't be seen  
8 immediately. And Hospira believes that this is not  
9 just a Hospira issue. And it was said very well in  
10 the ISMP newsletter that fixing blame on FDA, the  
11 pharmaceutical industry and medical device companies  
12 isn't the answer. We all need to join in a  
13 concerted effort to get all key stakeholders to work  
14 together. And I'm going to turn the presentation  
15 over to Tom to talk about some case studies that  
16 we've had at Hospira and some recommendations.

17 DR. WILLER: Thanks Mary. Labeling has  
18 come a long way over the years and in this slide  
19 you'll notice a variety of methods used to assist  
20 reading the labeling such as different colors,  
21 graphics, font size and even white space. We've  
22 tried to do a whole different variety of things to  
23 differentiate the products. There's a tremendous  
24 advancement since the early 1980s when I worked at  
25 Beecham Labs where we had simply two colors for our

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 labels. All human products were in blue ink and all  
2 vet products were in green ink. Medical  
3 practitioners actually had to read every label.  
4 That's sort of a new concept today seemingly.

5           What I'd like to show here is examples  
6 of labeling on the primary container. You kind of  
7 see the way we've tried to differentiate them.  
8 Notice the differentiating conventions on the  
9 strength. We've used some vertical bars and the  
10 differentiating the vertical bars depending on the  
11 individual concentrations. See the extra-large font  
12 for part of the drug name, namely dopamine. This is  
13 called tall man lettering as Mike pointed out and we  
14 use this for drug names that might be confused with  
15 similar names, such as dobutamine.

16           And again, as Mary and Mike and others  
17 have pointed out, we do have a little bit more  
18 ability for foil over-wraps because they have more  
19 printable space than we have on the flexible  
20 containers. As Mary pointed out, flexible  
21 containers generally are printed online from plastic  
22 containers that were actually buying the - I'll call  
23 it virgin flexible material is actually folded,  
24 sealed and printed online. So we don't print  
25 anything ahead of time. It's all done in one

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 continuous operation, therefore making changes  
2 rather a big activity. Again, notice the  
3 consistency of labeling information that you see on  
4 these compared to - to support the inside container.

5 And as Mike pointed out, we tried to put the flip  
6 side of important information, any information for  
7 our products when we can. But as he also pointed  
8 out, this is a significant additional expense. It  
9 basically doubles the cost of labeling. The goal of  
10 course for labeling is communication and the  
11 clearest possible way to do this is to try to  
12 support patient safety. This may be done via human-  
13 readable printing or via machine-readable bar codes.  
14 We've look at that also.

15 Now, this is interesting to Mary and I  
16 because we work a lot with trying to improve our  
17 labels. And in the 1990s we worked a lot with Jerry  
18 Phillips at FDA to try to come up with a system to  
19 review similar-sounding or similar-looking labeling.

20 Here's an example of a frequent conundrum for a  
21 drug company labeling department trying to create  
22 new labels. There are more than one drug that  
23 starts out with the letter 'H' of course. In this  
24 case, drugs are used in the same area of the  
25 hospital. Differentiating the labeling is crucial.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1       So here are examples of labeling strategy to  
2       differentiate heparin. And you can see the  
3       different ways we've tried to do it.

4               I heard a proposal this morning that  
5       said there ought to be a standardized presentation  
6       of labeling information. What a great idea, but not  
7       a simple one to implement. For these three  
8       products, we've tried to put the key information in  
9       different locations so that it does look different.

10       But be very careful if we try to move forward with  
11       a standardized approach to labeling, like we always  
12       want the concentration to be at the beginning of the  
13       drug name or at the end of the drug name. Great  
14       idea. It's going to lead to them all looking the  
15       same. And again, we're trying to use, one of the  
16       other speakers, Mr. Duffy or someone else was  
17       talking about human factors. That's very important  
18       in label development.

19               So here's our strategies for labeling  
20       and differentiating heparin. Note the information  
21       in red and the information in black. As Mary  
22       pointed out, we have a limited number of colors that  
23       we can use and we have a quarter inch space between  
24       the colors. So if we went to more colors or we went  
25       to red/black/red, we'd still need another quarter

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 inch of lost space. Note that the key portion of  
2 the product name was shortened to highlight its key  
3 position while the complete name is lower in the  
4 label. This greatly helps communicate the product  
5 name and the concentrations to the user. So it  
6 serves no purpose to just have this full name on  
7 here and possibly just delete this information. And  
8 so we've tried again to highlight the critical and  
9 important pieces of information, namely the two USP  
10 units or the 25 USP units, one for - two USP units  
11 for arterial line, 25,000 for pulmonary embolism.

12 Here, please note the use of large font  
13 and the effort to highlight the difference between  
14 the product names with the goal of helping to  
15 prevent similar product names being mixed up again  
16 in a busy hospital setting. Hextend uses the  
17 exaggerate 'X.' It looks sort of ridiculous, but it  
18 sticks in your mind, and that's the whole purpose of  
19 labeling differentiation. And after you kind of  
20 look at it awhile it seems kind of cool, so I really  
21 admire the people that came up with this idea. Also  
22 note the different placement of the 6 percent before  
23 Hetastarch.

24 Under label enhancement, as Mary pointed  
25 out, Hospira takes our labeling responsibility very

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 seriously. In the early 1990s we created a label  
2 enhancement committee that meets monthly to review  
3 the selected labeling. We examined two similar  
4 pieces of labeling and see if there might be areas  
5 for improvement. As noted in this slide, there  
6 usually are things that can be done with white  
7 space, font differentiation, word and concentration  
8 sequence, graphics, tall man lettering that I  
9 previously mentioned. You can kind of see them all  
10 here and how they do look quite different.

11 Is there anything that could be deleted  
12 from the primary container? And we believe yes.  
13 All information on the primary container is repeated  
14 from the foil over-wrap, from the product insert and  
15 from many companies' websites and by the end of 2006  
16 we're told that all electronic copy of labeling, the  
17 insert, will be on the National Library of  
18 Medicine's website DailyMed. So there's multiple  
19 places to get the full labeling information in  
20 addition to the limited space on a product label.  
21 Could the primary labeling be streamlined to reduce  
22 redundant information and thereby freeing space for  
23 a larger print? We believe yes and we're going to  
24 present some ideas here.

25 So again, for tall man lettering it

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 leaps out at you the differences between the two and  
2 that's the whole point here. Tall man lettering  
3 provides clear differentiation between somewhat  
4 similar names. And as one of the speakers pointed  
5 out, if there is a growing or a list from the FDA of  
6 preferred conventions for tall man lettering or for  
7 future products, that's a great idea. And if we  
8 move forward on expanding that name, someone should  
9 take the lead, possibly OGD and look at the drugs  
10 that are coming off of patent for the next five  
11 years rather than looking at the past. There's a  
12 great rush right now for new generics to enter the  
13 marketplace and it's important that we think about  
14 this proactively. And again, labeling review time  
15 at OGD sometimes takes awhile as they go back to see  
16 what's on a branded product. It's after the fact  
17 that OGD attempts to standardize some of this  
18 labeling into the 21<sup>st</sup> century kind of concepts of  
19 label improvement and this takes time and redundant  
20 effort, I think.

21 So here's how we currently label some of  
22 the products. Notice the huge amount of real estate  
23 that's devoted to the "each 100ml contains"  
24 statement in which every ingredient is normally  
25 written out in full. Is this needed? Is this

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 statement needed here or could scientific notation  
2 be used, for example? Make it a little easier to  
3 see. As noted in the previous slide, this is  
4 repeated from the over-wrap in the package insert as  
5 well as readily being available online. We have the  
6 capacity to print lowercase letters if we could  
7 increase the font. One of our problems with  
8 printing on plastic online is the plastic is  
9 flexible and it stretches when it's hit with the  
10 heat imprinted printing process. So because of the  
11 font sizes, if we go to uppercase/lowercase, the  
12 lowercase letters are smaller. And for us, I know  
13 it sounds ridiculous, but the lowest we can print  
14 with clarity is 7pt font and that's not a font that  
15 I think the medical community would like us to be  
16 printing at, yet we're constrained by the huge  
17 amount of information. It's a bit difficult to  
18 read.

19           However, there are other options. Let's  
20 look at the same three labels after being revised.  
21 Now, we've added white space. Looks very different.

22       And we've added paragraph breaks. And again, look  
23 how different this one is from the preceding one.  
24 We used scientific notation. We've  
25 uppercase/lowercased the label. We've bolded the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 caution. Mike had mentioned that earlier as a great  
2 idea and we put in larger font sizes. And this is  
3 the case where we really didn't remove anything, we  
4 just used scientific notation. So it's a  
5 spectacular improvement I believe.

6 We're excited to be here and to be able  
7 to present some ideas for discussion. We  
8 enthusiastically support re-evaluation of product  
9 labeling to help enhance patient safety and help  
10 reduce medication errors in part potentially due to  
11 labeling. We encourage any efforts for the same  
12 standards to be applied in all FDA review divisions  
13 in the development and review of drug labeling.

14 Now, in industry we're encouraged  
15 frequently to think out of the box. And so we  
16 thought about possibly putting in a smiley face for  
17 pediatric dosing, or possibly this is labeling that  
18 is for the future. However, in more seriousness, in  
19 summary, we're in an exciting time of examining the  
20 criteria for evaluating what is a good LVP label.  
21 We support any strategy to review aspects of what  
22 should be the mandatory information on an LVP label  
23 and what can remain only in the package insert. We  
24 support considering the removal of some redundant  
25 information that is in the LVP over-wrap and the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 primary container. The fewer words that are on the  
2 LVP container label, the larger we can make the  
3 remaining critical verbiage to identify the drug  
4 name, concentration and warning information. Dr.  
5 Mary Baker and I look forward to the outcome of the  
6 important meeting we're having today in evaluating  
7 drug names for similarities as well as overall  
8 evaluations of important labeling content. Thank  
9 you.

10 (Applause)

11 DR. VAIDA: Thank you very much. If we  
12 could - you could stay if you want. And if I could  
13 have the speakers from this morning's programs come  
14 up and take a seat. And in your program with the  
15 agenda in that that you received this morning  
16 there's also a set of questions that we had hoped to  
17 answer throughout the day today both with the  
18 morning session and the afternoon session, some of  
19 these discussion questions, and I actually have them  
20 up on the screen here. There are microphones at  
21 your places and if what you could do is raise your  
22 hand if you have a question and then I will point to  
23 you and hopefully be able to get this right. And  
24 there's a button on the microphone so make sure that  
25 you put the microphone on and then when you're done

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 with the question to shut it off. And if you want,  
2 you could direct them to individual panel members.  
3 So do we have any questions to start with from the  
4 audience? Anyone have anything? Yes.

5 AUDIENCE MEMBER: I have a question for  
6 the FDA. Does the FDA require all these products to  
7 be reviewed prior to marketing, and if so do you  
8 require submission of the final color printed label  
9 for evaluation before you give market authorization?

10 DR. DUFFY: Well, the answer to the  
11 first part is that yes we do review. We need to  
12 review and approve the label prior to marketing.  
13 And that's a process where the company would provide  
14 copies of proposed labeling, and this can be  
15 provided in mockup. It need not absolutely be  
16 provided, the final printed label be provided, but  
17 that's clearly more helpful. But we do need to see  
18 at least a mockup in full color in full size for our  
19 evaluation. And it's a matter of, in the course of,  
20 I don't know how many people are familiar with the  
21 approval process, but at the end of a review cycle  
22 the entire label is essentially negotiated. And the  
23 focus is primarily upon the insert label, the  
24 indications and the warnings and all those - all the  
25 other aspects of the drug that were developed during

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the clinical trials. But another key component  
2 would be the immediate container label, the carton  
3 and any other related labeling that goes with the  
4 product itself.

5 Now at FDA the insert label is primarily  
6 the responsibility of the clinical division and the  
7 product itself, the immediate container carton, et  
8 cetera, that part of the labeling is the  
9 responsibility of the chemistry manufacturing  
10 controls group. And we work in collaboration with  
11 the medication errors division, the safety group and  
12 a full evaluation is made both from a clinical - the  
13 immediate container label is a collaborative effort,  
14 review of the immediate container label is a  
15 collaborative effort with the clinical, the safety  
16 and the manufacturing people.

17 DR. VAIDA: Thank you. Yes?

18 AUDIENCE MEMBER: My question is also to  
19 the FDA. My question has to do with generic  
20 labeling. When we submit labeling as part of our  
21 submission with the generic labeling, we will try to  
22 remove some of the redundant text that's on our  
23 smaller labels and put it on a container label and  
24 it is quite a few times met with resistance by the  
25 labeling reviewers that they would like that on

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 there because it's on the innovator's labeling.  
2 Will this initiative then be able to allow us to do  
3 that, or will we have to wait until the innovator's  
4 labeling has made all of these changes before the  
5 generic will be able to make these changes?

6 DR. DUFFY: Generic labeling is supposed  
7 to be the same as the innovator except where there  
8 are specific obvious differences that need to be  
9 made - changes that need to be made. For example,  
10 the manufacturer, the name of the manufacturer. But  
11 the labeling does need to be the same as the  
12 innovator. Some minor variation in appearance is  
13 acceptable, but the content needs to be the same.

14 AUDIENCE MEMBER: The content is the  
15 same in essence because our labels are just - our  
16 container label may be smaller so we cannot fit the  
17 entire storage statement on the container label, or  
18 we may not be able to fit "each ml contains." So it  
19 will be on the carton label as allowed in the CFR,  
20 yet as I said, it has been met with resistance from  
21 the OGD, the labeling reviewers stating that because  
22 the innovator has it that we also need it. I'm just  
23 - that's where I'm asking that question towards.  
24 Will that then change with this initiative?

25 DR. DUFFY: I don't know the answer to

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that. But the basic principle is that the generic  
2 product should follow what is on the innovator's  
3 label. Now if there are space limitations, that's  
4 clearly an issue that needs to be discussed. Simply  
5 provide adequate rationale for the changes that  
6 you've made and presumably it would be - if it's  
7 reasonable it would be accepted.

8 AUDIENCE MEMBER: Hi. I have a question  
9 again for the FDA following to that question. It's  
10 like if a product that is generic now and they  
11 discover, like Mike Cohen reported in his report,  
12 many medication errors based on a generic name, and  
13 if they want to follow it, would you accept it even  
14 though it wasn't what they call in the innovator  
15 original labeling packaging? I hope I make myself  
16 clear. We have a lot of medication errors that we  
17 reported in a lot of drugs like has been mentioned  
18 is going generic. I had asked the generic company  
19 about something. They said oh, we can't do it, it  
20 goes back to the innovator. They have to do it. So  
21 in terms of patient safety, if they, how you say,  
22 approach you saying, okay, we're not following the  
23 innovator, we're changing the labeling concept with  
24 a high alert drug or whatever it is, would you allow  
25 that through because you know many multiple reports

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 being given, like ISMP, USP, that are a joint  
2 collaborative effort. Would you expedite that or  
3 you would send it back to the innovator waiting for  
4 them to correct it? That's my question.

5 DR. DUFFY: I mentioned that the generic  
6 label can be different in certain ways from the  
7 innovator and one of the ways, one of the  
8 justifications for having differences is safety.  
9 What the process would be at the agency would be  
10 that we would discuss the change and the rationale  
11 for it and we would permit a change and the agency,  
12 if the agency felt that this was a safety issue we  
13 have procedures for going back to the innovator and  
14 raising the topic and seeking to make changes if  
15 they're appropriate there as well. The matter of  
16 timing, I'm a little uncertain whether the generic  
17 would be permitted to change before agreement was  
18 reached with the innovator, but if we find that  
19 there's a safety issue in the labeling we would  
20 certainly address it for all manufacturers.

21 AUDIENCE MEMBER: Okay, thank you. That  
22 was my concern.

23 DR. VAIDA: Mike, did you want to?

24 DR. COHEN: Just a little bit of follow-  
25 up. This really is a serious problem because we do

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 recognize problems out there, we hear from the field  
2 and we do report them. We try to communicate them.

3 And we recognize that there really is a need for  
4 change and it can go on literally for years before  
5 that change is eventually implemented. I'm really  
6 concerned about this inconsistency and you know not  
7 to put FDA on the spot, but the enormous amount of  
8 time it's taking for example to get guidance to the  
9 industry and to their own people within FDA. And  
10 this is what's causing some of the inconsistency and  
11 it's terrible. I mean, we have calls from companies  
12 for example, they'll ask us because we can freely  
13 discuss things with them obviously, and they'll ask  
14 us for you know how do you think FDA will react to  
15 this or react to that. We'll give feedback to the  
16 company based on what we've been told by people  
17 within FDA and then they'll actually make a change  
18 and then submit it you know with a new product for  
19 example and it'll get rejected by another person  
20 within FDA. So that's a very serious issue I think  
21 and it's really affecting patient safety and I  
22 really think we have to do a much better job. We've  
23 been told for example guidance statements are coming  
24 out now for the labeling and the packaging since the  
25 1990s. I heard Jerry Phillips talk about that in

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 1998 or 1999. For example, the way some of the  
2 label expression of the concentration and how much,  
3 for example, you know should a vial of 10ml express  
4 the entire amount in the container primarily and  
5 then per milliliter. Where should it appear, should  
6 it be within the same rectangle so you can see both  
7 pieces of information or should it be per milliliter  
8 and then the volume elsewhere. There's no guidance  
9 out there and everybody does their own thing and the  
10 nurses get confused. They see it one time in one  
11 way and they see it another time in another way and  
12 it causes very, very serious errors. Fatal events.

13 And for this to go on since 1999 and probably even  
14 before that is just, it's terrible. You can't have  
15 that continue. And I'm sorry to have to put it that  
16 way or you know, but really it's a serious issue and  
17 we've got to get something done with these guidance  
18 statements to move things forward. I don't know  
19 what's holding it up.

20 DR. VAIDA: Anyone else? A question up  
21 here?

22 AUDIENCE MEMBER: A number of the  
23 speakers have talked about how do you reduce label  
24 clutter and I think one of the speakers mentioned  
25 that one possible way is using scientific notation,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 but are there other thoughts as to how one can  
2 reduce label clutter since that seems to be a  
3 recurring theme?

4 DR. VAIDA: Anyone want to start with  
5 that?

6 MS. DREWS: Well, I think probably one  
7 of the most obvious ways to reduce label clutter is  
8 to take a critical look at the clutter and to  
9 determine what really is critical product  
10 information that needs to be put on that label. I  
11 don't know that I personally am fully in agreement  
12 with scientific notation and this is just an  
13 anecdotal story that I'll tell you, but we've  
14 actually had customers that have called us up and  
15 said can you tell me what NaCl means? So you know I  
16 don't think that we should assume that everybody  
17 that is looking at these products are skilled  
18 clinical practitioners. I think there are you know  
19 we really need to look at the flow of the product in  
20 the clinical environment to ensure that the people  
21 that are actually placing the product in the  
22 inventories are able to understand the labels. And  
23 that gets to the human factors I think that I might  
24 have mentioned related to understanding scientific  
25 abbreviations as well as language.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 DR. DUFFY: Well, I think one way that  
2 this could be addressed would be through label  
3 comprehension studies. Developing different  
4 appearing labels that highlight certain aspects of  
5 the label, include or delete others and see whether  
6 or not people actually in a kind of almost clinical  
7 setting would be able to comprehend the label. I  
8 think the human factors is a very important aspect  
9 to label development, there's no question about  
10 that, and the comprehension studies I think are key.

11 DR. VAIDA: Any other comments from the  
12 panel?

13 AUDIENCE MEMBER: Kind of tagging onto  
14 that last comment and this question's addressed to  
15 the panel in general. To what extent are human  
16 factors engineers or other experts in that field or  
17 in the fields of human cognitive science involved in  
18 evaluating or assisting in the design of these  
19 labels? For any of you.

20 DR. WILLER: I'm with Hospira and most  
21 of our products are generics so we run into the  
22 issues raised before. If the innovator's got it,  
23 we've got to have it. If the innovator's got all  
24 the clutter as we talked about here then we've got  
25 to have the same amount of clutter. Again, we're

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 very, very constrained by the labeling space issue  
2 and is all that information needed for today. Does  
3 the practitioner - does the nurse administering the  
4 product read the "each ml contains." I don't know.

5 Perhaps it's more important for the pharmacist who  
6 selects the medication, but at the administration  
7 end of it is all that information beneficial? And  
8 again, your idea of a cognitive study might be  
9 useful.

10 DR. VAIDA: Any other?

11 AUDIENCE MEMBER: Actually, the person  
12 before me just had my question, but I don't think I  
13 got an answer that I understood so I'm going to just  
14 restate it one more time. And that is from an  
15 industry standpoint, if you could just comment to  
16 the quantity of human factors engineers or cognitive  
17 psychologists that are actually present in your  
18 companies that look at the labels are able to look  
19 at usability studies when these labelings come out.  
20 If you could comment to that.

21 MS. DREWS: I'll give it a shot. I  
22 don't know. Like Hospira, a lot of the products  
23 that I get involved in are generic products, so we  
24 are - the only labeling design that we really have,  
25 the only labeling design process is literally a copy

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 from the innovator label onto our current container.

2 That is not to say, however, that when new products  
3 are in development that there are not, and maybe  
4 there's some other folks in the audience that could  
5 speak to this a little bit better. You know, when  
6 we do have novel products that we're developing new  
7 labels for, I believe that we would involve a human  
8 factors analysis in that and that would be part of  
9 our clinical appropriateness type of activities  
10 before the product were approved for launch.

11 DR. COHEN: I'd like to comment as well.

12 Part of the problem I guess is that there really  
13 isn't a heck of a lot of research as far as you know  
14 what makes for a good label, what should be  
15 positioned in certain locations, how large should it  
16 be. You know, some of the things we've heard about  
17 putting the strength before the product name versus  
18 after, below, above. If we had enough room I think  
19 on the label we probably could end a lot of these  
20 problems by making the numbers large enough, et  
21 cetera. But when I say not enough research, even  
22 the use of tall man letters. There's only one study  
23 that we even know of that actually shows at least  
24 some benefit to that. Most of the practitioners,  
25 their gut feel is it's really helpful, but there's

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 not a lot of research even with trademark and  
2 medication errors or non-proprietary name and  
3 medication errors to the extent where it's very  
4 difficult to get people to make the changes that we  
5 think are necessary. So that's one thing.

6 I think what a lot of the companies have  
7 done which I think is a great idea, especially in  
8 the area of trademarks, is involve practitioner  
9 panels to look with a critical eye at the product  
10 name or in this case it could be the packaging and  
11 the labeling. The Institute of Medicine Committee  
12 on Preventing Medication Errors which I served on  
13 made that recommendation that you know companies  
14 should involve practitioners, that there should be  
15 an analysis of the labeling, the packaging, the drug  
16 names with feedback. So that's at least somewhat  
17 helpful. It allows them to position the product in  
18 the area that they use it. But I think we do need  
19 more research and probably the human factors folks  
20 could help in that area.

21 DR. DUFFY: No, I think that these  
22 comments are good, that the human factors studies  
23 really would be beneficial. I don't think there's  
24 any question about that. But in my experience the  
25 primary focus is on the trade name and look-alike

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 sound-alike kinds of studies, whether or not it's  
2 easily remembered, you know. That's the focus.  
3 It's from a commercial perspective primarily, rather  
4 than emphasis on safety.

5 DR. COHEN: Yes, we've seen hardly  
6 anything with a requirement for labeling and  
7 packaging. I think almost all of the companies now,  
8 if they're coming out with a new product before they  
9 you know determine with finality what that trademark  
10 is going to be, that's so important to them that  
11 they will in fact test that out in the field. They  
12 have a lot of practitioners involved. There's  
13 several groups that do that. And it's very helpful  
14 I think. But that has not crossed over to the  
15 labeling and packaging for the most part. It should  
16 be there. I know it adds some expense but it can  
17 save a lot of grief and obviously a lot of patient  
18 harm if it's done. So I think that's something that  
19 we'd like to see a requirement. That was mentioned  
20 in the IOM report.

21 DR. VAIDA: Yes.

22 AUDIENCE MEMBER: I'd like to follow up  
23 one more question on that comment. When one talks  
24 about you know getting input from the practitioners  
25 on the label, which particular practitioner are you

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 looking at? For example, are you looking at the end  
2 user who's at the bedside, perhaps the nurse, or are  
3 you looking at you know the pharmacist or the person  
4 ordering the drug because obviously there's package  
5 inserts, there's the cartons which are present  
6 initially, but by the time you get to the bedside.  
7 So when you're designing the label on this final  
8 container who are you designing it for?

9 DR. COHEN: You would be looking  
10 primarily at the end user. That is, the nurse-  
11 patient interface, the doctor-patient, the  
12 pharmacist-patient interface. But it's not just  
13 there. It could also be in the pharmacy. I mean,  
14 you'd want a wide array. And a lot of it is  
15 product-dependent too. Where it's going to be used.  
16 You might - if it's going to be used in the  
17 operating room obviously you'd want to involve  
18 anesthesiologists, nurse anesthetists, et cetera.  
19 So when these studies are designed, for example for  
20 trademarks, that is all taken into account. And  
21 they go right for the people that are going to be  
22 working with these products. That's a big part of  
23 it. They actually have a standard process. I kind  
24 of outlined it on one of the slides. We didn't have  
25 time to go over it, but you know who will prescribe

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 it. How does it even get into inventory. Who will  
2 prescribe it, how is it processed in the pharmacy,  
3 who will mix it, and it goes on and on all the way  
4 up to the point where it's actually given to the  
5 patient. All those individuals can be involved with  
6 the packaging and labeling study.

7 AUDIENCE MEMBER: I'm sorry, I just  
8 wanted to respond to your comments, Mike. I really  
9 appreciate hearing that the end users need to be  
10 involved in the evaluation of these products. I was  
11 an IV pharmacist for 20 years and an end user and  
12 experienced you know some of the challenges that  
13 we've talked about.

14 Once more to kind of turn back to the  
15 human factors issue, there's a lot of science -  
16 you're right, there's not a lot of research about  
17 how labels might best be presented or formatted, but  
18 there is a good bit of science and research about  
19 how human beings process information. And I think  
20 that there's an untapped resource in that field for  
21 applying those principles here, it just hasn't been  
22 done yet. So I'd just like to offer the comment  
23 that perhaps companies could look a little bit more  
24 closely at employing the expertise of these people  
25 to help us with these problems.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 DR. COHEN: By the way, can I just  
2 finish off? Thank you, that's an important comment  
3 to make, but I want to finish up with something I  
4 said earlier that just popped into my head. In the  
5 area of trademark review, there's at least some idea  
6 of how to do that. There's no official guidance at  
7 this point I guess, but it has been mentioned in  
8 some statements that have come out of FDA. But  
9 that's something that FDA could lay out you know.  
10 How should this analysis be done, the failure  
11 analysis. How should it be done, who should be  
12 involved. There could be some guidance for that as  
13 well and I think that would be important to have.

14 DR. VAIDA: Yes?

15 AUDIENCE MEMBER: We heard three  
16 presentations about what's currently required,  
17 either from USP or FDA about what labeling is  
18 required at the current time. What I didn't hear  
19 was why. I mean, we've identified at least  
20 indirectly a great deal of the labeling which may or  
21 may not have any value to the practitioner at the  
22 bedside. So why is it there?

23 DR. VAIDA: Maybe Diane or Jim?

24 MS. COUSINS: I can give you a  
25 historical perspective only so far back.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 DR. VAIDA: A good question to basically  
2 go through with the process. We heard some of the  
3 synergy here with the USP and the FDA. Do you want  
4 to?

5 DR. DUFFY: Well, I'm not sure how to  
6 respond to that. Things do evolve and one - you  
7 know, there's a - when you conceptually think about  
8 having a label, what you start out with is trying to  
9 be complete. And so I think the human tendency is  
10 to say well, if you want to express what the product  
11 is you should list what is in it. So for example  
12 some of the electrolyte solutions or total  
13 parenteral nutrition products, vitamin solutions,  
14 many, many components present. And so conceptually  
15 you think well, you want to say what it is, the  
16 identity as I had mentioned. There is a regulation  
17 requiring that identity be expressed. So the  
18 tendency would be to say all right, all the  
19 components need to be there. Therefore, that LVP  
20 you figure oh it's pretty good size, it's big, may  
21 as well go ahead and use that territory and fill it  
22 up, when I'm not sure whether or not the  
23 practitioner really needs to - first of all, is  
24 anyone going to read it? And secondly, is it really  
25 necessary for safe administration of the product?

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 This is debatable I think and frankly we'd like to  
2 hear comments from people about you know  
3 practitioners, people from industry, what their  
4 feelings are in terms of what is really necessary on  
5 a label. I had mentioned in my presentation that  
6 there are some minimum requirements in the case  
7 where there isn't much territory on the label. Now,  
8 how about a label where it's larger where you could  
9 for example have much more than that expressed? Is  
10 it really necessary? This is something that can be  
11 discussed.

12 Now, in terms of the review at FDA, one  
13 primary concern is safety in review of a label. And  
14 so if an argument can be made by the manufacturer  
15 possibly based upon a human factors study or  
16 something of that nature, that's something that we  
17 would certainly want to hear about and you could  
18 develop a rationale which we certainly, if it were  
19 persuasive I would think we would agree with it. If  
20 the clutter could be reduced and therefore prevent  
21 medication errors, I think that could be a very  
22 persuasive argument.

23 MS. COUSINS: I think I'm over the  
24 shock. I think I'd like to say just generally  
25 speaking, and it kind of keys off your word

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 "evolving." When USP standards are created, they  
2 are reflective of the best thinking at that time by  
3 the expert committees that create those proposals.  
4 But those proposals also go out for public comment.

5 And as you saw with the joint committee from the  
6 early '90s, there are comments that come back that  
7 may require the proposal to be modified in a way  
8 that sometimes it compromises you know the opinions  
9 of all the parties that be. I think the most  
10 important part about that process though is that it  
11 is a continuous revision process. So where we are  
12 today does not have to be where we are tomorrow or a  
13 year from now. And so the purpose of my  
14 presentation earlier was to let you know that there  
15 are things that can change, even things as drastic  
16 as changing the regulations as they did in the early  
17 '90s that can accommodate the best thinking of the  
18 time today. So I would encourage you to keep that  
19 in mind as we move forward. Really, what we decide  
20 on as standards at some point in time may no longer  
21 be the best thing to be doing. But we need to hear  
22 from you.

23 DR. WILLER: One of the problems with  
24 drug safety and patient safety as we think of better  
25 ways to have labeling. An example would be,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 "Warning: Contains sulfites." Great idea. So the  
2 agency said put it on there. It's rare to never  
3 agency has put this on but takes something else. So  
4 when we put the new "Warning: Contains sulfites" on  
5 there we've got to reduce the size of everything  
6 else on the label. So have we accomplished the goal  
7 of that important new information? I can only think  
8 of one instance and maybe other experts would  
9 remember more of FDA ever allowing us to remove  
10 something. That was the warning federal  
11 prescription law. And here again it was almost a  
12 perfect move by the agency, or at least by the law-  
13 writers, the people who wrote the law, which was  
14 they wanted the Rx-only put on there. What's the  
15 importance of the word "only"? It's either an Rx  
16 drug or it's not. I'm not aware of the same Rx drug  
17 being OTC and Rx at the same time with the same  
18 name. So again, we've got to put on that extra  
19 wasted space for O-N-L-Y. It's a small thing, but  
20 all these things add up in the very, very restricted  
21 space that we have.

22 And you know we try to do the best we  
23 can. We hear competence and complaints as I do from  
24 my relatives about labeling being too small. I'm as  
25 irritated as anybody that we're going to 8pt type or

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 something. It's hard for us to print that and so we  
2 would like to have it larger for the patient safety  
3 issues, but we're sort of constrained.

4 DR. VAIDA: Yes?

5 AUDIENCE MEMBER: Just wanted to give a  
6 little bit of an opinion to the person who asked the  
7 question about where did these regulations come  
8 from. And certainly I don't work for USP or FDA,  
9 but I believe it's rooted in public policy from when  
10 the FDA was not the FDA as we know it today, but was  
11 sort of an infant group as a part of the Department  
12 of Agriculture. And I think that this all developed  
13 as a part of that and has become what it is today.  
14 I think Tom that you make an excellent point with  
15 labeling that when we do have to add something that  
16 the agency wants us to add, they seldom ask us to  
17 take anything off. And you do end up with a lot of  
18 label clutter. And I really like the presentations  
19 this morning and Mike, I see what you mean about  
20 label clutter. We all have that and I thought that  
21 Tom had a very good label that he put up that used  
22 the chemical symbols and had the white spacing and  
23 everything. But one concern that I have about  
24 taking a lot of information off of the labels is  
25 what Vicki brought up, the legal sensitivities.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Because the package insert seldom follows this  
2 product to the bedside or to the end user and so you  
3 have to rely on that label that's on the actual  
4 product, the unit of use. And I sometimes have a  
5 little bit of a worry if we take a lot of  
6 information off, are we then going to move ourselves  
7 into a failure-to-warn situation where the users  
8 will say, well if I had had this information on the  
9 label, I would not have made that mistake. So I  
10 just wanted to, always being the conservative in the  
11 group, card-carrying conservative, I just wanted to  
12 bring that up that yes I think that we can make  
13 changes and good changes to the labeling, but at the  
14 same time we have to look at these other  
15 considerations about that the package insert doesn't  
16 follow - the box doesn't follow along and you end up  
17 with this product with a label that needs to have  
18 all of that information on it.

19 DR. COHEN: Keep in mind too, you know  
20 we're in the age now of you know machine-readable  
21 code, RFID, things like that that you know perhaps  
22 can bring that information right to the bedside.  
23 For example when the nurse scans the bar code or you  
24 know reads that RFID chip that might be embedded in  
25 the product they could get that warning information

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 very easily. So we have to think about the future  
2 too.

3 AUDIENCE MEMBER: No, I agree absolutely  
4 and Tom also made a good point that labels are  
5 available on the internet. You know, you can get  
6 this information all the time. But in the actual  
7 hospital setting where - and they may be in an  
8 emergency situation and people are extremely busy  
9 and running around and grabbing a product, they  
10 don't have time to go to the internet to look up to  
11 get information on that product. And I think that  
12 you know you really have to have a certain amount of  
13 information on that label.

14 DR. BAKER: But some of the information  
15 though doesn't really contribute. You know, "Usual  
16 dosage: see insert," doesn't tell you much other  
17 than to look for the package insert and you're  
18 hanging the bag and it's like well now what. So I  
19 don't think that that's really providing  
20 information. And also, can we condense some of the  
21 verbiage. "Use aseptic technique, consult with  
22 pharmacist if available" takes up a heck of a lot of  
23 space.

24 AUDIENCE MEMBER: No, I absolutely  
25 agree. All I'm saying is that if we do start to

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 remove information from the labels, we have to take  
2 everything into consideration and especially the  
3 reviewer differences at FDA and real problems. We  
4 do have real problems in terms of doing a generic  
5 label and having to be similar to the innovator.  
6 And we at B Braun have tried to add geriatric  
7 information and pediatric information to package  
8 inserts for some of our products and have been told  
9 that we cannot put that in there because the  
10 innovator doesn't have that information in their  
11 package insert. So you know there are constraints  
12 that we have to live with and it would be nice if we  
13 could put those things into a generic package  
14 insert. But again, the agency is constrained as  
15 well because they have to live with the same  
16 regulations we do.

17 DR. VAIDA: Up here first. We'll come  
18 back and then I think Jerry has a question.

19 AUDIENCE MEMBER: It's exciting that  
20 we're looking at standardizing labels and I think  
21 Dr. Cohen mentioned about machine-readable code. My  
22 concern is that when you look at bar code  
23 technology, there really isn't a standard format and  
24 there are so many different ways that manufacturers  
25 either put information or don't put information that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 I think if we're going to try to gain real estate  
2 and share information there has to be  
3 standardization in the type of information that can  
4 be machine-read so it can aid either at a bedside  
5 scan or in a pharmacy scan or even if a material  
6 handling scan. So just I think it's absolutely  
7 critical notwithstanding the labeling that has to go  
8 and be printed on the bag is that the bar coding  
9 format is standardized so we're all using the same  
10 format so it has the same amount or the same type of  
11 critical information that can be shared by all  
12 users.

13 DR. VAIDA: Okay.

14 AUDIENCE MEMBER: I want to offer my  
15 apologies. I wasn't meaning to attack. The lady  
16 below expressed me much more eloquently than I do.  
17 My concern was that in this discussion that we in  
18 fact take a look at what we do now and ask ourselves  
19 why we do it because it may be there's a good  
20 reason. And in our haste to clean up the labeling I  
21 did not want to throw out the baby with the  
22 bathwater.

23 DR. VAIDA: Very good comment. Jerry?

24 MR. PHILLIPS: I think we can find the  
25 origins of FDA's labeling regulations in the Food,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Drug and Cosmetic Act when it was originally done.  
2 There are labeling regulations that were put in the  
3 Act itself or in revisions to the Act. And then FDA  
4 then implements those through the Code of Federal  
5 Regulations through rulemaking that elaborate more  
6 on the intent of what Congress put in the Food, Drug  
7 and Cosmetic Act. Just to change the "Caution:  
8 federal law" statement required a change in the  
9 Food, Drug and Cosmetic Act itself and then a change  
10 in the Code of Federal Regulations. So that is  
11 quite an intensive process to go through from the  
12 agency's perspective and Congress. Thank you.

13 DR. VAIDA: Yes, sir.

14 AUDIENCE MEMBER: Yes, I had a very  
15 similar thought as a couple of things that have been  
16 expressed. We sort of have an 800-pound gorilla in  
17 the room here to a certain extent. I think several  
18 of the presentations have made it quite clear that  
19 space is the issue. And a lot of the priorities and  
20 values of different kinds of information. For  
21 instance, we have discussion about complex studies  
22 of human factors analysis. Well, if some of the  
23 fine print, some of them even inactive ingredient  
24 statements, et cetera, could go away or be dealt  
25 with in a prompt fashion, so many of these other

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 issues become so much easier. But we have the  
2 momentum problem because we sort of have a  
3 disconnect between the safety issues that should be  
4 a primary public health issue being expressed here  
5 by all sides, and yet you have an act from Congress  
6 and a whole set of regulations and the timing  
7 mismatch between the level of concern and the cycle  
8 time to get any of that changed. I mean, we  
9 recognize that FDA, you know what would you do, say  
10 take your existing regulations and tell the FDA  
11 reviewers to exercise a lot more discretion? I  
12 wouldn't do that if I was an FDA reviewer or  
13 somebody you know finalizing the labeling.

14           So how do we get a mechanism maybe  
15 similar to this but more focused, getting to higher  
16 levels of the agency or the USP or both. Because  
17 the transmission of transmitting all this good  
18 energy to the road and getting somewhere as Dr.  
19 Cohen said just doesn't seem to be there. A line  
20 takes 10 years to get authorized to change. So  
21 there's a mechanistic problem in the industry-  
22 government interface here in getting these things on  
23 a higher priority, having I don't know a blue ribbon  
24 committee or something that could get whatever's  
25 necessary in the Act and the regulations on a much

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 faster turnaround time. The generic companies.  
2 It's very impressive how few options they have. You  
3 know? I've dealt with generics as well as brand  
4 products and there's just no latitude with a generic  
5 reviewer. They are constrained to say basically you  
6 have to have the same. Until the innovator does  
7 their thing there's nothing I can do for you and you  
8 can't do any of that innovative stuff. So there is  
9 a disconnect between public you know health  
10 priorities and the mechanisms of these changes. And  
11 something on an organizational level needs to be  
12 done better I think to get a higher priority for the  
13 issues.

14 DR. VAIDA: Tim?

15 AUDIENCE MEMBER: The thought occurred  
16 to me that we've talked a lot about size and size  
17 constraints. And if you think about say a syringe  
18 that's used to add to an IV and how little  
19 information is required on that, but that same IV  
20 has a whole bunch. Is it because you have the size  
21 so you can, or if you don't have the size you don't  
22 have to? I mean, it kind of seems like if you think  
23 about just a tablet or a capsule in a unit-dose  
24 package has virtually no information, but all of a  
25 sudden IVs have a ton of information. And I'd ask

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 any of the nurses who are in here, have you ever  
2 read that bag of dopamine besides the - and in fact,  
3 a comment about that and it relates to human  
4 factors. Most of the nurses select dopamine as 400  
5 and 250 or 800 and 250. They don't - and those  
6 aren't even connected, but yet that's the way that  
7 at least with smart pumps all of the libraries are  
8 set up as far as I know. But it seems to me that we  
9 have a real double standard and I don't know how we  
10 get by with it with the same medication that might  
11 either be an oral or an injectable, or an injectable  
12 and an IV. What's the difference? I mean, why do  
13 we have to have all that information on one and not  
14 on the other?

15 DR. VAIDA: What - and that, actually I  
16 was going to have - we've heard a lot about the real  
17 estate from both of the industry speakers, that  
18 there's very little real estate. We hear a lot  
19 about what is really needed on there. And actually  
20 as a question, there was some changes made. Diane,  
21 when you gave a historical perspective there were  
22 some changes made on that labeling. What do we have  
23 to do to basically take a look at that information  
24 that's needed on there? What is the process? And I  
25 would imagine it's beginning with USP. And does it

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 actually have to go all the way back as Jerry said?

2 It doesn't sound like there was actually, it went  
3 to Congress or anything else at that time to make  
4 some changes. What would you see as an outcome of  
5 looking at some of that information? Even not  
6 taking into account how the drug appears or how the  
7 concentration appears which I think we all hear  
8 there needs to be guidance. There needs to be some  
9 guidance. But how would that process start? And  
10 would that be going back to USP?

11 MS. COUSINS: I think the first thing  
12 that needs to happen is there needs to be agreement  
13 on the issues. You know, when we talked about  
14 clutter and someone asked the question, I mean there  
15 were different perspectives on what's clutter. So I  
16 think the first thing is we have to define the  
17 problem and we have to agree to what the issues are.

18 Then I think we have to look at where, you know the  
19 requirements, the laws, the standards interface with  
20 what we think is the best thinking of this time for  
21 what ought to be and evaluate what could be done to  
22 address those things. There are many places USP  
23 doesn't have standards and we could create them and  
24 that's very easy to do. I say very easy, but  
25 certainly easier than sometimes revising. You might

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 think it would be just the opposite, but sometimes  
2 that's not the case. So I think that we just have  
3 to proceed in a methodical way, and this is  
4 certainly a great first step, to start to gather the  
5 parties, identify the issues, look within the  
6 context that we are operating in and then determine  
7 where we need to be. Where's the best thinking at  
8 this time and how do we get there? Because if we  
9 talk about the constraints we're going to be  
10 constrained. If we think without constraint, we'll  
11 have a better idea of the ideal. And I think we  
12 have to think like that. It's true it's difficult  
13 to change laws, but I've never seen a better fan for  
14 a fire than an IOM report. So this is gives us  
15 certainly at USP a lot better way to move forward in  
16 these areas than ever before.

17 DR. VAIDA: Any comment? Yes?

18 AUDIENCE MEMBER: I'm also speaking from  
19 a generic perspective, so the Office of Generic Drug  
20 Labeling Review keeps getting asked questions, but  
21 Mr. Duffy I do have a question for you. Some of the  
22 things I've experienced, I have gotten a deficiency  
23 from the agency asking me to use tall man letters  
24 only to have it rescinded a month later asking me  
25 not to use tall man letters, although another

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 generic company is on the market with tall man  
2 letters. I also have gotten - everything I sent in  
3 I put total strength per total volume and I've had  
4 label reviewers tell me not to. I've also,  
5 everything that I sent in begins "Usual dosage: see  
6 package insert" but as a generic I constantly get  
7 comments back telling me that I must put exactly  
8 what's on the innovator. For example, "See  
9 accompanying insert for dosage administration."  
10 Even though I try my best to constantly reserve real  
11 estate, my question is what sort of training goes  
12 into label review? That might be a really big, wide  
13 question, but is there any kind of subjective  
14 training that goes into OGD label review where -  
15 because I argue these and I'm not usually  
16 successful.

17 DR. VAIDA: Carol?

18 MS. HOLQUIST: I can help Eric try and  
19 answer that. I actually used to be a labeling  
20 reviewer in the Office of Generic Drugs. So how do  
21 you get training in there? You learn the  
22 regulations. And you learn the regulations. The  
23 regulations say you have to have a usual dosage  
24 statement. But what also binds generics, as we  
25 heard before, is they have to be the same as the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 innovator. I'm kind of surprised that you would get  
2 some feedback on changing your usual dosage  
3 statement to me because it seems like what was on  
4 there was okay. Jerry can probably speak better to  
5 why maybe they would require something like that,  
6 but I can speak to the epi. I think what you're  
7 referring to with the tall man lettering is actually  
8 - and this is something I wanted to get feedback  
9 from the panel as well on - is that you know now  
10 everybody's saying tall man lettering, yes, it's the  
11 next best thing. You know, it's going to create -  
12 it's going to minimize all these errors, especially  
13 with established name confusion. But what I think  
14 I'm also afraid of is that if we overuse it, we're  
15 going to dilute the effect. And in the case where  
16 you go a rescinded letter I believe is when a  
17 company wanted to highlight epi on the label and it  
18 was not a product that contained epinephrin. And we  
19 thought, at least I know from a safety perspective  
20 we thought highlighting was, I think, I believe it  
21 was Epirubicin was putting epi as highlighting epi  
22 so that it wouldn't get confused with other rubicin  
23 products. And we thought from a safety perspective  
24 that that really wasn't the best use of tall man  
25 lettering, that there could be other ways that we

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 could differentiate that product so that it wouldn't  
2 get confused with other rubicin products. So I  
3 think that's a question I have too.

4 I might not have answered all of your  
5 questions about labeling reviews, but the label  
6 reviewers, they do go, you know, they get trained  
7 hands-on by other labeling reviewers who have been  
8 there from you know time on. There's team leaders.

9 But they have to follow whatever the innovator has.

10 So if the innovator has something on there, they're  
11 going to ask you to put it on there. There have  
12 been times when there has been an error that we have  
13 asked the innovator to change it based on the error.

14 It may not be to remove some sort of statement on  
15 the label, but it might be to actually change the  
16 trade dress of that particular product because the  
17 error may be related to the fact that the vials all  
18 look alike. So there are ways that you can minimize  
19 your errors from a generic perspective, it just  
20 really depends on what the issue is. It's not that  
21 they can't do anything at all.

22 AUDIENCE MEMBER: May I also ask is  
23 there an upcoming list? I believe Mr. Willer  
24 referred to this also. The tall man lettering list  
25 that is on the FDA website is quite dated. I can't

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 even remember the date, but I know it's been several  
2 years. And as Mr. Willer alluded, there's a lot of  
3 products coming off patent very soon that tall man  
4 lettering would be very good for and an updated list  
5 would help in some of these issues. But some of the  
6 label reviewers will allow me to put "See package  
7 insert" and some will not. So it's very  
8 inconsistent on the label review.

9 MS. HOLQUIST: Yes and I think if you  
10 have problems with the inconsistency, I think you  
11 really need to bring that to the attention of the  
12 Director for the Office of Generic Drugs because if  
13 there is, you know, you're hearing from one group in  
14 OGD that it's okay, but you're hearing from another  
15 group in OGD it's not, they can get together. You  
16 know, if they're made aware of it they can get  
17 together as a group and say this is what we're going  
18 to come up with and they have a standard. It's a  
19 small you know amount of people. That wouldn't be a  
20 difficult process.

21 With respect to the list of tall man  
22 lettering, basically the list that's only up there  
23 is the list that we knew of that we actually asked  
24 people to change which was the list that came from  
25 ISMP. What we're finding is that a lot of

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 manufacturers are doing tall man lettering on their  
2 own and slipping these things in in what we call  
3 annual reports which because they consider it as a  
4 minor and editorial change, where to me I don't  
5 think tall man lettering is a minor and editorial  
6 change. For the example of the Epirubicin. And I  
7 think that was a case that brought it to our  
8 attention and so now our group, because we're so  
9 concerned about this, is trying to take control of  
10 it and we're trying to work with not only OGD but  
11 new drugs too, if anybody comes in with that request  
12 or they see something like that in an annual report  
13 that they at least you know ask us about it because  
14 they think it's a good idea. And I recognize that  
15 things are going to be coming off patent, but it  
16 gets back to the point do we want to highlight every  
17 generic product with tall man lettering. I mean, do  
18 people think that's a good idea, or do we think it  
19 may minimize the effect.

20 DR. COHEN: Well first of all, I agree  
21 with a lot of your comments. And I do have a  
22 problem with everybody using tall man letters  
23 helter-skelter for unknown reasons in some cases.  
24 And I mentioned before, I've actually seen a couple  
25 of cases now where the tall man letters that were

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 emphasized actually made it look like it was a brand  
2 name. And obviously the whole idea of USAN and your  
3 non-proprietary name development is you know, it's  
4 opposed to doing something like that.

5 But it isn't even just the  
6 pharmaceutical product labeling that's using tall  
7 man. Infusion pumps, smart pumps now have the drug  
8 libraries and they're using it. The pharmacists are  
9 using it individually in their hospitals and there's  
10 inconsistency there, the way that it's done. The  
11 letters that are emphasized are not always the same  
12 even between two companies. I've seen that happen  
13 already.

14 So again, you know a lot of this is  
15 leadership. It's somebody's got to take charge  
16 here. Even in the last conversation that we had  
17 about you know where do we start, what Alan was  
18 talking about. Somebody's got to embrace this and  
19 say you know here's how we get this going. Here's  
20 who the players are. Let's bring these people  
21 together and you know maybe work on individual  
22 problems one at a time. I don't know but one of  
23 them is certainly going to be tall man letters  
24 because that - the growth has just been unbelievable  
25 since the 15 or 20, whatever it was, were approved

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 by FDA. And I absolutely do not agree that with  
2 some of the ones that are being used, no question  
3 about it. Like epi would not be a good idea,  
4 definitely not. So somebody's got to be.

5 DR. VAIDA: Comment by the panel? With  
6 that we'll take one more question.

7 AUDIENCE MEMBER: I have a question.  
8 Are we also looking at the way these products are  
9 being used? You know years ago - I speak to my  
10 mother who's been in the nursing profession for 40  
11 years. You used to go to nurses training and you  
12 used to - you picked up the bag, you read it, you  
13 hung the bag, you read it, you spiked the bag, you  
14 read it, and that was part of their training. And I  
15 find now that with every, you know with all the  
16 cutbacks in every part of our society, that a lot of  
17 these nursing training stuff that seems so important  
18 at the time have slipped away and there needs to be  
19 also some accountability in the training in the  
20 healthcare profession as well. I have seen  
21 complaints come where the bags are clearly two  
22 different - you can't - they are so far different  
23 from each other, but we still get a complaint of a  
24 medical error in a hospital and it turns out to be  
25 it's because they're in the storage room where the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 letter, you know the one product starts with "O" and  
2 the other one starts with a "P" and in the alphabet  
3 that's how they're stored, and they were hung that  
4 way. And I think there needs to be more emphasis  
5 and regulations also in that part of the industry as  
6 well. I think cutbacks hurt everybody and you just,  
7 you know you have to read the label.

8           And I think we can do a lot of things  
9 here, but I think we need to work within the  
10 hospital setting. You know, years ago you would  
11 hang three bags. Now, you saw a picture there.  
12 There's 20 bags being hung. How can any individual  
13 keep track of that? And are we doing anything,  
14 looking at some of the things we could do in the  
15 hospital or pharmacy setting?

16           DR. VAIDA: Was there one more question  
17 here? In the middle? Did you have a question  
18 before I end?

19           AUDIENCE MEMBER: For just a second,  
20 perhaps to change the focus. Several of the  
21 speakers - I'm speaking here as a practitioner.  
22 Several of the speakers have mentioned cost, the  
23 cost of changing fonts, of several colors. Can you  
24 just give us an order of magnitude? What are we  
25 talking about here in terms of the label cost? How

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 big a fraction of the cost of the product is that?

2 MS. OLINGER: I can address that a  
3 little bit I think. I don't think it's as much the  
4 cost of printing the label once you get going, but  
5 it's to change an ink like they said previously, you  
6 have to validate that. You have to do leechables,  
7 extractables, everything that goes with that so that  
8 the cost of validating and qualifying a new ink can  
9 be in the hundreds of thousands of dollars. And  
10 changing the label for, as Mary said, if you've got  
11 a couple thousand drug products and in our case we  
12 extrude the film, do the whole process right on the  
13 manufacturing line. To make changes to that  
14 sometimes requires re-tooling a manufacturing line  
15 and shutting that line down totally so that you're  
16 not doing any production at all on it. And these  
17 are not high-margin products. You know, that if you  
18 have to shut down you lose a lot of money. So it  
19 becomes an extremely expensive proposition for a  
20 company to make massive changes. So I hope I  
21 addressed that.

22 DR. VAIDA: Okay. Before we break for  
23 lunch here I - we still have our afternoon that  
24 we're going to hear from another manufacturer and  
25 also some practitioners and then we're going to have

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 time for some public comments. And hopefully we  
2 will have some closer conclusion at the end of the  
3 day. It does sound like there are a couple of  
4 issues. One is the actual safe labeling of the  
5 medication, the way concentrations are which we  
6 heard from people, even controversy on tall man  
7 lettering, but there also is this issue on real  
8 estate that does sound like when I hear about even  
9 if you're adding something, not taking something  
10 away. In my prior background as a hospital  
11 pharmacist, if we would add drugs to formulary, we  
12 would always be asking what are we going to take off  
13 of formulary so we're not just continually building  
14 the formulary. But it does seem like there are  
15 those couple issues here. One is addressing that  
16 safety of the naming of the drug or how that font  
17 appears and that, but also is there some other issue  
18 on just talking about what is the other needed  
19 information on there on the label.

20 So with that we're going to break for  
21 lunch. There's a cafeteria downstairs. There's  
22 also some other, if you're familiar with the campus  
23 I guess there's some other eating places along the  
24 campus here. And we're going to reconvene here at  
25 12:45. So we'll reconvene here at 12:45. Thank

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 you.

2 (Whereupon, the foregoing matter went  
3 off the record at 11:32 a.m. and went back on the  
4 record at 12:51 p.m.)

5 MS. BECKER: Thank you all for returning  
6 from lunch. I hope you enjoyed that little respite  
7 and are ready to dig right in to the next session  
8 where we're going to change our that a little bit  
9 here and listen to the practitioner perspective on  
10 labeling. And our first speaker is Debora Simmons.

11 Debora is the Associate Director and Investigator  
12 for the Institute of Healthcare Excellence at the  
13 University of Texas MD Anderson Cancer Center and is  
14 a member of the United States Pharmacopeia Safe  
15 Medication Use Expert Committee where I've had the  
16 pleasure of working with Debora for a couple of  
17 years now. Debora is a founding advisor and board  
18 member of Citizens Advocating Patient Safety, a  
19 partnering safety coalition of consumers that helps  
20 healthcare advance a safety culture through  
21 alliances with the national and international  
22 healthcare communities. Debora is program manager  
23 for the University of Texas's Close Call Reporting  
24 System which has 10 reporting hospitals and over  
25 10,000 close calls in its database. Debora is the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 program manager for the Healthcare Alliance Safety  
2 Partnership, the first non-punitive error reporting  
3 program in the country. This partnership with the  
4 State of Texas Board of Nurse Examiners and 10  
5 participating hospitals allows nurses to report  
6 errors without fear of reprisal by the regulatory  
7 agency. Debora sits on several state and national  
8 level committees influencing safety concerns and  
9 regulatory issues. She's a clinical nurse  
10 specialist in critical and acute care and also  
11 teaches clinical nursing. Debora is a member of  
12 Sigma Theta Tau, is a Virginia Henderson Fellow and  
13 is the recipient of the 2006 Research Leadership  
14 Award from the Texas Nurses Association. Debora?

15 MS. SIMMONS: Well, thank you for having  
16 me here with you today. Can you hear me okay in the  
17 back? I always make sure with these things. I'm  
18 always I'm only hearing myself and you're all out  
19 there going huh? What's she talking about? Thank  
20 you so much for having me here today. You're some  
21 of my favorite people because of the work you do and  
22 so hopefully I'll be able to add a little bit to  
23 this presentation quickly as I go through and kind  
24 of keep to our timeline today and give you kind of  
25 the perspective of these nurses that we keep talking

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 about that are the ones there that are picking out  
2 these IV bags and getting confused about the labels.

3 And I can kind of give you the perspective from the  
4 nurses' eyes.

5 I'm going to just briefly go through -  
6 when I was trying to think of what would be  
7 interesting for you to hear about, I came up with  
8 kind of four big buckets of areas that might be of  
9 interest to you. I'm going to try not to quote a  
10 lot of research to you because I think this group  
11 has seen the research that's out there. I can show  
12 you some of the gaps. I'd like to share with you  
13 some perceptions of information that nurses have,  
14 kind of give you a challenge around that, talk to  
15 you about the limitations of nurses and the work  
16 environment and the task load as well.

17 First of all, perceptions of  
18 information. What's the on the label for parenteral  
19 containers. I challenge you to go to a clinical  
20 area and walk around, kind of do a randomized trial  
21 here, random meaning walk the halls, and just ask  
22 the nurses that you see what's on the parenteral  
23 containers. Because the first thing they're going  
24 to ask you is what all is a parenteral container  
25 because nurses don't think that way. They think

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 about what they need in their workplace to get their  
2 work done. And I want you to keep thinking about  
3 that as I go through this because I will tell you,  
4 if you put a bunch of nurses on an island and did  
5 Survivor with them, at the end of the show you'd  
6 have a well woman clinic and you'd have - everybody  
7 would be inoculated and everybody would be in great  
8 health and their cholesterol would be down because  
9 they are very task-oriented. That's what we do. We  
10 come into a situation and we make things work. And  
11 so the way that they think about things is what do I  
12 need to do in order to fulfill this for my patient.

13 And that's going to be their motivation. That in  
14 itself is a wonderful thing. That in itself is a  
15 bad thing because they will do what they need to do  
16 to get that work done.

17 So on your illegal - because we're not  
18 going to get consents here - walkthrough to talk to  
19 nurses, ask them what's on the parenteral container,  
20 get those answers back, and I'll tell you this is  
21 what I got. What I got was they need to know what  
22 the amount is, how much is in there. They need to  
23 know if there's a drug in there or not. They need  
24 to know concentration. A couple of them said  
25 expiration date and they need to know the route,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 what it's for, and that's it. So I was really kind  
2 of pleased to hear you talk this morning because  
3 this is what I keep hearing from you over and over  
4 again and I'm kind of surprised at the consensus  
5 that I'm getting out of this group. Is that there  
6 is a finite group of very important facts that we  
7 need to know on these containers. The rest of it, I  
8 was asked at lunch if a nurse ever reads those.  
9 Upon occasion we do. We do when you've got a  
10 patient that's got something exceptional, when  
11 you've got a different drug that you're not used to.  
12 Other than that, that information is not something  
13 they usually use. So when you see something like  
14 this where you've got 10 milliequivalents of  
15 potassium in one bag and 20 in the other, and  
16 they're in the same bin in the same drawer on the  
17 bottom so you have to stoop over and look at it,  
18 it's very easy to see how these look very similar.  
19 And if you just miss that one number, then you're  
20 going to pick up the wrong bag in this situation.  
21 The implications for this, I think time and time  
22 again I can say this, and I think you've already  
23 said it to me is that nurses need only the essential  
24 information for the task at hand. And if you  
25 consider that they are the highest population you

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 are going to be dealing with in administering these  
2 IV fluids, I think that's a call to action there to  
3 simplify the information. If it's not, then perhaps  
4 I can show you a few more things that are going on  
5 in nursing that will change your mind.

6 One of the things you might ask as you  
7 walk the halls is where are the nurses because right  
8 now in the United States there's an 8.5 percent  
9 shortage in nursing. And I'm not going to spend a  
10 lot of time on that. It's multi-factorial why this  
11 has happened. It's got to do with Baby Boomers.  
12 It's got to do with opportunities for other say  
13 careers where you don't have to stay up nights and  
14 weekends and work all the holidays. It's got lots  
15 to do with what's going on with the industry. But  
16 the fact is right now there's at least an 8.5  
17 vacancy rate. And some of our smaller hospitals  
18 where we do consulting in smaller towns where  
19 there's critical access hospitals in Texas, they  
20 will tell you if one of their nurses goes down,  
21 that's it, the hospital about closes because they  
22 may have only five or six nurses in a small town.  
23 So we've got a great shortage here both in our  
24 metropolitan areas and in our urban areas too. And  
25 the Health Resources and Services Administration

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 projects that the nursing shortage should grow by  
2 about 1 million nurses by the year 2020. I don't  
3 see that having any relief so far and in the  
4 meantime you might be thinking about this, that the  
5 average age of a nurse is about 46.8 years of age.  
6 I don't know where they got the 0.8 thing. But  
7 anyway, what you have before you now is a little  
8 greater than average older nurse here giving you  
9 this lecture. And the study that Buerhaus actually  
10 put out gave us some more interesting news in that  
11 the growth in nursing, the nurses that are coming  
12 back into nursing are over 50 years old. So I would  
13 say that now we've got kind of a middle-aged nursing  
14 population here that we're dealing with.

15 Well, there's some bad news about that.

16 And that is of that growth factor, I find over age  
17 45 - I don't know if you've noticed this, but we all  
18 tend to get a little bit farsighted. And so the  
19 small print is difficult, impacting nearly everyone.

20 And they say by you know 55 it's 100 percent of the  
21 population is affected. Letters start to look  
22 fuzzy. In my own case I noticed I started wearing  
23 these all the time, in the clinical area, much to my  
24 chagrin I just had to take them to the grocery store  
25 because I couldn't figure out what was on the box in

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the grocery store. And we start trying to  
2 compensate for that. But we have not compensated  
3 for that in the workplace of nurses at all. We have  
4 not put better lighting in. Reading is extremely  
5 difficult in low-light situations. I now have these  
6 high-intensity lights over my desk, I have it over  
7 my reading chair and we have done nothing about that  
8 in the nursing workforce.

9 In fact, this actually is like the rest  
10 of my slides, we just went walking with our camera  
11 one day through some of our consulting hospitals and  
12 this is a neonatal intensive care unit. Now, do you  
13 see a problem with this picture? This is actually  
14 during the day. This is a low-light stimulation  
15 environment. And when I asked well what do you do  
16 if you need to prepare medication, what they told me  
17 is we go here under the lamp. Well, you and I know  
18 that you can't always go under the lamp. When  
19 you're in a high-intensity situation where you have  
20 to respond to patients' needs, got a lot of things  
21 going on, that's just not going to happen.

22 The other problem that we have with  
23 vision, and this is across the board too but  
24 especially is kind of influenced in age is that  
25 maturity decreases our ability to discriminate

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 cluttered situations. So if you've got your little  
2 greater than average nurse here walking around  
3 teaching clinical nursing students and we've got a  
4 patient going by with this IV pole that's got  
5 multiple bags up there, what do you think the  
6 chances are I'm going to be able to read all those  
7 labels? Pretty poor. And if you know human nature  
8 and the way that we work and the way cognitively we  
9 put things together, you start realizing how these  
10 things begin to happen. Because we similarity-match  
11 and we go with what's familiar with us and we make  
12 those assumptions, not consciously by the way folks.

13 This is all unconscious. This all goes back to the  
14 human factors and usability facts that we need to  
15 deal with in clinical situations.

16 So this is the slide that Mike Cohen  
17 used earlier that I also will take license with.  
18 Because if you think about the yellow labels here on  
19 these IVs and across the board, differentiating  
20 between each one of those much less unraveling the  
21 spaghetti of tubing is going to be a challenge.  
22 This is not the nurse's only patient either. You  
23 know, this is one patient, maybe one of two, in an  
24 intensive care situation one of three or four. But  
25 when you start adding those numbers together, this

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 task becomes even more daunting.

2 This is an ECMO unit. This is actually  
3 an IC unit with an ECMO patient running. As you can  
4 tell again we've got much visual display here, a  
5 clutter of information that's being presented to you  
6 at one time. Now, this is flat information in the  
7 work environment. I'm not even talking about trying  
8 to go back and find the finite details and minutiae  
9 that make taking care of this patient safe that  
10 comes out of the package inserts where the font, as  
11 you have aptly pointed out is very small. We're  
12 trying to get all of that information down there.  
13 And besides that, for package inserts, do we really  
14 know how to present that information so the most  
15 important information is presented in a way that it  
16 comes out to the practitioner? I am recalling  
17 something that Mike Cohen would speak to much more  
18 succinctly about the Denver nurse case where they  
19 were looking for the route of administration for  
20 that drug, and they were looking in the package  
21 insert and they did not find it. Now, on one hand  
22 you may have someone that tells you well, you know,  
23 they just weren't vigilant enough, they just didn't  
24 look enough. But over and over and over again when  
25 we've done error analysis we've seen careful,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 thoughtful practitioners trying to find information  
2 and they do not find it. We've simply got to learn  
3 how to present this information in a better way so  
4 people can discern between the pertinent points.

5           So here's the other good news about the  
6 work environment in nursing if I haven't cheered you  
7 up so far, and that is new products are added daily.

8       If you're a new nurse on the unit and you're just  
9 working in that unit in a usual fashion, what you  
10 feel like is that you're in the middle of tidal  
11 waves of information. You get new products in  
12 constantly and despite the best efforts of the  
13 pharmacy and everyone else to in-service to bring  
14 the information to bear, you're just not going to  
15 get it. It's going to come to you and you're going  
16 to open a patient's drawer for medications and pull  
17 out something you are not familiar with. What we  
18 know now by human factors analysis and cognitive  
19 analysis of some of these errors is that people at  
20 that time go with what they know. The human brain  
21 works in a pretty predictable fashion in that we  
22 look for things that are common to us, that feel  
23 comfortable to us and we put those two facts  
24 together. We kind of work like a Windows file  
25 system in that we start seeing something unusual in

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the environment and trying to make it fit like  
2 something else. So if you wonder why some of these  
3 new products come out and they make spectacular and  
4 horrible errors with it, start looking for something  
5 that looks like that. And if you can gain the trust  
6 of the clinician well enough, they will tell you  
7 well it looked like this so it must have been that.

8 And that in itself is something very important for  
9 us to learn in this industry is that that's the way  
10 our minds work and that's what we will do when  
11 presented with unique problems.

12 The labels vary. Our hospital is on a  
13 purchasing group and so I know because we're a state  
14 institution, we try to be fiscally responsible and  
15 good stewards of the money that we are entrusted  
16 with, we try and make the best purchasing decisions  
17 we can. And when I talk to the purchasing  
18 department what they tell me is well you know, we've  
19 got a price break on this and if we go with this  
20 then we can save this much money for the hospital.  
21 And you know in these days and times it's a really  
22 hard sell for me to go back to the financial officer  
23 and say we need to change our purchasing practices  
24 because if you really look at the margins that we're  
25 dealing with now in the industry it's very, very

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 important for us to have that financial outlook so  
2 that we keep our industry going and we keep the  
3 patients coming through. So we get labels, we get  
4 different products from different manufacturers all  
5 the time. And for the nurse at bedside that feels  
6 like random acts of violence I think sometimes.  
7 They're going about their day and all of a sudden  
8 they're presented with something they've never seen  
9 before and they have to problem-solve right then and  
10 there on how to deal with it.

11           There's a lack of consistency. I think  
12 you have proven that to the point where I really  
13 don't even need to speak to it much this morning.  
14 As I watched your slides go by, I see a lot of  
15 efforts in trying to change these labels for the  
16 font, for the background and for the color. And I  
17 will tell you right now it's a mishmash out there.  
18 It's just a roll of the dice what you're going to  
19 get at bedside and then you're going to have to deal  
20 with it. The other problem with that though is  
21 this. Remember I talked about the fact that we  
22 similarity-match. We do that so unconsciously in  
23 normal human operations - and this is even past  
24 nursing, pharmacists do it, that's the way our  
25 brains work - so that we are going to go with what's

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 in our data file here and we're going to match to  
2 what we saw before. So now if we've got a little  
3 bit of a change in that we zero in on the tall  
4 letters and the tall letters are a little off. Now  
5 you've got them hanging the wrong bag.

6 Low or no light. Have you ever walked  
7 through the units at night? It's completely dark in  
8 there. We're trying to get the patients their rest  
9 and you know, some of the errors that we've looked  
10 at through our system in the last couple of years  
11 have been in the middle of the night, especially  
12 pediatric units where they just got a baby to sleep  
13 and they're trying to keep the baby asleep, trying  
14 to give everybody their rest and they take a little  
15 bit of a shortcut and kind of work with it in the  
16 no-light environment. And there's incentives for  
17 that isn't there? No one wants to wake up the  
18 patient and wake up the baby. Nobody wants to wake  
19 up the parent. So you take that little bit of an  
20 edge there and now you've got an error going  
21 through. All of these kind of are contributory  
22 factors. Can you put your finger on just one and  
23 say well that was it? Probably not. What you look  
24 at is with all of this in the milieu you're going to  
25 get these kind of errors. Constant distractions.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 I'll talk a little bit more about that in a minute.

2           The other piece I wanted to bring to you  
3 and kind of talk to you about is the emphasis on  
4 task completion in nursing. That again and again  
5 with the nursing shortage and the different  
6 shortages that we have faced and kind of the re-  
7 engineering that healthcare does over and over  
8 again. I don't know how many of you are in hospital  
9 systems, but you've probably gone through a couple  
10 of consultants in the last years I would imagine. I  
11 was in one hospital. We went through three in four  
12 years. We were all like bomb-struck you know at  
13 that point because we had people coming and saying  
14 well you know if you do a time study it should only  
15 take this much time so change this process, so  
16 change that process. And the real emphasis then  
17 becomes how do you get these things done. Get these  
18 things done. And remember what I said about nurses'  
19 orientation being I'm going to get this work done in  
20 this period of time. When you add to that that  
21 their incentives are on task completion, on getting  
22 it done in a certain time period, then we've got  
23 another recipe for disaster because as our human  
24 nature takes over, we start trying to get those  
25 tasks done. And so we start dropping off these

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 other things that we know are safe practices as we  
2 go along.

3           What you'll find sometimes when you look  
4 at error reports is you see failure to follow policy  
5 and procedure. I don't know if you've ever run  
6 across that before, but that seems to be the  
7 causative factor that somebody will stick that on  
8 there. Well, the real problem with this error is  
9 they didn't follow policy and procedure. And my  
10 second challenge for you today is to go look at your  
11 policies and procedures and kind of look through the  
12 time period that it takes to complete that task and  
13 then multiply it by the number of patients and then  
14 multiply it by the number of drugs and now multiply  
15 it and then add in all the distractions that we have  
16 in all the other tasks. And what we've done is set  
17 up some pretty unrealistic expectations in a lot of  
18 areas by doing that. And I'll confess to you today  
19 I've written a lot of those policies and procedures.

20       They were eloquent. I think I was the only one  
21 that read the full thing. They were very long. But  
22 did I actually see if someone could operationalize  
23 that in clinical practice? I don't think we've done  
24 that. So it's time for us to kind of get away from  
25 this idea about not following policy and procedure.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1       And when we have a tendency to go there, we need to  
2       ask ourselves what was the situation at the time,  
3       what was the number of tasks that person had to  
4       complete and what was their motivation for not  
5       following policy and procedure.

6               The other piece that follows into this  
7       is again going back to human factors and looking at  
8       cognitive analysis of some of the situations you  
9       realize that we look but fail to see many times. We  
10       will look at something, fail to see it, or we will  
11       see what we want to see. And we've demonstrated  
12       that over and over again. The more familiar the  
13       color, the shape and the type, the more likely we  
14       are to similarity-match. And this is grounded in  
15       the human factors science, it's been around in other  
16       industries. Other industries deal with this. We  
17       have not approached this in healthcare and certainly  
18       not worked with it with labeling. We definitely  
19       need more attention to this area. So we do get  
20       things like 20mEq looking like 10mEq and during all  
21       of this we've got distractions going on.

22               And here's the one little piece of  
23       literature I'll bring to you. Tess Pape did a study  
24       on innovative approaches to reducing nurses'  
25       distractions. And what she actually did was she

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 took this bright orange stuff like they put on the  
2 people that are working on roads and put these big  
3 orange aprons on nurses that said "Leave me alone,  
4 I'm giving medication," and actually put them out in  
5 the units. And what she found was it worked for  
6 just a few days and then everyone was immune to it  
7 and started distracting them again. That tells me a  
8 couple of things. One of the things it tells me is  
9 the tasks are so pressing that they are moving past  
10 those thing and so we really need to spend some time  
11 looking at where are nurses giving medications. The  
12 other thing that's kind of interesting if you've  
13 seen the medication carts that roll around the  
14 halls, we put nurses in the middle of a hallway to  
15 prepare medications, one of the high-risk and  
16 demanding tasks that they have with critical  
17 thinking skills and we wonder why they make mistakes  
18 while they've got everything else going around them  
19 and all this noise, call bells, everything else  
20 going on. USP again from the database has shown  
21 time and time again that many of the errors, three-  
22 quarters of the errors in this particular study were  
23 influenced by distractions. This one, distractions  
24 and workload cited as contributing factors.

25 I would say we have definitely proven

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 there's distractions, but in the meantime what we've  
2 done, this is the industry's answer to that, is we  
3 have bagged them and tagged them and now we're  
4 tracing them through the hospital. We've put tracer  
5 tags on the nurses so we can track them on these  
6 little GPS maps and then we've got little  
7 communication devices, either walkie-talkies or  
8 we've got telephones. Now the telephones are  
9 particularly nice for us because you can give that  
10 phone number to the family of your pediatric patient  
11 so while you're in the hallway preparing your  
12 medications you can have the family also calling  
13 you. One particular response to that in 2002 I  
14 think you might find interesting is that on Labor  
15 Day a group of nurses put a box in the middle of the  
16 unit and put all their tracer tags in the box and  
17 then the box disappeared because they felt like it  
18 was an invasion of their privacy because they'd  
19 actually been tracking their break time and seeing  
20 how many minutes they were spending in the break  
21 room. So obviously this is not an answer is to go  
22 ahead and put tracer tags on them. We've got to go  
23 a step past that and actually look at the cognitive  
24 and physical workload of nurses and make changes in  
25 the environment so that they are able to complete

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 these tasks safely. I especially liked their  
2 statement was that they had a concern because  
3 increasing corporate industry's effort routinize and  
4 speed up the complex work done was in a time of  
5 chronic under-staffing. And we all know that  
6 patients are not getting less complex that they're  
7 dealing with.

8 Just a word on computerized systems real  
9 quick. There's challenges to cognitive performance.

10 Perrault and others in the aviation industry talked  
11 about the way that people "trust the computer." We  
12 have found over and over again in our work that  
13 people trust automatic dispensing machines. When  
14 you go in there and you put it in the computer that  
15 you want heparin, out comes that drawer, you believe  
16 that you got what you programmed in. But we also  
17 know that humans are the ones stocking those  
18 drawers. And so what we see is people taking out  
19 10,000 units of heparin and giving it instead of  
20 1,000 units and coming up with horrible results.  
21 Over and over again. So automation on one hand is  
22 good. On the other hand it is not and will lead us  
23 down another path. Also, we say that we need to do  
24 this because they won't apply the five rights. The  
25 next time someone says "five rights" you can tell

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1       them that you know there's plenty of evidence out  
2       there now that that was absolutely the wrong type  
3       message to teach nurses because you can be right on  
4       all five of those and still make a medication error  
5       that's dire for your patient.  It's an unrealistic  
6       requirement for the workload that we've got now and  
7       absolutely for the information load we've got now on  
8       their medications it's not reasonable.

9                       This is just an example we got out of  
10       the close call system.  I wanted to show you two  
11       labels that got confused.  This actually came out of  
12       an automated dispensing machine.  They were getting  
13       ready to do a procedure where they passed a probe  
14       with a patient hoping they got lidocaine out and  
15       when they opened the bottle luckily lindane shampoo  
16       has a rather distinctive smell and so they  
17       recognized what they had and were able to stop it.  
18       So even with a color differentiation it came out of  
19       an automated machine and they trusted it.

20                      Stocking in drawers in these automated  
21       machines again is a problem.  I was talking to some  
22       of you at lunch and asking why do these things need  
23       to be opaque.  I understand that some of that's cost  
24       but I'll tell you, when you dump all of these in a  
25       low drawer because these things are heavy and they

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 want to keep them in the bigger drawers, the deeper  
2 drawers, it is really difficult to look down there  
3 and to be able to differentiate because of lighting  
4 and looking through that wrapper at that point. The  
5 other thing is some of these dispensing machines,  
6 you know if you're asking someone to reach over  
7 their head in order to identify something chances  
8 are they're not going to. And the medication load.

9 Three to four patients is our load at Anderson and  
10 we've got one of the best patient loads I think in  
11 our medical center. Each one has an average of  
12 about 20 medications. So it's 80 chances per shift,  
13 80 simple chances, this doesn't even count  
14 everything else that's going on, to make an error.

15 I couldn't help but look in our close  
16 call database to see what we had gotten as far as  
17 close calls. Now we collect information from front  
18 line providers about when they have near misses,  
19 when they actually almost make an error and it's  
20 anonymous. We came up with of the 7,300-some  
21 medication errors that are reported in that database  
22 a pretty significant, 633 were attributed to  
23 labeling and packaging errors, problems with the  
24 labeling and packaging. Which I find some  
25 consolation in because I think what it says to us is

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that they're actually to take a minute and think  
2 about the label that they were looking at and say  
3 yes, that was a contributing factor, that was a  
4 problem and perhaps labeling/packaging would be  
5 something I could change to make it better.

6           Implications for research. I think I  
7 could preach to the choir now which is my favorite  
8 thing to do and say that we need applied research.  
9 We've already gone through the demographics of this.  
10 We've gone through the occurrence rates of this. I  
11 think all of us agree, the public agrees that there  
12 are medication errors and there are problems with  
13 it. All of you agree that there's a problem with  
14 the amount of information that's presented there and  
15 we have quite frankly moved like a herd of turtles  
16 through peanut butter on this issue. It amazes me  
17 the lack of agility in healthcare for responding to  
18 these type of problems. You know, that we have  
19 discussed this over and over again and we can't come  
20 to a solution. It's kind of a little embarrassing  
21 at times that we are not able to be agile enough and  
22 to take a lead and take a stance and move forward on  
23 this so we can actually make a difference. Because  
24 all this time I've been talking they've been out  
25 there pulling these medications and giving these to

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 patients. You know, time is ticking as we go along.

2 We need more applied research about the  
3 work environment of nurses. Luckily an IOM report  
4 came out supporting that. I highly recommend it,  
5 Transforming the Work Environment of Nurses, an  
6 excellent, excellent report on keeping patients  
7 safe. We need to look at physical and visual  
8 limitations and actually make some changes in the  
9 workload accordingly to that and step bravely out  
10 there and look at cognitive load. What is the  
11 amount of information, how are we teaching critical  
12 thinking skills, how are we supporting critical  
13 thinking skills? Because as the shortage moves  
14 further, we are not going to be supporting it more.  
15 We're actually going to be finding more and more  
16 shortcuts as we go along through this process.

17 So kind of my conclusion of all this is  
18 that we can't change cognitive functioning. This is  
19 going to be the human condition. We can't perfect  
20 human performance and reversing aging is pretty  
21 futile. The time and gravity thing, I don't think  
22 we're going to make much of a dent in it. But the  
23 best reduction strategy is actually anticipate these  
24 errors which I think we've already proven we need to  
25 and design systems to prevent them. So I would hope

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that some of you would walk away from this saying  
2 that you could do applied research or if you  
3 actually did make an intervention in the clinical  
4 area and then measured those results so the industry  
5 will follow. At this point that's what's needed and  
6 I think it's what's going to move us forward. James  
7 Resen says that you can't change the human  
8 condition, but you can change the condition in which  
9 they work. And I will tell you, there's not very  
10 many nurses here today, but that the nurses that are  
11 out there I'm sure would support that as well.  
12 Thank you so much.

13 (Applause)

14 MS. BECKER: Thank you, Debora. Now you  
15 know why I like working with her so much. Our next  
16 speaker will give us the pharmacy perspective.  
17 Timothy Lesar, Dr. Lesar, is the Director of  
18 Pharmacy and Patient Care Services Director for  
19 Diagnostic and Therapeutic Services at the Albany  
20 Medical Center in Albany, New York. He has served  
21 on the faculty of the University of Minnesota and  
22 the University of Illinois at Chicago. Dr. Lesar's  
23 research and practice has focused on understanding  
24 and improving the medication use process with a  
25 focus on medication errors and deficiencies. He has

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 participated in numerous patient safety initiatives  
2 and collaboratives. He is a member of the Joint  
3 Commission's Medication Safety Advisory Group and  
4 the FDA Drug Safety and Risk Management Advisory  
5 Committee. He's a recipient of the ASHP Award for  
6 Achievement in the Practice of Pharmacy and Health  
7 Systems in 1991 and 1998 and the ISMP Chair's Award  
8 in 2000. Dr. Lesar has more than 90 publications in  
9 the medical literature. He received his BS in  
10 Pharmacy from the University of Wisconsin-Madison  
11 and a Doctor of Pharmacy degree from the University  
12 of Minnesota. He completed an ASHP residency in  
13 hospital pharmacy practice at Bassett Healthcare in  
14 Cooperstown, New York, and a fellowship in  
15 pharmacokinetics at the University of Minnesota. We  
16 welcome Dr. Lesar.

17 DR. LESAR: Good afternoon. I'd like to  
18 thank ISMP and FDA for inviting me today. It's an  
19 honor and a pleasure and it's nice to see some folks  
20 that I haven't seen for awhile. I'm going to be  
21 presenting from the pharmacy perspective here and  
22 I'll - a little bit difficult to see that, right?  
23 But when I thought about what to present I thought  
24 I'd present again what our world is like and how  
25 these things interact with our world.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1                   You know from an introductory  
2                   standpoint, just to say that when I look at our day-  
3                   to-day functions, improving the design of parenteral  
4                   fluid both large-volume, small-volume parenterals as  
5                   well as the labels the pharmacy places on products  
6                   really are needed to reduce risk. They produce  
7                   risk, they can help reduce the risk. And also,  
8                   everybody understands that in the pharmacy world and  
9                   elsewhere in healthcare we're trying to reduce the  
10                  number of things that we have to actually prepare.  
11                  That is, we have to change the way it comes from the  
12                  manufacturer. And I think this is something you're  
13                  going to see more in the future, but it will never  
14                  be eliminated. We'll always have 500g neonates and  
15                  400lb athletes in our hospitals. So while we can  
16                  move toward more pre-made materials which will make  
17                  labeling by the manufacturer more critical, we'll  
18                  also have that we change those products and we add  
19                  additional labels to products that the manufacturer  
20                  makes. And certainly we're seeing a growing number  
21                  of products and often very complex products with  
22                  complex dosing structures on a frequent basis that  
23                  enter into our system.

24                         But we do think there's been substantial  
25                         improvement in labeling over the years, but we still

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 I think our day-to-day experience, the things I see,  
2 the things that my staff brings to me and says oh,  
3 look what we did, the risk management reports that I  
4 read, our quality reviews all demonstrate that we  
5 still have a lot of risk and a lot of errors that  
6 are occurring. So clearly further efforts and I  
7 think this is a great first step. I think Mike's  
8 point about somebody's just got to take charge of  
9 this, take hand on this and move this forward is  
10 really required so that we can take care of our  
11 patients in a more safe manner. And I think one of  
12 these things - and this process is really going to  
13 require some very robust risk assessment that looks  
14 at the context, looks at exactly what's happening  
15 and understand that things are different in  
16 different parts of the organization. The pharmacy,  
17 if we have to prepare something the label means a  
18 little bit something different than if it's pulled  
19 off the shelf by a nurse. So every place that you  
20 see these things being used, the context is  
21 extremely important and so you're going to get a lot  
22 of people saying this is most important on the label  
23 and you might say this is most important. It really  
24 depends on what the context of that label is. And  
25 so it will be a difficult process, but I think it's

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 doable.

2                   And so key point. This has to be -  
3 whatever we do, whatever you do, whatever decision  
4 is made, this has to be done in terms of the context  
5 in which the products are being used, both in the  
6 person who's using it. A great discussion of what  
7 the nurses are thinking when they're using it. I'll  
8 try to provide you some information on what the  
9 pharmacist is thinking and what environment they're  
10 in. And also that - understand that healthcare is  
11 highly dynamic. Just because they do it one way in  
12 one institution or on one floor of the institution  
13 does not mean that it's not done differently in the  
14 same institution down the hall or by a different  
15 individual. Very dynamic, very different and each  
16 situation creates its own sets of risk.

17                   And so when evaluating potential  
18 problems, I think it's important that everybody  
19 understands what the flow of a product is through a  
20 healthcare system. And this is a slide that I've  
21 used in the past to try to explain to people who  
22 don't work in healthcare system why something that  
23 looks perfectly clear, perfectly safe isn't once we  
24 start using it. And the point is that once you  
25 introduce anything into the healthcare system,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 whether it's a new product, a new drug, even a new  
2 process, there are many, many factors that it  
3 interacts with that were not thought of, not  
4 predictable in how they interact. So anytime you  
5 input anything into the healthcare system we're  
6 going to create errors and it will be - they'll be  
7 very understandable in hindsight, but not  
8 predictable in foresight.

9           And I think it's important that you  
10 understand what the flow cycle looks like in most  
11 parenteral products. And if you look at, you know  
12 one of the things is we do when we decide we're  
13 going to buy these products. Sometimes the  
14 formulary committee decides you're going to buy  
15 something that's going to decide that we'd have a  
16 product in the organization used depending on what  
17 the needs or types of patients you have. There's  
18 contracting, as was already mentioned. We're  
19 primarily a Baxter hospital. We primarily have  
20 Baxter products. Some hospitals might have Braun,  
21 some might have Hospira. Depends on contracting.  
22 What happens if there's a shortage? What happens if  
23 there's a recall? All of a sudden we have different  
24 products. But there's a decision made. These  
25 things are purchased and they're really - they're

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 purchased and they're received into the  
2 organization, usually into a storeroom. We happen  
3 to have our own storeroom. But also central supply  
4 distributes most of the large-volume parenterals.  
5 Even the potassium-containing large-volume  
6 parenterals go to the floor. They don't go through  
7 the pharmacy. All right? So there are two  
8 different ways some agents are actually distributed.

9 We get them, they sit in our storeroom. Pharmacy  
10 needs them. They come up to the pharmacy and they  
11 are placed on different storage areas in the  
12 pharmacy. Depends on where we're going to need  
13 them. These are always done by clerks, techs, never  
14 done by pharmacists. Mike showed you some of the  
15 boxes that look the same. So we've actually had  
16 situations where we bought through purchasing got  
17 the wrong ampicillin, multi-dose 10g vial that  
18 looked like a 1g by another company. We never had  
19 the 10g before. And believe it or not it went  
20 through this whole system, made the whole cycle  
21 because somebody made a mistake in purchasing.

22 So anywhere along this process you can  
23 see errors that get into the system. But once this  
24 gets somewhere down in the pharmacy, and I'll show  
25 you what that looks like. And then out of that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 stock, the working stock, a technician or a  
2 pharmacist selects that product. They may label it,  
3 they may prepare a drug dose with it and then we  
4 send it. We distribute it. And this may be - we  
5 may distribute it as a unit dose in a cassette. We  
6 may send it to the refrigerator on the unit. We may  
7 place it in a automated dispensing machine. And  
8 believe it or not, we do think about what that  
9 product looks like. Those automatic dispensing  
10 machines you saw what was called a matrix drawer.  
11 That's a drawer that's open and you can select  
12 different products. We have almost eliminated those  
13 from our organization because people were picking  
14 the wrong things out of that matrix drawer or got  
15 the wrong one, put it back in the wrong matrix. So  
16 our drawers don't allow that. They light up or only  
17 one of those boxes open at a time. Or we've taken  
18 that type of thing off the floor so nurses don't  
19 have the opportunity to make that error. So you can  
20 make a lot of decisions in here about trying to  
21 reduce that risk.

22 So they move up, off and on, then they  
23 get closer to the patient. Now they're on the floor  
24 somewhere for the nurses to give. But remember, our  
25 goal here is to provide to the nurses a low number

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 of things to select from, and those things that they  
2 can select from that are accurately labeled and  
3 easily identifiable and limited. So they don't have  
4 to do a lot of selection and make those errors. And  
5 then of course the nurses are going to give that  
6 drug. And also in here it's not just nurses. If  
7 you go to the operating room it's the  
8 anesthesiologist, the OR nurses, sometimes OR techs.

9 It's the profusionists, it's the dialysis techs in  
10 the dialysis unit. Go to the cath lab it might be  
11 the - they'd have cath lab assistants now who do  
12 these things. Who's ever doing these things, these  
13 again differ wherever you go in the organization.  
14 So what's critical to them varies and what  
15 environment they're in in terms of their selection  
16 of the product varies quite a bit.

17 If they're not administered or if  
18 they're overstocked or whatever, things are then  
19 returned to the pharmacy. Guess what? They've got  
20 to be identified and placed back into the stock  
21 again. So actually you can see where things have to  
22 be identified numerous times. So every place you  
23 see a spy glass we've got to identify these  
24 products. Sort of all around the system, multiple  
25 places to identify.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1                   Now, welcome to our IV room. We are a  
2                   630-bed hospital. We have a large 50-bed neonate  
3                   intensive care unit, Level IV. So we have 500g  
4                   neonates. We have multiple, multiple intensive care  
5                   units, pediatric, adult, intense, medical, cardiac,  
6                   neurology. And so we have just about everything.  
7                   We have transplant patients. We run the whole  
8                   gamut. So we see, we have to provide through our  
9                   central pharmacy we provide drugs to all of those  
10                  patients. So our IV room is large. We dispense  
11                  about 1,200 a day that we actually prepare and  
12                  label, IVs that are prepared. And these are just  
13                  some of the places. Look, here's multiple drawers  
14                  like this containing over-bagged IVs, shelves,  
15                  refrigerators, and so that's what it looks like.  
16                  Very, very hectic. Make a lot of things that are  
17                  needed immediately and multiple people working.

18                         And so I was just going to go through  
19                         and hit many of the items that were already talked  
20                         about but from our perspective. One of the things  
21                         that was discussed were over-wraps. In a pharmacy  
22                         department, much of what we select has an over-wrap  
23                         on it. Over-wraps are critical in terms of our  
24                         ability to identify there what we see. When we  
25                         select an agent, we're selecting for the most part

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 something already with an over-wrap. So this is  
2 what they look like. This is a pretty clear picture  
3 of what over-wraps look like when we select a  
4 product. How many people would think this is clear?

5 These are two different drugs. So these type of  
6 over-wraps, they should be eliminated. Go to the  
7 foil ones.

8 Here's a foil wrap. Look at the  
9 difference. This is - I squeezed down so the  
10 moisture inside the over-wrap makes this more  
11 visible. But you can see the difference. Here's  
12 over-wrap paper nicely - you can actually read that.

13 This really is unacceptable. Over-wraps are  
14 terrible. So here you go, they clearly obscure the  
15 label. And by the way, in the pharmacy they stay on  
16 until use. We don't have a lot of these products in  
17 our Pixis machines, in our base cabinets, but you  
18 can see if this was in one of those matrix drawers  
19 on the floors how easy it would be for that to be -  
20 for someone to make a mistake, to simply put it back  
21 in the wrong slot and easy to make an error.

22 They're very difficult to read. You really have to  
23 take the example of the poor lighting. They're  
24 almost - they're very, very difficult to see. So  
25 over-wraps should be easy to read. Just over-wraps,

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 and we have shelves full of them, drawers full of  
2 drugs in over-wraps that are similar to that.

3           The refrigerators are very similar.  
4 Refrigerators will contain drugs that are either not  
5 stable at room temperature or drugs that we have  
6 prepared, ready for use. So this is one of our  
7 refrigerators. Here's another one of our  
8 refrigerators, some syringes. Here's the small-  
9 volume, some are large-volume parenterals. The  
10 yellow labels are patient labels that have been  
11 added over the top of the manufacturer label. So  
12 refrigerators are always in short supply. They take  
13 up a lot of space. We could not squeeze another one  
14 into our IV room. And this is also true if you go  
15 out to the floors. We take these products and we  
16 place products like this, we take those to the  
17 floors and put them in the refrigerators on the  
18 floor every day. And some of those floors, some of  
19 those refrigerators are essentially - in the  
20 intensive care units look like this. And the nurse  
21 is going to go in there and select the right drug.  
22 Somebody selects it, puts the wrong one, puts it in  
23 the wrong bin, all of a sudden you have trouble  
24 identifying that drug. So environment and context  
25 are extremely important in terms of looking at how

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 these things interact. So to say, to hold a product  
2 in your hand and say gee, and hold two of them say  
3 yes, these look pretty different. You can see you  
4 start placing them in a context like this, things  
5 don't look so different anymore. So the printed  
6 products are never handled in isolation. They're  
7 always bunched together. They're always kept in  
8 close proximity, okay?

9           So there you go. That's just a drawer.  
10        I opened up a drawer in our IV room. You tell me  
11        if I placed a similar red and black-labeled product  
12        in that drawer that I could tell the difference. So  
13        when a tech goes to get that, we don't go just get  
14        one of these usually. We have over 550 patients in  
15        our hospital at any one time. When a tech goes in  
16        there batching things, they go in say I need 15 of  
17        these. They take 15 of them out. Do you think they  
18        look at every single one? Or even if they looked at  
19        every one, do you think they would recognize the  
20        difference if there was one wrong one there? No,  
21        they wouldn't. So you can see where the over-bag  
22        and the similarity now create a tremendous risk for  
23        error. And remember, this is what - somebody took  
24        this out of a box that Mike showed you, put them  
25        into the drawer, one of our techs or clerks did

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that, and now this is how they sit. And if they  
2 were to grab 15 but only use 12, somebody had to put  
3 them correctly back into the drawer.

4 And this is just a good example of a  
5 shelf, kind of like you saw before with large-volume  
6 parenterals. Here's foil-wrapped one. Here's over-  
7 bagged one. Here's another foil. So it's very easy  
8 to see how things get placed on the wrong shelf or  
9 selected from the wrong shelf. So the other thing  
10 in this room, I didn't show any people, but believe  
11 me there's people. There's maybe eight or ten  
12 people in this room at any one time, pharmacists and  
13 techs, clerks moving the materials. So this is a  
14 high volume of work, lots of things that have to be  
15 done right away. There's a huge supply chain  
16 function. That is, it's a materials management  
17 function. We are trying to maintain a limited  
18 number of working stock in the right places. But  
19 pretty much there's a huge turnover because we have  
20 limited space, plus the more - if you don't want to  
21 have your inventory so large, that you have problems  
22 with expiration dates and things that if you have  
23 too many obviously you have an issue with selecting  
24 the wrong product. IVs, the huge number of IV  
25 products that we go through. Remember, we have a

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 lot of custom-made products that we have to make  
2 because of our population variation. So we have a  
3 large number of different products.

4 Disruptions. Very common, as was stated  
5 before. And this is very reliant on human  
6 resources. We are a hospital that's about 40  
7 percent into bar code administration. In the  
8 pharmacy we use robotics to dispense most of our  
9 oral drugs, but we don't use them at all in our IV  
10 room. And we also use bar code to load up our Pixis  
11 machine. So to check the Pixis material, then to  
12 get them into the right drawer in the Pixis machine  
13 we also use bar code. But in terms of the IV room,  
14 there's not really good products out there for us to  
15 use bar coding in the IV preparation part of the  
16 pharmacy department. So one of the most critical  
17 areas is in IV preparation and we really don't have  
18 some of the technology that's going to be really  
19 applicable to making doses for neonates. Some of  
20 it's becoming available and we'd like to apply it as  
21 we go along. But again, it's highly variable and  
22 highly dependent on human performance and often once  
23 we make a product, it's very - you can't tell. You  
24 can tell if you have two tablets in your hand, but  
25 you can't tell if you put 1g or 2g of a drug in a

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 bag anymore because it's a clear solution.

2           So the other issue. I talked about  
3 purchasing. So product lines. Remember, product  
4 lines look very similar because it's typically  
5 product dress and companies have a typical way they  
6 want to make their product look. And so products  
7 that come from the same company tend to look the  
8 same. Different companies though, I do agree they  
9 do look different. However, there are chance look-  
10 a-like situations. And so drugs do tend to look  
11 different. Here's a Braun bag that we tend to  
12 stock. Most of them are Baxter products which look  
13 like this. And the contracting pretty much  
14 determines that in our organization. However, if  
15 there's a shortage, we run out of something, have to  
16 borrow it, there's a recall, all those things could  
17 require us to produce - to order in other different  
18 types of products. And here's an example of product  
19 line. Dopamine. There's a tall man, but when I  
20 went and said - when I went in to take my pictures,  
21 I said okay you know give me dopamine because I was  
22 just looking, I was going to take a picture of tall  
23 man. So the pharmacist went okay, I'll get them.  
24 He went to one drawer, got this. He took about 10  
25 steps and down an aisle and got this one. Took

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 another 10 steps and got this one. He said oh, we  
2 have to separate them because we get these mixed up  
3 all the time. All right? So you can see, you know,  
4 it seems - they're definitely dopamine, but it's so  
5 easy to confuse them because they look so much the  
6 same across the product. So people adapt.

7 Across product lines there's chance  
8 look-a-likes. I saw this riconazole over-bag and I  
9 think they are very distinguishable. But the  
10 problem is in an area, in a place like Albany  
11 Medical Center is we maybe purchase something else  
12 and if another company decides to have color dress.

13 There's lighting issues, there's color vision  
14 issues. There's a chance, just like we know from  
15 other types of products that something is going to  
16 appear that looks similar or appears similar to  
17 somebody as something else that has a distinctive  
18 look. So oftentimes a distinctive look is  
19 advantageous until something that's made by somebody  
20 else totally different also has somewhat distinctive  
21 look like that, and people will confuse those  
22 things. We clearly see that.

23 I think Mike showed Brevibloc foil wrap.  
24 Another label. Different colors differentiate the  
25 two concentrations. This product is actually what

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 we would consider very good at this point. I'm just  
2 waiting for something else to show up that looks  
3 like that. Blue line here says injection. Nice big  
4 letters. Pre-mixed injection. May start with a `B'  
5 who knows. This could easily, given - if something  
6 came with the same color, could easily be mixed up  
7 even though it's a different drug name because that  
8 distinctive color and that distinctive look. Right  
9 now it's a great example.

10 How should you express the drug name?  
11 How would we like to see the drug name? This is a  
12 bad picture, but this happens to be a Xerox of a bag  
13 that was involved with an error in the pharmacy so I  
14 thought I would just use it. This is Gentran -  
15 Dextran 40. Look at this label. Gentran 40.  
16 What's this? 0.9 percent sodium. Look at the size  
17 of that. Then down here it says you know it says  
18 injection. Then it says Dextran 40 and 0.9 percent  
19 sodium chloride. And you can see oftentimes things  
20 are picked by our technicians, prepared - the  
21 pharmacist checks them. You can see, what is  
22 Gentran? Goes back to that. What is Gentran?  
23 Well, Gentran is Dextran. The technicians do not  
24 know that when we hire them. They have to learn.  
25 Many people don't know. It's not a common brand

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 name that people use. No doctor ever orders  
2 Gentran, they order Dextran 40. So again, brand  
3 names. This is stressed here. Everything we do in  
4 the pharmacy is really based on a generic name. We  
5 enter into the pharmacy computer by generic names.  
6 Any label we produce has first the generic name.  
7 The generic name is the primary identifier. We  
8 translate - most of our labels have both a generic  
9 and a brand name on, but the first name is always a  
10 generic name.

11 You ask me, the first thing here should  
12 be the generic name and in bold, the largest font.  
13 Don't tell me what's in it until much smaller if I'm  
14 interested. Don't tell me how you buffer it. I'm  
15 not really interested in that until I need to  
16 specifically look for that information. Okay. But  
17 here it's very difficult to tell what is this. Tall  
18 man lettering. Another point. Very nice. Here's  
19 dobutamine, dopamine. They jump out at you. This  
20 line, why is that there? I don't know. That's very  
21 interesting. Who decided to put the line there? I  
22 wasn't sure when I started looking through these  
23 products again, I don't remember ever that being  
24 discussed ever in any literature, but very  
25 interestingly you know it looks like that's the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 whole word. And I'm just waiting for the error, for  
2 the techs to think oh this is just the salt or  
3 something. Dopamine - and you can see, it looks  
4 pretty distinct. So then what I did, I just took  
5 the color out. Just an example, here's how it would  
6 translate into the IV, the product. This is what it  
7 would look like that would come out of our pharmacy  
8 system. It would come with this label, patient's  
9 name would be here, tells you what the drug is.  
10 Here's our bar code so the nurse uses it when she  
11 bar codes it, when she gives it. And so it does  
12 translate there.

13 Talk about tall man, you talk about  
14 consistency. We're trying to be consistent in our  
15 tall man. Tall man in our IV labels, in our  
16 automated dispensing machines, in our electronic  
17 formulary, in our pharmacy computer system and  
18 hopefully it will eventually be our CPOE system, in  
19 our medication administration record which is  
20 pharmacy-generated, or in our electronic monitor.  
21 And so when we started looking at this we had to do  
22 exactly that. All of a sudden we noticed that the  
23 tall man lettering differed across our system  
24 because somebody would look at something for one  
25 source and one of our systems - from one of our

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 systems, but for the IV labels they looked at  
2 something else. And this became a real problem.  
3 They said well gee, here this manufacturer uses  
4 this. And I would look at that. I use - tend to  
5 use what's listed in Lexi-Comp which I believe is  
6 the same as ISMP because Lexi-Comp is our drug  
7 information supplier so they use it, they produce  
8 our electronic formulary and they also produce our  
9 drug - one of our online drug information systems.  
10 So it's there. There's not much I can do to change  
11 that. So we try to be consistent from our drug  
12 information resource so we try to make our  
13 medication administration record, the pharmacy  
14 computer and our IV labels all match. But you can  
15 see if we've done that and a manufacturer decides to  
16 use different tall man lettering, you can see what  
17 the problem is. So tall man lettering needs to be  
18 standardized and it should be controlled through  
19 either a standards within the organization - through  
20 the manufacturers or by regulation.

21 But look what happens when you take the  
22 red and the coloring out. You know, all of a sudden  
23 while that may stand out at you, I don't know. I  
24 would see a tech who sees this all of a sudden. I'm  
25 just telling you and a tech grabs it, puts a patient

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 label on it, prepares it for the pharmacist. The  
2 pharmacist doing 24 things went in, they're calling  
3 staff in the emergency room and people are screaming  
4 at them because we're not getting the drug fast  
5 enough. All of a sudden because the tech was able  
6 to take this product and they confused it, the  
7 pharmacist might not pick up the error. Redundancy  
8 is important for that double-checking in our system  
9 is important. I'm not so sure sometimes we aren't  
10 making our own set of errors.

11 But you can start to see what some of  
12 the differentiation starts to make its own problem.

13 And in terms of us trying to differentiate it in a  
14 system that is complex, it starts to become quite  
15 problematic. And you see some of the things we try  
16 to differentiate in certain systems are problematic.

17 And the other thing - we also mentioned  
18 understanding - we often talk about what people  
19 would understand and the suggestion that somebody  
20 would ask what NaCl is. That doesn't surprise me  
21 very much at all. There are a lot of people who  
22 work within the drug distribution process who just  
23 are not savvy. They don't understand drug names.  
24 They don't understand how drugs are named. They  
25 don't understand the difference between the drug and

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the salt. There's a lot of issues like that that  
2 keep coming up. And so you can tell that the people  
3 who - and if one person makes an error can then lead  
4 somebody else to make an error as well. And so you  
5 can see things that make a difference.

6 So here again, color, talked about  
7 color. While it makes a nice difference here it  
8 leads to error here. And so I think it's a - use of  
9 color has a major problem is that in isolation it  
10 looks good. In certain selective areas it looks  
11 good, but as the number of items accumulate, the  
12 number of things we have, I think color leads to  
13 error. Color actually I think has even more of an  
14 impact on somebody's recognition of an item than  
15 does form. So anything - and there's fewer colors  
16 than there are forms, that is, names. So I think  
17 color is actually a problem. I think it should be  
18 used extremely - in extremely rare cases if at all  
19 to help differentiation. Because it's just going to  
20 accumulate. When you put it in an environment like  
21 this, things start to really look alike. This is a  
22 good example where things that are black just look  
23 alike. And the names look pretty similar, sodium  
24 chloride versus dextrose. This is just a good  
25 example of - we send the vials of the drug in with

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the bags to be prepared into our clean room to be  
2 made. And so often these things are sitting next to  
3 each other in another bin. All they do is tumble  
4 in, or somebody says oh that one fell out and put it  
5 in the wrong bin. All of a sudden somebody who  
6 thinks they should be the same thing, they aren't.

7 So and this is some prepared IV  
8 products. I'll talk about - only mention that  
9 color, believe it or not in our pediatric system we  
10 use color. But and you can see here. Here's our  
11 pink, our yellow and our blue. But they don't mean  
12 specific products. Yellow - I mean pink, that's for  
13 patients who are 0kg to 5kg. We have standardized  
14 concentrations for them. Blue is for patients who  
15 are 5kg to 20kg and yellow is for anybody over 20kg,  
16 including adults. And these are books that tell us  
17 how we make each of those specialized products that  
18 we make for those patients. The labels are all  
19 yellow. We don't differentiate them by color. We  
20 don't differentiate the product by color, but we  
21 have identified that this type of patient gets this  
22 kind of product. And it has a quite different  
23 dynamic than picking things by color. We found that  
24 actually to be a very effective process. So here's  
25 color, two drawers, as I said you can open up.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 We've really tried to avoid having two of these  
2 products in drawers right close to each other or one  
3 on top of each other because you can see two  
4 different drugs piled together, there's not much to  
5 tell the difference, is there? Especially when you  
6 add the over-wrap. So color is bad if you ask me.

7           What about labeling? What should be on  
8 the - what should be the name? Here's magnesium  
9 sulfate, foil over-wrap. It says this is - they're  
10 very reflective. We have fluorescent lights and  
11 lots of them in the IV room because the IV room you  
12 want to have a lot of light because you see a lot of  
13 words and it's easy to read. But you can see  
14 because of the reflectiveness of these products all  
15 of a sudden things start to get obscured. And Mike  
16 showed you some of the bags, the way they fold. And  
17 1g, this is 1g of magnesium sulfate. It's  
18 interesting. Here's 4g and here is the 1g. So they  
19 have 1g total and that's how we usually give this  
20 drug, but again here's the concentration, 40mg per  
21 ml. And over here 10mg per ml. And they do  
22 differentiate. Do you know that the 40g bag is 40mg  
23 per ml? The 40g bag used in obstetrics. So you can  
24 start to see obviously we keep those things way away  
25 from these because it's not hard to see how those

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 things differ. But also you start to see where  
2 these things become prominent. We almost never see  
3 anybody order magnesium sulfate. They give them 100  
4 cc's of 40mg. That's not how it's ordered. It is  
5 ordered as 1g, 2g or 4g. This should be more - in  
6 this type of product if you ask a pharmacist, this  
7 is the operable 4g in 100 cc's. That's the operable  
8 function. It's not 40mg per ml. We would see in a  
9 product like this, this should be not - this should  
10 be the prominent. This confuses people. We've got  
11 another product that's this. So 1g is important.  
12 So as I said, context. If you give the whole dose,  
13 typically that's how it should be expressed. If  
14 you're giving it a drip, typically it's  
15 concentration that's important. And this just goes  
16 to show you that this becomes what your eye comes to  
17 is this 40mg.

18 What about the operable value? Here's  
19 dopamine. Right, we have these different  
20 concentrations. And look how we express the  
21 concentration, 3200mcg per ml. And that's good  
22 because dopamine is dosed usually in mcg per kg per  
23 minute. So this is operable. And this is probably  
24 okay as an identifier. For these type of drugs it  
25 probably does make sense to have both the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 concentration - the total dose, total amount  
2 contained in bag and the concentration expressed  
3 appropriately. But this should be done  
4 consistently. I think we're always looking over  
5 bags, how much is this. Some of them are in boxes,  
6 some of them are over here, some of them are over  
7 here. This makes them start to look like - but if  
8 there was some way that we could be a sequence, some  
9 display makes a difference.

10 Now what about zeroes? Lots of zeroes.

11 Zeroes confused people. Decimal point errors are  
12 not uncommon. Somebody calculates a dose, they make  
13 a tenfold error. Just I think, I bet while things  
14 are dosed a certain way. Here's 2500mg in 250 ml's.

15 Why did you tell me that? Why wasn't it 2.5g in  
16 250 ml's? And you gave me 10mg per minute of  
17 Brevibloc. That, sometimes the boluses are given in  
18 milligrams but it might be dosed in milli-mic's per  
19 kilogram or milligrams per minute. Just funny how  
20 this is expressed. Dopamine again, I hate to pick  
21 on any of these, but it's a good example. So dual  
22 expression is important, but how it's done I think  
23 really needs to be addressed by the human factors  
24 people because I'm not sure exactly how it is. I  
25 know that we see errors because of this.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1           Couple of points again, going back to  
2           that extra information. Here's that Gentran 40, you  
3           know. So why is all this stuff on here? Why do  
4           they tell me that there's all this. Look how big  
5           this is and then you tell me in pretty big font  
6           again down here. I don't know why that's done.  
7           That doesn't make any sense. We never read this  
8           stuff. We don't really care how it's buffered. I  
9           can go to the package insert, I can go online. I  
10          think those points are very valid. So all that  
11          stuff you think has to be on there, nobody ever  
12          reads it. And if we do it's because we have a  
13          problem and we need to.

14                 What about the patient labels? Here's a  
15                 good example. Here's that dopamine bag we would  
16                 take. We're going to put one of our labels on it.  
17                 What happened to all that stuff that was on there?  
18                 It got covered up, right? This is how all of our  
19                 dopamine bags look. If the nurses take one out of  
20                 there, in an urgent situation they can't take them  
21                 out of their - they put a label on it over the same  
22                 spot. Here's more patient labels. Here's some  
23                 prepared small-volume. These happen to be  
24                 chemotherapeutic agents. We put another big label  
25                 on it. What did it cover up? All that stuff that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 was so important. Also, here's a patient label.  
2 Interesting how they - now these things come  
3 together and we'll talk about human factors.  
4 Gentran 40, sodium chloride. The pharmacist enters  
5 into the computer the patient was supposed to get 3  
6 percent sodium chloride, 500ml. Technician goes and  
7 selects - going looking for this. What do they  
8 find? They find sodium chloride, 500 cc's. It's  
9 not the right concentration but to them it might be  
10 close enough. This goes to the pharmacist. Look at  
11 this. What caught their eye here? It wasn't this  
12 and it wasn't this. It was sodium chloride. Well  
13 gee, not a big surprise is it? So here's a classic  
14 example where human errors, you know. This  
15 statement, this is what caught their eye. So you  
16 can where expression and what's on the label can  
17 make a huge difference. Now this is a very nice  
18 visual example of an error caused by that.

19           And the last point to sterile water.  
20 Again, sterile water you know our point has always  
21 been keep them - just don't let it get out of the  
22 box. That is, it goes only one place in our IV room  
23 into one drawer and the problem is as I mentioned  
24 there's lots of places where things can get  
25 diverted. You know, if somebody makes a mistake in

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 central supply and orders sterile water or something  
2 and it ends up on a unit because someone picked up  
3 the wrong box because it was labeled poorly as Mike  
4 showed, ends up on a rack somewhere. Somebody says,  
5 you know somebody's looking for dextrose 5 percent  
6 in water and they see water, they pick it up and  
7 they give it. So you know, differentiation of that  
8 bag. There are certain bags that maybe perhaps we  
9 should make them very differentiated with very bold  
10 warnings on them. Use some of that real estate to  
11 say that. And I think the clear thing though is  
12 that they also, no matter what we do with it it has  
13 to not be available to be selected from.

14           And so in the product cycle we have to  
15 identify things multiple, multiple times and that  
16 humans don't identify things the way we want them  
17 to. So the things that we're trying to talk about  
18 here and make it our ability to select products in  
19 that context really has to consider what that  
20 context is like and that is very cluttered, very  
21 dynamic with a lot of people making very quick  
22 decisions, people trying to work quickly, people  
23 again doing the things that they're familiar with.  
24 They're going to select the things that they most  
25 think match what they're looking for and they're

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 going to choose it. So there does need to be  
2 standardization across the products. There was an  
3 effort made with OTCs. I'm not saying that was  
4 perfect, but that was done. Some decided that we're  
5 going to make OTC labels standardized.

6 Distinguishing features are helpful until something  
7 else has similar distinguishing features. We need  
8 to minimize the amount of information. I'll  
9 reiterate that point. We need to design these  
10 things to accept patient labels. We're putting bar  
11 codes on things. When we put patient labels on  
12 things, that typically means we don't have open  
13 stock on the floor for the nurses to select them  
14 which is a good thing, but we're going to cover it  
15 up with a patient label coming out of the pharmacy.

16 And so we need to understand what also the context  
17 of use does to the recognition of the labels that we  
18 decide are good. And we also need to make a system  
19 that's more responsive to change and I think that's  
20 been said as well.

21 So those are kind of the pharmacy  
22 standpoints. There's many other things that can be  
23 talked about in very specific circumstances, but I  
24 think that those are the high points and I'll stop  
25 there and I'll thank you for your kindness.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 (Applause)

2 MS. BECKER: Thank you, Dr. Lesar.

3 We're going to switch hats again and bring back the  
4 manufacturers perspective and some initiatives that  
5 have been created. Susan Olinger is the Corporate  
6 Vice President of Regulatory Affairs for B Braun  
7 Medical Incorporated and has served in that capacity  
8 since October of 2004. In her role as Corporate VP  
9 she oversees the staff responsible for both device  
10 and drug regulatory affairs in the United States and  
11 Canada as well as interacts with B Braun medical  
12 regulatory affairs staff worldwide. Prior to  
13 joining B Braun Medical Ms. Olinger was employed as  
14 Director of Regulatory Affairs for both Ono Pharma  
15 USA Incorporated and Abbott Laboratories  
16 Incorporated. She received her BS in Physical and  
17 Life Sciences from Wilson College. In addition, she  
18 has completed course work for her Master of Science  
19 degree in Biomedical Science from Hood College and  
20 in Health Law from DePaul University. She is  
21 currently pursuing her juris doctorate from Concord  
22 University.

23 MS. OLINGER: Thank you very much. Good  
24 afternoon everyone and thanks very much for inviting  
25 B Braun to be a part of the meeting today. While

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Shawn is putting up the presentation, I've been very  
2 interested in the presentations and especially  
3 Debora's when she was talking about the visual  
4 limitations and the low light conditions in the  
5 hospitals and so forth. And I was smiling to myself  
6 because I made my husband install a 10-light  
7 chandelier in our master bathroom so that I would  
8 have more light in there. And for those of you who  
9 were brave enough to stay at the Pooks Hill Marriott  
10 last night, I was pleased to see that they had done  
11 a lot of renovations, but the counters in the  
12 bathrooms were so wide that I was virtually crawling  
13 up on the counter to get close enough to the mirror  
14 without my glasses. So I understand those  
15 limitations that people go through.

16 For those of you who are not familiar  
17 with B Braun, and I do pronounce it B Braun  
18 partially because that's the way the Germans  
19 pronounce it. We are a German company. And also  
20 because people tend to not ask if I can get them  
21 good prices on toasters and electric shavers. B  
22 Braun is actually a very old company, about 169  
23 years old. In Germany the corporate headquarters  
24 are B Braun Melsungen AG and if you're in Germany  
25 that's B Braun Melsungen AG is the way they say it.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 We're headquartered in the United States in  
2 Bethlehem and Allentown, Pennsylvania. About 30,000  
3 people worldwide. And we have a product portfolio,  
4 and I apologize for my typographical error, of about  
5 4,000 finished goods and about 12,000 finished  
6 components.

7 I will be able to get us back on track I  
8 think in terms of time today because a lot of the  
9 things that are in my presentation have already been  
10 discussed ad infinitum, like lettering and color  
11 differentiation and so forth. So I'm not going to  
12 spend a lot of time going over that, but I have  
13 taken some notes as the presentations have gone  
14 through and maybe I can come up with some different  
15 things that we could discuss in panel discussion.  
16 So I wanted to talk a little bit about - again about  
17 lettering, sidebars and the upright and inverted  
18 positions, a little bit about color differentiation,  
19 watermarks, symbology and bar coding.

20 So we go back again to the lettering.  
21 And this is an example of the tall man lettering.  
22 Again this is our duplex line of cephalosporins  
23 where we do have tall man lettering, but not on all  
24 of our duplex products, not on all the ceph  
25 products. One of the reasons for this is because we

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 have - some of these are ANDA products, some are NDA  
2 products. And we talked earlier about there was  
3 some difference in the latitude that OGD has with  
4 labeling as compared to what the NDA review  
5 divisions have. So we have not been allowed to put  
6 tall man lettering on all of our cephs, but we do  
7 have it on a few and I just wanted to show you  
8 these. I do think it's a good thing to have it on  
9 this line because we have CefuROXIme, CefaTAXim,  
10 CefTRIaxONE, CeFOXItin. These names are very  
11 similar I think and I think that the tall man  
12 lettering really helps with these particular  
13 products. But I also agree that there is a big  
14 danger with overexposure in using the tall man  
15 lettering. And FDA does have this defined list of  
16 products for which you can use that. And the  
17 cephalosporins I will tell you are not on that list,  
18 but we do have the tall man lettering. It has been  
19 approved by the FDA. But I will say that I agree  
20 with those of you who have spoken before me that  
21 these labels are cluttered.

22 Symbology. B Braun, Baxter at the time,  
23 Abbott now Hospira in a HIMA task force did develop  
24 this scheme for labeling. The dextrose, the three  
25 different concentrations and you can see the symbols

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 that have used. I think that that actually looks  
2 good on these labels. But again, throughout the  
3 presentations I've seen that what I thought looked  
4 good on the labels didn't necessarily translate to  
5 what looks good the end users. So I think there is  
6 a lot of work that we can do in those areas. But I  
7 think these are easily identifiable and these types  
8 of changes with a symbol like that I believe are  
9 relatively easy for us in industry to implement on  
10 our labels.

11 Here are examples of some sidebars that  
12 I think add additional differentiation. Makes the  
13 name more prominent on the label. It makes it a  
14 little more easily identifiable. And as you can see  
15 on the heparin we've got some color differentiation  
16 as well here. The inverted bar I think adds as well  
17 because these labels you can read whether they're  
18 hanging on the IV stand or whether they're laying in  
19 a drawer or a bin. So I do think that the inverted  
20 bar adds a little bit of differentiation to the  
21 label.

22 Colors and symbols again. And with  
23 these we've got the concentration in a different  
24 color. But I see the point that people have been  
25 making today. If you look at this it reads very

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 differently from here. We've got different units on  
2 there. And I do think that standardization of the  
3 way we do the units could be something that we could  
4 work together with industry, with FDA and with the  
5 users in order to develop better labeling in that  
6 regard.

7           This is an example of from B Braun's PAB  
8 line where we've used a color differentiation for  
9 the metronidazole, the dextrose. What we've got is  
10 red for pre-mixed drugs and then black for the drugs  
11 that can be mixed. And then for our PIC line for  
12 the sterile water, the basic irrigation products and  
13 for the urologic irrigation and so forth we've got  
14 some color differentiation there as well with the  
15 red, yellow and green. But again, the lettering is  
16 still all black. And you can see that we've got  
17 room here for bar codes on these. So there is not a  
18 lot of real estate left on these labels, but I think  
19 they don't look quite as cluttered as some of the  
20 others.

21           Watermarks are another thing I think  
22 that can distinguish a label. And this is an  
23 example of two that we have. And I'm actually very  
24 ambivalent about the watermarks. I believe that FDA  
25 doesn't care for them too much. I like the way you

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 can actually see this on the label. I think it  
2 stands out a little bit. On the other hand, I think  
3 that it really detracts from the text on the label  
4 and makes that hard to read.

5 And bar coding, that was - actually the  
6 Coordinating Council for Medication Error and  
7 Reporting had recommendations on bar coding, that  
8 they should be scannable and human-readable, they  
9 should have the NDC number, the lot and batch number  
10 and expiration date. They should be down to the  
11 unit of use, a standardized location on the label  
12 and they also recommended wraparound labels. Well,  
13 the final bar code rule went into effect last year.

14 I don't know if all the companies have implemented  
15 them yet. I know that some companies, including B  
16 Braun, had to ask for an extension in order to  
17 implement the bar coding. It was more difficult  
18 than expected because of the equipment, getting the  
19 equipment working correctly to put the bar codes on  
20 the manufacturing line and the fact that we had to  
21 shut down our manufacturing lines in order to get  
22 the bar coding up and running and to get that  
23 implemented. So I don't know if everyone has been  
24 able to do that yet. It did pose some difficulties  
25 and some logistical problems. It was expensive for

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 us to implement that. However, our bar codes do  
2 conform to these requirements.

3 Wraparound labels, we're actually  
4 looking into that at B Braun because we're looking  
5 at a new packaging configuration for some of our  
6 products and we are looking at wraparound labels and  
7 whether that would be good for this particular  
8 product. But again, even bringing a new container  
9 to the market, it takes a long time and it takes a  
10 lot of money, in the millions of dollars to  
11 introduce a new container. The one thing I wanted  
12 to talk about as well, the standard location of the  
13 bar code label. That again is logistically  
14 difficult for a company to do, to standardize that.

15 So, some obstacles. The bar coding  
16 requires that the end user has the equipment to read  
17 that and the equipment to read the bar code as we  
18 have done that. I think that color differentiation  
19 and you've heard a lot of that today from everyone.

20 I think everyone here agrees that color coding and  
21 color differentiation is not the final answer. And  
22 I've heard a lot about standardizing the labels so  
23 that all the manufacturers have a very, very similar  
24 label. But then I also saw in the last presentation  
25 that all those labels looking the same can lead to

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 some confusion as well. So I do have a little bit  
2 of concern about standardizing those labels so much  
3 that you really can't distinguish not only between  
4 manufacturers but between product lines and types of  
5 products. So I wouldn't want to add too much more  
6 confusion there. And the companies will always want  
7 to have some differentiation so that you know whose  
8 company's label you're dealing with.

9 Over-wraps, I wanted to talk about that.

10 It wasn't a part of my presentation, but I've heard  
11 about over-wraps today as well. We don't put the -  
12 we would not put the over-wraps on if we didn't have  
13 to because it is an extra cost. It takes more time  
14 to do it. We would like to eliminate that, so maybe  
15 that is one of the things that we should be working  
16 on as a group, industry, FDA and the users so that  
17 we can see how we could eliminate over-wraps on  
18 these products if we can.

19 And back to standardization of labeling.

20 Maybe we could standardize more the way we do the  
21 concentrations and the strengths and the units on  
22 the labels. That may be more helpful than trying to  
23 standardize in other ways. And then again,  
24 eliminating some of the information that's on the  
25 labels, I think those are three things that we

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 should probably work on as a group to try to do.  
2 And although eliminating a lot of the information on  
3 the labels could go back to actually amending the  
4 Act, the Food, Drug and Cosmetic Act, so all of  
5 these changes are not as easy as we may like them to  
6 be.

7           So just in summary the industry response  
8 to labeling issues has been bar coding, color  
9 differentiation, symbols, watermarks and lettering.

10       But as we said earlier today, we really are  
11 required to follow the agency's regulations on  
12 labeling and the agency itself is constrained in  
13 what they can do with labeling, especially with  
14 generic products because the generics have to follow  
15 what the innovators do. We think that - I think  
16 that color-coding leads to more of a reliance on the  
17 color than the text and at the end of the day  
18 there's no substitute for reading the labels.  
19 Again, I think we should work as a group on  
20 minimizing the information on the labels as much as  
21 possible, designing based on what the end user  
22 wants, and these are points that I took from the  
23 last presentation because I think they're very  
24 valid. I think they're things that we can work on  
25 and that they may give us a good result. And the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 last one is room for patient label if the pharmacy  
2 has to label and put on there. So that's all I  
3 have. Tried to keep it brief. Again, thank you  
4 very much.

5 (Applause)

6 MS. BECKER: Can I have all of the  
7 speakers join us up front? I think the ones even  
8 from our first in the morning. They said they  
9 wanted you to come up and answer questions if  
10 necessary. There should be enough room. It might  
11 be tight. I actually have another request. If you  
12 have a question, if you could please identify  
13 yourselves so we can get that down. That would  
14 help. Now that everybody's cozy up here. Questions  
15 for our panel? In the back?

16 MS. MCGAHAN: My name is Chris McGahan.  
17 I'm with Abraxis Bioscience. And the question that  
18 I have is for the pharmacist and the nurses. Given  
19 that there's a lot of extra information on the  
20 labels, a lot of our labeling has spaces to put  
21 patient information, time that it was opened,  
22 patient's name. Is that something that really gets  
23 used, or is that just part of the extra junk that  
24 should come off?

25 DR. LESAR: For the most part it's just

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 extra things. It's either going to get covered up  
2 or it's going to be ignored. Even right down to  
3 thinks like what's the salt of the drug. Even  
4 saying things like injection. You can say why are  
5 you telling us injection. To me, most of that stuff  
6 is extraneous, not important at all. But to that  
7 end user we can always look up in our system when we  
8 decide to make something, everything is  
9 standardized. We're going to look up what the  
10 buffers are, can we make it, what the stability is,  
11 that's all going to be built into this process.  
12 These are controlled through other mechanisms than  
13 somebody holding the bag and reading it. So many of  
14 those things are already constrained by  
15 organizations such that they become not important  
16 because there is not - they're not a variable that  
17 is important that has already been constrained by  
18 some other system in the organization. So you're  
19 not choosing between the fact that that information  
20 doesn't provide anything for you to choose among as  
21 it were. So it's not really important or that's  
22 already been considered.

23 MS. SIMMONS: Am I getting it straight  
24 that you're telling me that on the actual  
25 medication, the IV bag you have room for that?

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 MS. MCGAHAN: No, more like on the PVP  
2 bottles and some of our other, like 30ml, 50ml  
3 bottles. We'll have on them spaces that'll say the  
4 patient's name, it'll say the time that it was  
5 opened, it'll say initials of nurse. I don't know  
6 that - that's my question is if those type of things  
7 are actually being used or if it's just taking up  
8 extra room. Because it'll just say date, time, and  
9 there's little lines to write this information in.  
10 But as I'm seeing, if it's coming from the pharmacy  
11 it looks like another label is being put on instead.

12 MS. SIMMONS: I will tell you that  
13 nurses have many, many, many places to document  
14 those things. And it's documented on the MARs,  
15 depending on what kind of system they have in place,  
16 the bar coding and things like that. I would really  
17 - I would very much doubt they ever look at that.

18 And you know in all honesty too, with  
19 due respect to the industry and what you're putting  
20 on there, we really don't care about what company  
21 produces it either. So we really don't care about  
22 trademarks and that sort of thing. And for most  
23 nurses I think if you do your walkthrough as I  
24 suggested they're going to say who is that. Because  
25 again what they're looking for is that essential

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 information. They have to get that particular task  
2 done safely.

3 DR. LESAR: If you look at our IV labels  
4 that we place on a bag that we have manipulated it  
5 has very little information on it. It has the name  
6 of the drug obviously. One of the things is we take  
7 that label and put it on the right drug. It has to  
8 be there. It might have an expiration date which  
9 once it's come out of the over-wrap that dating is  
10 placed by us. It's no longer - that bag doesn't  
11 know when it was taken out of the over-wrap and when  
12 it's been taken out of the refrigerator. So some of  
13 those things, the initials typically are the  
14 signature of the pharmacist and that's actually  
15 pretty much a requirement for us to be able to track  
16 who checked that bag. Well you can do that by logs,  
17 you know. It's always been a tradition that doesn't  
18 leave the pharmacy unless it has that written  
19 initial on it. So there are some things on there  
20 that that's not particularly what I would call  
21 extraneous information. But we've often been asked  
22 by nursing interestingly enough to add all kinds of  
23 things to these labels. And we've actually been the  
24 ones that are saying you know does this drug need,  
25 double-check is this a high-alert drug. That often

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 has to do with safety as well. And actually we've  
2 been sort of against that because we think it just  
3 clutters the label and obfuscates some of the other  
4 important information. So to your point is I think  
5 we try to reduce that. In some cases you know  
6 that's not quite possible, but we work pretty hard  
7 to keep that information pretty small. But some of  
8 it you just have to have.

9 DR. COHEN: I just want to remind people  
10 too that most of our healthcare organizations I  
11 guess outside of ambulatory care are accredited in  
12 some way and there are accreditation requirements.  
13 So in the past few years much more emphasis has been  
14 placed on having pharmacists prepare a lot of these  
15 doses. So before where some of the drugs that you  
16 might be talking about had to be labeled by nurses  
17 up on the nursing units, that's actually done now in  
18 the pharmacy. So it wouldn't be a bad idea to have  
19 somebody in your company kind of stay in touch with  
20 the various accreditation requirements. For  
21 example, in the operating room environment there  
22 were some new requirements through National Patient  
23 Safety Goals for labeling of products. And that's  
24 actually created somewhat of an industry in some  
25 ways for some companies.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 DR. LESAR: I just might also add that  
2 there's tremendous limitations to the pharmacy  
3 system labels that I think could be a whole other  
4 discussion about - our ability to create labels that  
5 differ. We struggled, we had to talk people into  
6 allowing us to do tall man lettering onto our IV  
7 labels for instance. So I think there's some  
8 limitations there in terms of what our abilities are  
9 as well.

10 MS. BECKER: Thank you. Yes?

11 AUDIENCE MEMBER: Dr. Lesar, you  
12 mentioned the potential opportunity to put dosing  
13 units on the IVs. And while I would agree with  
14 that, I think we have to be really careful. We  
15 measured the variability in a hundred hospitals in  
16 their drug libraries and their smart pumps and we  
17 found as many as 11 different dosing units for one  
18 drug. And so I think the amount of variability that  
19 actually is in practice, whether the drug is being  
20 dosed as milligrams or micrograms, whether it's  
21 dosed as grams or milligrams. Magnesium was our  
22 all-time winner with 11 dosing units. So putting  
23 dosing units on there and the concentrations, it's a  
24 double-edged sword I think. Something we need to be  
25 really careful. Obviously it's not good practice to

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 have so much variation, but it's just that's the way  
2 it's developed and we were surprised. We're now  
3 looking at 250 hospitals and we're finding even more  
4 variability than we found in the original hundred.  
5 So the concentrations are less variable even though  
6 that's what JCAHO has focused on, but the dosing  
7 units - and then when you throw in bolus doses which  
8 are almost, they're always different units than what  
9 you have for continuous infusions. It makes it even  
10 more complicated.

11 MS. BECKER: Yes?

12 MR. BRUGER: Andy Bruggar, Baxter. I  
13 was interested in the pharmacy labels that are  
14 applied to the containers. Are there standards as  
15 far as the size of those labels or the content of  
16 the information that goes on those labels?

17 DR. LESAR: I don't believe there's any  
18 standards. I mean, it sort of depends on who's your  
19 vendor, what kind of printers you use, obviously  
20 your software. There are typically what we would  
21 call what would be the standard: date of  
22 preparation, the patient's name, drug,  
23 concentration, total amount. There are some  
24 actually lists of what has to be on the label. You  
25 know, JCHO actually defines what the minimum

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 labeling needs to be and so some of that is actually  
2 defined through JCHO. And you know typically it  
3 varies from hospital to hospital, but the standard  
4 elements are going to be there.

5 DR. COHEN: I just want to say that  
6 we've actually been working with some of the  
7 computer system vendors and we've actually started a  
8 process to help somebody come up with official  
9 standards. We've actually been interacting with  
10 practitioners in these companies and have put  
11 together some standard label formats. And there are  
12 some constraints like you know not enough space in  
13 certain fields you know to do what we would like.  
14 It's not the easiest thing in the world to do, but  
15 there are two label formats that we have been  
16 working on. One is already finalized. Another one  
17 is in process and we're close to it and we can  
18 provide more information about that. Or maybe  
19 Allen, are you - Allen Vaida, are you familiar with  
20 where we are with that at this point? Stewart's  
21 project? Oh, okay.

22 DR. VAIDA: Yes, I think what we were  
23 saying as Mike was saying too, we're working with  
24 some of the vendors with that but I'm not familiar  
25 with anything else.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 DR. COHEN: Okay.

2 DR. LESAR: I will say how hungry we are  
3 for that type of information that the minute we saw  
4 that it was printed off my computer, given to my  
5 computer guy and said we need to match these  
6 standards. So I think that those are the type of  
7 things that as practitioners that we are looking  
8 for. So I mean the importance of that, we know it's  
9 a problem and we wanted to have the minds come  
10 together about what this should be.

11 DR. COHEN: That's exactly what's  
12 happening. You know, one particular computer system  
13 vendor has many different hospitals and they're all  
14 telling them to do something different and they  
15 would like to have a standard way to please all  
16 their customers. So that's why we've been  
17 interacting with them to do that.

18 MS. BECKER: Okay. Question in the  
19 back?

20 AUDIENCE MEMBER: Yes, I have a comment  
21 related to the same thing with the labels and it's  
22 related to placement and to bar coding. You know,  
23 the manufacturers are doing one thing with respect  
24 to where they put the bar code on there as well as  
25 where they put the labels. And the pharmacies and

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the hospitals, I'm with a pharmacy outsourcer and we  
2 do the same thing with respect to trying to put bar  
3 codes and label placement where we want to put it.  
4 And if you look at, I'll give you an example on the  
5 LVPs. I mean there's hundreds of millions of LVPs  
6 sold with saline, dextrose, lactated ringers, et  
7 cetera, and pharmacies are adding drugs to what  
8 percent of them? Let's say 30 - 40 percent, 50  
9 percent. And they're putting their own label on top  
10 of the manufacturer's IVs. Well here's a problem I  
11 can absolutely tell you I've been in a lot of  
12 hospitals and I watch to see where that pharmacy  
13 label gets placed with a drug in it over top of a  
14 manufacturer's IV bag of a plain saline or a plain  
15 LR, something like that. And just like I saw up on  
16 Dr. Lesar's label, got a great label but you didn't  
17 cover up the sodium chloride up at the top and you  
18 know whether that's routinely the way you do it or  
19 whether that's just the way one technician did it,  
20 it now says sodium chloride, the underlying label  
21 from the IV manufacturer, and now it's got the drug  
22 with sodium chloride underneath on the pharmacy  
23 label.

24 Well, one of the other issues that it  
25 raises is sort of a race for the middle of the bag

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 by the bar coding because as we all know these  
2 curvatures are not always you know read. You put a  
3 bar code on the outside of an IV bag, it doesn't get  
4 read very well. I as a pharmacy outsourcer have  
5 been asked when I put my label on it with a bar code  
6 can I cover up the manufacturer's bar code label  
7 from the Baxters or the Hospiras of the world. Can  
8 I cover that up because now the nurses don't know  
9 which bar code to read. So I'm throwing out a lot  
10 of different things that probably could be commented  
11 on by any of the panel members, but one thing I  
12 observe is if we're looking at taking some of that  
13 large language off of an LVP that's in the center  
14 that may not add a whole lot of utility, maybe we  
15 could lower the base IV labeling into the middle of  
16 the bag, keep the big bold letters of saline and  
17 lactated ringers, et cetera, so when that pharmacy  
18 label goes over top of it it's no longer normal  
19 saline, it's a drug in normal saline and the bar  
20 code can be read. So I've covered a lot of  
21 different things here, but I'd love everybody's  
22 comments on that.

23 DR. LESAR: I'll make a comment about  
24 the double bar coding. You know, Mike's reported  
25 that in a couple of cases with some other products

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 but you know if you think about it, if a patient is  
2 on D5 or normal saline and the hospital happens to  
3 be bar coding the IV fluids, that patient who might  
4 be on dextrose, I mean 0.9 percent sodium chloride  
5 as an IV infusion typically is product-based. The  
6 computer doesn't know if they bar code that, that's  
7 an authorized product for that patient. They may be  
8 holding a drug that isn't that patient's or is the  
9 wrong drug for that patient and bar code simply the  
10 bag. The computer is going to say - the first thing  
11 if it doesn't alarm, they're going to hang that bag.

12 Do you understand? Or the IV pumps with IV bags.  
13 So actually that sets up a tremendous danger and as  
14 Mike said, there are certain products that actually  
15 have two bar codes actually on the drug products  
16 themselves. I think your point is taken very well  
17 with that. I think that we're going to see those  
18 type of errors as we extend bar coding into the  
19 parenteral solutions which I think is an eventuality  
20 anyway. I don't know how much that's being done.  
21 We decided not to do that at this time because of  
22 that specific problem.

23 MS. BECKER: Does anybody else want to  
24 address that? Yes? In the back.

25 MS. BENYA: Laurel Benyo from Ben Venue

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Labs and I do have a question. I also was here with  
2 Dr. Cohen about two years ago when we talked a lot  
3 about color in this same room and nothing came of  
4 it. And I guess my question is going to be rather  
5 adversary, but what is going to come out of this  
6 meeting? What is the next step? Who is going to  
7 take the leadership role? I am a generic drug  
8 manufacturer. My hands are tied by regulations in  
9 the agency. I cannot change my labels. So what  
10 group is going to take the action items from this  
11 meeting and go with it?

12 MS. BECKER: I guess I can open that up  
13 to ISMP and USP and FDA.

14 MS. COUSINS: I was going to say that we  
15 have three cosponsoring organizations here who will  
16 meet following this meeting and I can tell you one  
17 of them will be moving forward. I won't tell you  
18 which one, but no. I'm sure you'll see activity.  
19 It is the intention of all three organizations to  
20 use this information in a way that will benefit you  
21 ultimately.

22 DR. COHEN: And keep in mind please,  
23 ISMP is not a regulatory authority or a standard-  
24 setting organization. What we do is collect the  
25 information from the field, we do investigations, we

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 try to advocate for change but we have no real  
2 authority to do any of that. Even setting  
3 standards, you might have heard me say that you know  
4 we're trying to set some standards for labeling that  
5 we can take to someone else to make it official. So  
6 if that's necessary. It may not even be necessary  
7 in that case.

8 MS. COUSINS: And Mike, I would add that  
9 you do keep us all honest.

10 MS. BECKER: Okay. Hopefully we  
11 answered your question. Questions? Yes, Carol?

12 MS. HOLQUIST: Yes, I just wanted to  
13 comment a little bit on the color-coding because I  
14 heard that come up a couple of times today and that  
15 you know what came out of that. Well, I guess what  
16 came out of that is that we heard from a number of  
17 people that I guess there's inconsistencies in or  
18 differences of opinion in whether color-coding is  
19 good or not. We heard from some of the front-line  
20 practitioners here today that they don't like it.  
21 They're not in favor of it. However, we did hear  
22 from some other clinicians who said that's all they  
23 use, such as the ophthalmologist and the dentist.  
24 And so from a regulatory perspective it's very  
25 difficult to come out with a statement that says

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 we're not going to ever allow color-coding when in  
2 fact it's been found to be useful in certain  
3 circumstances. So I think what we took home from  
4 that meeting that day was that color-coding can be a  
5 problem and we have to be very careful when  
6 companies want to come in and implement new color-  
7 coding schemes that haven't been out there already,  
8 or there may be some improvements we can make with  
9 some of the ones that are already out there. Like  
10 for medical gasses, that's a color-coding scheme  
11 that's well known and if we went and said you can't  
12 use color-coding, that would have a very negative  
13 impact. So I think what comes out of these meetings  
14 you have to take into context everyone's opinion and  
15 sometimes it's very difficult to come out with one  
16 standard that works for everybody. So it's not that  
17 we're ignoring it, it's we have to tread carefully  
18 with any new considerations.

19 DR. COHEN: I just have one comment  
20 about that. Those of us that were here that day I  
21 think were - at least the practitioners and the  
22 folks from industry were kind of shocked to hear one  
23 of the proponents of the color-coding say it's great  
24 because that way we don't have to read the label, we  
25 can just pick up the container and you know start to

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 use it. So. And then knowing that within that  
2 particular field we actually have had a series of  
3 intra-product line mix-ups. In other words, that  
4 drug category would be mixed up because the category  
5 was color-coded, not the individual drug product  
6 which would be very difficult. So you know, and  
7 that's still going on too.

8 MS. HOLQUIST: Right. And I recognize  
9 that, and that's some of the issues, but I think - I  
10 don't think you're going to see an agency line that  
11 says you can't do it because in some cases it is  
12 found to be effective, especially with the medical  
13 gasses although there has been still mix-ups with  
14 that. But I think to revert back you know, we have  
15 to look forward and anything new that comes in I  
16 think we have to really scrutinize.

17 MS. BECKER: Other questions? Jerry?

18 MR. PHILLIPS: Jerry Phillips, Drug  
19 Safety Institute. A lot of things today we've been  
20 talking about the tall man letters. One of the  
21 reasons why we're doing tall man letters is the  
22 nomenclature system that's used in established names  
23 for generic names. And one of the parties that  
24 needs to be part of the discussion is the body that  
25 determines generic names which is the United States

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 - USAN, the United States Naming Council and the INN  
2 who approve generic names. We have lots of evidence  
3 of medication errors occurring between two generic  
4 drug products which is driving the tall man letters.

5 So in order to get to the solution there must be a  
6 discussion with that body about looking at this from  
7 a safety perspective probably. The system that's in  
8 current use uses a stem system which identifies the  
9 therapeutic category of that particular drug  
10 product. That has a lot of usefulness from a  
11 clinician's point of view, but it also introduces  
12 similarity. I don't have the answers. It's  
13 basically just a statement. Thank you.

14 MS. BECKER: Thank you. Elizabeth?

15 MS. MILLER: Hi, I'm Elizabeth Miller  
16 with USP. I'm a pharmacist that works with the Safe  
17 Medication Use Expert Committee. And there's been a  
18 lot of talk about enhanced or tall man lettering  
19 today and I wanted to share with you briefly the  
20 Safe Medication Use Committee is working on this  
21 issue. The committee has some concerns, one being,  
22 as many of you have raised in your presentations the  
23 effectiveness of tall man lettering, the paucity and  
24 lack of data to support not only its use but also  
25 what's the most effective combination of lettering.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Dr. Lesar, you pointed out very nicely that the  
2 stems might stand out as opposed to what is  
3 capitalized. Also, other mechanisms of enhancing  
4 lettering, for example we're showing a lot of mixed  
5 case, but I saw some interesting use of also mixed  
6 fonts. That's why they use the terminology  
7 "enhanced lettering."

8 Another one of their big concerns is  
9 standardization. One of you brought up in your  
10 presentations the fact that you might see  
11 manufacturers using one depiction of tall man  
12 lettering whereas you might see in drug information  
13 or in a computer pick list another way of  
14 representing that non-proprietary name. The last  
15 thing that their concern centers around is this  
16 dilution effect with the overuse of tall man  
17 enhanced lettering and how that could have negative  
18 impact on the practitioner using the product.

19 The committee is getting ready to survey  
20 users, nurses, pharmacists and physicians that are  
21 actually exposed to this tall man lettering and  
22 they're going to broadly disseminate an internet-  
23 based survey out to healthcare practitioners of all  
24 the allied healthcare professions. And what they're  
25 looking for is basically to see what the awareness

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 and recognition is in the field of the lettering as  
2 well as how it's used in practice. Are folks doing  
3 their own homegrown tall man lettering in their own  
4 systems? And to sort of get some of their  
5 perception of the effectiveness of how it's being  
6 used.

7 My question to you and what I'd like to  
8 bring back to the Safe Medication Use Expert  
9 Committee is do you have any recommendations for  
10 this survey? Would you like to see certain things  
11 asked of front-line practitioners about how you're  
12 using your tall man lettering or enhanced lettering  
13 on your products and if you had any other  
14 recommendations for things you'd like to see asked  
15 of the front-line practitioners?

16 MS. BECKER: Mike?

17 DR. COHEN: If you circulated something,  
18 you know I'd be glad to offer some suggestions for  
19 that rather than going over it right now. But I did  
20 have one thought. I was talking to Diane a little  
21 bit earlier, just an idea, but this tall man letter  
22 has been around now for several - of name pairs.  
23 And the companies I guess have been using that now  
24 for at least two years I guess on their labeling.  
25 Things like dobutamine and dopamine. I'm not sure

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 when the companies, Baxter I guess implemented that.  
2 Others have now as well. But it would be  
3 interesting to take a look at the medication error  
4 reports perhaps that have been sent either to your  
5 database with MedMarks for example or some other  
6 databases that exist in the country and then maybe  
7 even ask the companies if they've. You know, maybe  
8 if you put all this together with several of these  
9 name pairs we might be able to see that you know  
10 given IMS data showing a certain level of use of the  
11 drug and taking that into account, perhaps the  
12 number of error reports have actually gone down or  
13 gone up or stayed the same. You know, I just don't  
14 know. Maybe that's something that we could do that  
15 would be helpful to the committee.

16 MS. BECKER: Thank you, Mike. Any other  
17 questions? I don't want to miss anybody. All  
18 right, does the panel have anything?

19 DR. DUFFY: I have one question for the  
20 panel. In the international arena, what kinds of  
21 solutions to this problem have been arrived at other  
22 places? I'd be very interested to hear.

23 DR. COHEN: One thing they do is they  
24 don't use infusion bags as much as we do. They use  
25 syringes and syringe pumps for the most part to give

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 a lot of their IV medications. And that, you know  
2 that actually has - it's kind of been a barrier to  
3 some of the solutions that we've had. For example,  
4 in the United States not only have we changed the  
5 appearance of the vials of concentrated potassium  
6 chloride, but hospitals, acute care facilities that  
7 is and others have removed it from patient care  
8 areas. And we've been able to do that because the  
9 industry has brought us you know through their  
10 technologies pre-mixed solutions which have been  
11 great. And we don't have fatalities from injecting  
12 potassium chloride concentrate versus sodium  
13 chloride as we once did. That still continues in  
14 other countries, but there's not, you know there's  
15 not a product out there in some of the countries.  
16 They don't have a pre-mixed bag and even if they did  
17 I don't know that they would use it because they're  
18 so used to syringes. But that is really something  
19 that you know is different about other countries and  
20 that's happened.

21 MS. BECKER: Well, thank you very much.

22 We will have - oh somebody else? I'm sorry.

23 MS. BERWITH: May I ask a question  
24 please? Yes. I'm Geneva Berwith. I'm from the  
25 Penn State College of Medicine. I'm a medical

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 student. I'm actually going into the field of  
2 anesthesiology and I think that this meeting in  
3 itself has a big impact on my future career, the  
4 future of medicine and the future of nursing, the  
5 future of pharmacy, I mean every field. And so but  
6 just from my perspective I've seen people say there  
7 are various things that work, but they said that  
8 those same things don't work. The tall man  
9 lettering, the bar code scanning, the color-coding.

10 I heard good things and bad things, and many people  
11 have different opinions. And I think that we're a  
12 big powerhouse right here in this room of minds that  
13 can make some decisions. However, I think that thus  
14 far from what I've heard even the panel say  
15 decisions are being made based on trends. They're  
16 being made based on what the current practices are.

17 They're not being made necessarily based on  
18 evidence and we've already discussed the fact that  
19 there is not solid evidence out there right now  
20 saying what works best. And I think that committees  
21 work well to some extent, but in the culture of  
22 medicine in this day and age the next generation  
23 that's coming up needs to practice medicine based on  
24 evidence. I mean, that's - I'm sure you guys have  
25 heard it, evidence-based medicine. And I was just

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 wondering if there is going to be funding to go  
2 ahead and research these areas to see if these  
3 actually will work instead of just talking about it.

4 MS. BECKER: Comment?

5 DR. COHEN: Well, the Preventing  
6 Medication Error Report from the Institute of  
7 Medicine, if you look at that there's a whole  
8 section or chapter rather on research and there's a  
9 recommendation actually that people move - that  
10 researchers move more towards error prevention  
11 strategies and move away from the error rate type of  
12 research that's been done so much in the past. Not  
13 that that isn't still needed. Certainly in some  
14 areas it is, but moving more towards does a double-  
15 check work, does tall man lettering work, things  
16 like that that would help to prevent medication  
17 errors in the case of that particular committee. So  
18 I think there's some hope for that. For example,  
19 I'm sure AHRQ is taking that very seriously and you  
20 know in the future I'm sure some of the funding  
21 requests, the RFAs that come from them will probably  
22 be in that area.

23 DR. WILLER: Just one point from me.  
24 You've heard all the speakers today, especially  
25 Susan Olinger kind of summed it up well. The

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 ultimate reason there's medication errors is a lack  
2 of reading the label. And the things we propose  
3 today are ways to try to improve the visibility of  
4 the key parts of the labeling. And as you rightly  
5 point out, there isn't solid data that any one or  
6 all of them have an effect. We are experts in  
7 labeling or have a lot of experience in it and we  
8 believe that it's better than it was. When I  
9 started with Beecham Labs we had as I said two  
10 colors, green and blue, and it seemed to work fine  
11 then. But the trend came to color-enhanced labeling  
12 to improve the reliability of people getting the  
13 message. And so until there's more data your idea  
14 is a good one. For now we've got to do the best we  
15 can until the agency can make changes, until the law  
16 can be changed, until we can effect changes on our  
17 own. The ones we're doing now are the ones we can  
18 do without significant changes in the law. So it's  
19 the good ones we're making now. Better ones are  
20 going to come.

21 MS. SIMMONS: I think I have an opposing  
22 view for you. You know when we first started kind  
23 of this journey it was 1999 and we started looking  
24 at the demographics and that sort of thing and we  
25 were really an ignorant industry at that point.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Other industries where they had high-risk situations  
2 and critical situations in the nuclear industry and  
3 aviation recognized the limits of human performance,  
4 especially in high-risk situations such as  
5 anesthesiology which actually has made just probably  
6 the best strides for any particular discipline.  
7 They've been really ahead of us. What we know now  
8 is this. Humans perform in very predictable  
9 patterns. That's part of your cognitive psychology  
10 you'll go through. One of other interesting things  
11 that you learn as you go through working in clinical  
12 areas is that we all have minds that work very  
13 similar. We also have similar goals. And in the  
14 medical field that is doing the best thing we can  
15 for our patients.

16 It has come to my attention as I've  
17 spent more time looking at this that there's even  
18 more to it when you start looking at the science of  
19 causality which established well in very grounded  
20 literature and very grounded science and is  
21 evidence-based and that causality is not a single  
22 point. In fact, there's a term for that called  
23 single-point failure, when we assign causality to  
24 one particular subject or one particular cause.  
25 These errors that you see have multiple causes.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 They have multiple factors which makes them very  
2 difficult to chase quite honestly and makes them  
3 very difficult to solve. What we have done to this  
4 point since 1999 is identify many of those and  
5 actually been able to reduce the possibility of  
6 repeating some of these errors over and over again.

7 It is my hope that your generation after we have  
8 done this work will be even braver to speak up when  
9 these things happen so we can learn more about them.

10 I think at that point we'll actually be able to  
11 make even further strides. Until that point we'll  
12 have to keep just chipping away at that multiple  
13 causality there to reduce the possibility of  
14 failure.

15 MS. BECKER: Diane?

16 MS. COUSINS: Just two maybe  
17 disconnected comments from each other. One is that  
18 the USP's expert committees in fact struggle with  
19 that very question. They are always seeking  
20 evidence on which to base their decisions.  
21 Unfortunately many times there's not evidence,  
22 particularly in this area, and it gives the  
23 appearance of being non-responsive or providing an  
24 untimely response because they are looking for that  
25 evidence. So it is frustrating. As Elizabeth said

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 with the tall man lettering, they were looking for  
2 evidence of its effectiveness or not and really  
3 found neither even in looking in tangential  
4 industries. So I feel your pain on that one. I  
5 understand where you come from and I do think it is  
6 a challenge to all of us.

7           However, I will say too that one of the  
8 things that the National Quality Forum struggled  
9 with when it was trying to develop its safe  
10 practices was the fact that as they collected their  
11 evidence there were a lot of safe practices that  
12 really had no evidence. Taking potassium chloride  
13 off the floor and watching the number of deaths  
14 diminish to practically zero. Those they called,  
15 they had to call them something because they thought  
16 they're things that we ought to be doing even though  
17 we don't have evidence and they ended up calling  
18 them obviously beneficial practices I think is what  
19 they were calling them which I guess is the no-  
20 brainers that we call them. But you know I think  
21 there's a recognition that there are some things  
22 that make sense to do and I think it's an incredible  
23 challenge for us as we think about changing things  
24 like standards that are, you know, these are  
25 evergreen kinds of things that we're going to have

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 to live with for many years. And so there's a  
2 challenge for us in where does the line fall between  
3 these obviously beneficial practices and the  
4 evidence that we have that tell us these are the  
5 right things to do.

6 DR. LESAR: I want to comment that  
7 sometimes that evidence would actually be very  
8 difficult to get and some of the solutions may have  
9 nothing to do with labeling. As you mentioned, you  
10 know some of the constraints on availability and  
11 choosing may be the thing to do. You look at some  
12 of the technology like unit-based cabinets.  
13 Misused, those actually produce more errors. And in  
14 this case labeling became a critical part of open  
15 matrix automatic dispensing machines, I believe a  
16 major cause of errors that we saw in those types of  
17 machines. We eliminated the open matrix drawers and  
18 these things start to disappear. So you can  
19 actually look at that evidence. It has nothing to  
20 do with how well you can read the label and how many  
21 opportunities there are to misread the label as what  
22 you change. And those are the practices that would  
23 be actually fairly easy to document the  
24 effectiveness of and actually eliminate the need of  
25 determining how the label should be made. One

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 problem with that is of course the more you control  
2 the risk from any single-point error such as putting  
3 the wrong drug in the wrong matrix by the pharmacy  
4 actually increases the risk because people then  
5 become more dependent on the technology. So you can  
6 see where every error is just squeezing the balloon,  
7 but some of the answers may not be label in here.  
8 It may be practices.

9 MS. BECKER: Well, I think I heard that  
10 the FDA, ISMP and USP would take up the cause of  
11 what we heard today. I'd certainly like to thank  
12 all the speakers for their presentations and we'll  
13 take a break and be back at 3:15. Is that still  
14 good with - that sound good? 3:15 and Diane Cousins  
15 will moderate the public session. So we're looking  
16 forward to those comments also. Thank you.

17 (Applause)

18 (Whereupon, the foregoing matter went  
19 off the record at 2:54 p.m. and went back on the  
20 record at 3:18 p.m.)

21 MS. COUSINS: Okay, good afternoon  
22 everyone. We'll get started again if everyone could  
23 take their seat. We're about to enter into the open  
24 portion of today's meeting. There are five speakers  
25 who will be addressing you. Three of them have

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 slides and so we'll begin without further ado. We  
2 have 10 minutes per speaker and I'll use the clock  
3 at the back of the room for the speaker's purposes  
4 to timing. So I'll give you a one-minute warning,  
5 okay? Our first speaker today is Dr. Gerhard Maher  
6 from Schreiner MediPharm. Dr. Maher?

7 DR. MAHER: Good afternoon. Glad to see  
8 so many stuck around for the 3:15 part. I work for  
9 Schreiner MediPharm and just a couple of words about  
10 the company. It's located in Germany at this point  
11 and we make what people have been talking about here  
12 all day long. We actually make the labels and  
13 nothing else. So I think everybody else was  
14 concerned also what was inside. We are the ones  
15 that actually make the thing that's on the outside,  
16 the label.

17 Just very briefly the kinds of products.

18 When I thought about this is for IV, an IV focus.  
19 We make only specialty items so perhaps there are  
20 ways in which these kind of labels can be used for  
21 IV therapy that we're not aware of. Most of what we  
22 do are removable sections on labels for big areas or  
23 vaccines and biotech products. And you can see  
24 examples here of wraparound labels with removable  
25 sections, integrated texts we have. Products that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 have the instructions for use integrated. And we do  
2 these for - usually for very small containers, like  
3 I say for vaccines and so forth. I was just  
4 yesterday in Canada talking to the Vaccine Bar Code  
5 Initiative that's going on up there and right now it  
6 looks like things are tending towards going towards  
7 data matrix codes that would be printed online for  
8 vaccines up there including variable information  
9 such as lot number and expiration date. So pretty  
10 exciting stuff.

11 Then we also have labels with integrated  
12 hangers. It was brought up before what's happening  
13 outside of the U.S. and what was mentioned I think  
14 we also see. Not a whole lot of mini-bags being  
15 used, pre-mixed mini-bags being used in Europe at  
16 least or Japan. Mostly it's still bottle-based and  
17 a big portion of our business is to integrate the  
18 hangers into the labels so that when you attach a  
19 label to a bottle that you also just integrated the  
20 hanger. And then as everybody's concerned with  
21 anti-counterfeiting or tamper evidence we have a  
22 business group that deals with that also.

23 I'm going to address here more or less a  
24 small piece of the puzzle of what was talked about  
25 here today. Obviously 98 percent of what was

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 covered here today has to do with identifying what's  
2 in a pre-mixed bag. But I'd also like to focus a  
3 little bit on when admixtures take place and  
4 specifically when you add whatever's in a vial to a  
5 mini-bag somewhere in the hospital pharmacy or  
6 something, that there is some critical information  
7 from that medication that somehow does not get  
8 transferred to the mini-bag and therefore to the  
9 patient bedside. Having such a transfer of  
10 information I think is important for a variety of  
11 reasons that might make situations difficult at the  
12 bedside and we've talked about them a lot today.  
13 Just mainly human error and stressful work  
14 environments.

15 So how does this happen? It's fairly  
16 simple. There are peel-off - you peel off a section  
17 off the vial and attach it to the IV delivery  
18 system. For those that would do so and write the  
19 information on a tag or something no more errors due  
20 to wrong or illegible writing, and therefore things  
21 like black box information, specific warnings, "Do  
22 not inject this product into the spine" or something  
23 like that can be transferred and is accessible right  
24 to the patient's bedside. These peel-off sections  
25 that I think are a nice way to convey information

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 have a broad market acceptance primarily in Europe  
2 and Japan. They are just now starting up here in  
3 the U.S. You're seeing most of them again more in  
4 the vaccine area where documentation is pretty  
5 standardized. And what are some of the basic  
6 features of these? These are not paper labels.  
7 Paper labels don't work so all the products that we  
8 make are advanced plastic foil-based. So you print  
9 the variety of layers and glue them in silicone so  
10 the nurse or the hospital pharmacy, you can remove  
11 the section that needs to be removed and then when  
12 you stick it to the container that it's stuck to it  
13 doesn't come off again.

14 We did some basic research on peel-off  
15 labels and at the American Nurses Association just  
16 to look and see what do nurses think about peel-off  
17 labels. And it's pretty obvious they hate writing  
18 down information. They get complaints from their  
19 bosses that people can't read what they wrote down.

20 We hear a lot of information about when information  
21 is written down that there's a very high level of  
22 errors and a very, very high percentage thought that  
23 this would be something that they would like to  
24 have. And that's all I have. Thank you very much.

25 (Applause)

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 MS. COUSINS: Thank you. Our second  
2 speaker is Bona Benjamin from the American Society  
3 of Health System Pharmacists.

4 DR. BENJAMIN: Good afternoon. I am a  
5 pharmacist. In addition to representing the ASHP  
6 today I have practiced for about 20 years in  
7 hospital settings and most of that was spent in IV  
8 admixture areas and some of it in direct patient  
9 care. Most recently before coming to the ASHP I was  
10 the quality officer at the Clinical Center for the  
11 National Institutes of Health. But today I'm going  
12 to be speaking to you on behalf of ASHP in my  
13 capacity as the Director of Medication Use Quality  
14 Improvement.

15 ASHP's 30,000 members include  
16 pharmacists and pharmacy technicians who practice in  
17 a variety of healthcare settings including  
18 inpatient, outpatient, home care and long-term care.

19 The issues that were discussed in the workshop  
20 today directly affect our members who handle large-  
21 and small-volume parenterals as part of their day-  
22 to-day job responsibilities and it also affects the  
23 millions of patients who are treated with  
24 intravenous therapy. ASHP has been an advocate for  
25 improvements in drug labeling and packaging for a

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 long time. We have previously commented in these  
2 meetings and in other forums that the incidence of  
3 error where the appearance of the product was  
4 contributory indicates that current standards are  
5 either inadequate or inappropriately applied -  
6 current standards for labeling and packaging are  
7 either inadequate or inappropriately applied and we  
8 have advised the agency in the past to tighten its  
9 control over these activities.

10 ASHP's policies state that practitioners  
11 as well as industry should be included in decisions  
12 about labeling and packaging. We have endorsed  
13 research on the role of human factors and the use of  
14 human factors concepts to prevent error. While some  
15 of the examples shown today by practitioners  
16 indicate that there have been some positive changes  
17 and some response to some of these requests, most of  
18 them confirm our concerns that there is still much  
19 work to be done on the problem of poor  
20 differentiation among drug products. ASHP commends  
21 the FDA and the organizers of this meeting for  
22 recognizing and addressing issues associated with  
23 intravenous medication use, a high-volume high-risk  
24 process where errors have significant potential to  
25 cause harm.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1           Some of you may already know that ASHP  
2 perspective supports many of the views expressed by  
3 the presenters today. We would like to comment on  
4 four key points on behalf of our membership. The  
5 first is the application of human factors, the use  
6 of bar coding, collaboration and risk reduction, and  
7 FDA guidance and regulatory controls.

8           First with regard to the application of  
9 human factors principles. As this group has heard  
10 today, labeling and packaging practices for many  
11 large- and small-volume parenteral products  
12 continues to exhibit lack of application, under-  
13 utilization, or disregard for established human  
14 factors concepts for preventing errors as  
15 demonstrated by the lack of standardization,  
16 cluttered, ambiguous, or poorly visible labeling,  
17 confusion about the use of color-coding and  
18 dependence on practitioners to note subtle  
19 differences among labels. You've seen many examples  
20 of this last point. The one that really impressed  
21 me that I saw in more than one presentation were  
22 those three dopamine infusions, kind of the  
23 nightmare of the IV admixture supervisor and people  
24 working in the IV room. It's easy to understand  
25 when you see these examples how a nurse or a

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 pharmacist, even one who might not be working in a  
2 busy or distracting environment, could pick up the  
3 wrong product. ASHP is aware of FDA's current  
4 efforts to incorporate human factors concepts in its  
5 risk assessments. We recommend that the FDA  
6 continue to explore these techniques and maximize  
7 their use to detect the potential for error.

8           Secondly, ASHP is a strong supporter for  
9 the use of bar coding technology as one means to  
10 accurately identify medications prior to the  
11 preparation, dispensing and administration to the  
12 patient. ASHP supports current FDA regulations that  
13 require manufacturers to label all pharmaceutical  
14 product packages with bar codes that contain the NDC  
15 number for the medication. ASHP has also received  
16 anecdotal reports of situations in which the poor  
17 quality of the bar code provided by the manufacturer  
18 renders it unscannable, therefore eliminating any  
19 patient safety enhancing benefits. We strongly  
20 advocate that hospitals and health systems adopt bar  
21 code scanning technology to prevent patient harm and  
22 call on the FDA and pharmaceutical industry to  
23 ensure that bar codes placed on small- and large-  
24 volume parenterals as well as all other drug  
25 products are scannable.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Third, ASHP supports a collaborative  
2 approach to risk reduction, similar to what we've  
3 heard in this room today. The answers to questions  
4 being asked at this meeting are critical information  
5 for all the stakeholders and can help determine what  
6 changes are needed. And meaningful change must  
7 arise from a common understanding of all the issues.

8 ASHP believes that workable solutions can only be  
9 developed by consensus of all these stakeholders.  
10 And we again commend the FDA for collaborating with  
11 ISMP and USP and including manufacturers,  
12 practitioners, regulatory and accreditation agencies  
13 and patient groups in the meeting today. We would  
14 additionally advise the group that any proposed  
15 changes should also be evaluated by human factors  
16 experts and most importantly by pharmacists, nurses  
17 and physicians who actually handle these products to  
18 ensure the best chance for effective solution.

19 Lastly on the issue of guidance and  
20 regulatory control, the FDA should accelerate its  
21 efforts to incorporate relevant findings from  
22 today's workshop and other fact-finding meetings  
23 into more specific guidance on packaging and  
24 labeling and into regulatory standards. The agency  
25 should then rigorously monitor for compliance and

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 any adverse events associated with regulatory  
2 changes. Further, while acknowledging that changes  
3 represent significant challenges in implementation,  
4 ASHP reiterates that because patient safety is at  
5 stake, the importance and the urgency of addressing  
6 the issues presented today cannot be overstated.  
7 ASHP will be submitting more detailed written  
8 comments prior to the April 12 deadline. I would  
9 like to thank you for the opportunity to comment on  
10 this important issue on behalf of the ASHP  
11 membership.

12 (Applause)

13 MS. COUSINS: Thanks Bona. Our third  
14 speaker today is Jerry Phillips representing the  
15 Drug Safety Institute.

16 MR. PHILLIPS: Good afternoon. My  
17 name's Jerry Phillips. I am the President of the  
18 Drug Safety Institute which is a subsidiary of Brand  
19 Institute, a pharmaceutical consulting company that  
20 is involved in the naming, labeling and packaging of  
21 pharmaceutical products. And prior to me joining  
22 this company I was with FDA for 16 years and today I  
23 want to talk a little bit about some of the stories  
24 behind medication errors, my personal experience at  
25 the agency and then some recommendations.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1           The first thing I'd like to point out is  
2           that while at FDA we published an article in the  
3           American Journal of Health System Pharmacists in  
4           October of 2001 in which we looked at deaths  
5           associated with medication errors. In this we  
6           looked at the adverse event reporting system at FDA  
7           for a 6-year period from 1993 to 1998. And we  
8           identified some 5,366 medication error reports were  
9           identified for that 6-year period. Sixty-eight  
10          percent were classified as serious and approximately  
11          10 percent were - resulted in death. The product  
12          characteristics we identified and it's important in  
13          today's discussion that close to 50 percent of all  
14          deaths associated with medication errors in this  
15          timeframe had to do with injectable drug products.  
16          When we looked at pharmacological drug category, the  
17          CNS agents, the opiates of course lead in the number  
18          of deaths. Acetaminophen, cisplatin, vincristine,  
19          Brevibloc, lidocaine and the anti-infectives and  
20          antibiotics.

21                 Seventy-three deaths were associated  
22          with one product being given for another. Examples,  
23          potassium chloride instead of furosemide, heparin  
24          instead of sodium chloride in eight patients,  
25          cisplatin versus carboplatin instead, et cetera.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 And lidocaine being put in stock bins for  
2 Hetastarch.

3 Now, prior to me - when I joined FDA,  
4 today we had some discussions about being a labeling  
5 reviewer in the Office of Generic Drugs. And I  
6 actually was a labeling reviewer and one of my  
7 products that I was reviewing was metronidazole. So  
8 I want to tell you a little bit about from my  
9 experience as a labeling reviewer inside the FDA.  
10 On July 8, 1993, four products at a VA hospital  
11 received mivacron simultaneously at the same time on  
12 a hospital ward. They were intended to receive  
13 metronidazole. Instead they received mivacron which  
14 is a neuromuscular blocking agent. This resulted in  
15 two deaths and two serious injuries. Now, the  
16 packaging of this particular mivacron was in a foil  
17 over-wrap like we've seen today, but the foil over-  
18 wrap had no drug identification on the main panel as  
19 we saw today. So what you see is the opaque picture  
20 window there that you can identify the drug product  
21 sometimes. And what happened in this particular  
22 case was that mivacron was a new formulary item,  
23 came into the pharmacy. The pharmacy tech knew that  
24 he only had one product in his formulary that was  
25 foil-wrapped and that was metronidazole, so he put

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the things into the bin for that product. Then it  
2 got to the pharmacy. The pharmacy pulled it out of  
3 the bin, put a metronidazole label on the window as  
4 you see it there. It went to the floor. It went up  
5 there in the foil over-wrap and then the patients  
6 received it. So a lot of things went wrong here.

7 The agency actually looked into this.  
8 Since I was one of the reviewers for metronidazole I  
9 was looking at a paper label like you just saw and  
10 it seemed like it was a logical label to approve.  
11 But what was happening in different areas of FDA was  
12 11 different products being reviewed and approved by  
13 different people of the same sort. We of course  
14 went into negotiations with Abbott at FDA and it was  
15 negotiated for changing the labeling from all 11  
16 products that included the drug name and the  
17 strength and also alerting hospital pharmacy  
18 directors. And this of course is an example of the  
19 solution. And on the back, although you can't see  
20 that very well, metronidazole is on the back of the  
21 label. There were many lessons learned in this case  
22 including from the pharmacy and the hospital system  
23 to what FDA does. And if you look at it, we were  
24 approving drugs at FDA and still do in a silo-type  
25 system.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1                   Now, I'd like you to think about CDER  
2                   and FDA as a hospital. We know that medication  
3                   errors occur from one hospital to the next and I'd  
4                   like you to think about FDA as one big large  
5                   hospital system with different therapeutic drug  
6                   products. Nineteen separate hospitals working  
7                   together, 2,000 employees, common set of operating  
8                   principles, but sometimes communication doesn't  
9                   occur between one division to the next division, et  
10                  cetera.

11                  So my intervention strategies include  
12                  that both FDA and industry must be able to consider  
13                  the actual environment in which the product will  
14                  coexist and interact with other products and the end  
15                  users. And today I'm proposing that FDA think about  
16                  an FDA pharmacy which would serve as a human factors  
17                  lab where you basically would have an inpatient  
18                  pharmacy just like you would walk into a hospital  
19                  and an outpatient that would be equipped with all  
20                  the labels of those products. FDA already has the  
21                  authority to ask for labels, labeling and packaging  
22                  to be sent to the FDA. And that human factors lab  
23                  would be used in a pre-marketing arena so that you  
24                  could - any reviewer could walk into that pharmacy  
25                  and look at how their label is going to fit into the

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 environment in which it would be used. Also, in a  
2 post-marketing arena you could look at it from a  
3 medication error perspective.

4 Industry should adopt a failure mode and  
5 effects analysis which is a tool used in the  
6 engineering and the device world quite a bit, but  
7 hasn't been incorporated into the drug world as  
8 much. And use root cause analysis to determine the  
9 potential error causes of these intravenous solution  
10 errors and then implement appropriate solutions.  
11 Practitioner input is paramount via market research,  
12 getting expert opinions, focus groups, or any type  
13 of a market research design to redesign the labels  
14 and packaging.

15 Now, some particulars. We heard this  
16 today. The strength needs to be very prominent.  
17 You need the total quantity of the active ingredient  
18 for injectables. Color and boxing or those types of  
19 things can help to differentiate between one  
20 strength and the next strength. We should avoid  
21 using confusing expressions, such as Fosphenytoin  
22 equivalents, PE units, using different types of  
23 salts. We should try to standardize our units of  
24 measure, milliequivalents versus millimoles versus  
25 micrograms, et cetera, and issue an FDA guidance

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 accordingly. Color. We should avoid color-coding  
2 whenever possible and use color only to  
3 differentiate important information on the label.  
4 And I think it's important to avoid standardized  
5 color formats for all labels within a company line  
6 which happens regularly. For content, the most  
7 important things are the proprietary name, the  
8 established name, the strength, the route of  
9 administration and any special warnings and that's  
10 what we should see. We should think about  
11 standardizing the placement of that information.  
12 FDA has standardized the placement of information  
13 for consumers in the over-the-counter drug products  
14 and maybe we should be considering standardizing the  
15 location of these important things on prescription  
16 drugs. I also would recommend that we amend  
17 201.100(b)(5) that requires inactive ingredients to  
18 be on an IV label but keep that in the package  
19 insert. Thank you very much.

20 (Applause)

21 MS. COUSINS: Thanks Jerry. Our next  
22 speaker is Dr. Miriam Klein from Woodhull Medical  
23 and Mental Health Center.

24 DR. KLEIN: Okay, my name is Dr. Miriam  
25 Klein and I'm the Medication Safety Officer and

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 Clinical Pharmacist at Woodhull Medical Center  
2 located in Brooklyn, New York. The reason for my  
3 interest to improve injectable medication labeling  
4 is the result of a personal tragedy during infancy.

5 I had experienced irreversible profound severe  
6 bilateral central neural hearing loss due to a  
7 medication overdose by a newly licensed  
8 pediatrician. This inspired me to become a clinical  
9 pharmacist and to help other healthcare  
10 practitioners avoid medication error. With the  
11 support of my pharmacy director Sheila Neiman we  
12 have spearheaded a national campaign with  
13 pharmaceutical manufacturers and national patient  
14 safety organizations to improve medication labeling  
15 system in order to avoid medication errors.

16 The purpose of meeting today with the  
17 FDA, ISMP and USP on improving patient safety by  
18 enhancing the container labeling for parenteral  
19 infusion aligns with our mission. This is one of  
20 the important facets of improving medication  
21 management system. It is the injectable vials and  
22 ampules that requires more attention. The FDA  
23 should support the concept that IV labels on  
24 injectable medication should be removable and  
25 transferable to syringes, medication containers and

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 IV fluid. This will be an additional feature  
2 supporting patient safety. It will help avoid  
3 medication error. By correct labeling, we can help  
4 assure the delivery of the right drug, the right  
5 concentration and the right dose.

6 All healthcare facilities across the  
7 United States face the same common goals, patient  
8 safety and by extension preventing and avoiding  
9 medication errors. One of the continuous challenges  
10 they face is maintaining compliance with the JCAHO  
11 medication management standards and its national  
12 patient safety goal. A critical part of JCAHO  
13 national patient safety goal number 3 is medication  
14 safety. Requirement 3(b) states, "Label all  
15 medications, medication containers, that is  
16 syringes, medicine cup, basin or other solution on  
17 and off the sterile field in perioperative and other  
18 procedural settings."

19 One troublesome area that affects every  
20 single healthcare facility is the management to  
21 ensure that all injectable drugs transferred to  
22 syringes, medication container or IV fluid are  
23 properly labeled at all times. This dramatically  
24 affects patient safety. Although much education is  
25 given to healthcare providers, there is still a flaw

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 in the system. Whenever the patient arrives, they  
2 transfer medication from the injectable vial to the  
3 syringes, medication container or IV fluid bag,  
4 there will be instance of non-compliance in labeling  
5 medication.

6 One of the biggest challenges facing  
7 anesthesiologists and surgical nurses in the OR is  
8 labeling medication. Handwriting the drug label is  
9 time-consuming, it causes delay which compromises  
10 patient safety. To hand-write the drug name and  
11 concentration on a syringe label, medication  
12 container or IV fluid bag is prone to error and can  
13 be labor-intensive. Illegibility, incomplete  
14 medication name or writing the wrong concentration  
15 can be dangerous to patient safety. Because the  
16 path is so arduous that those that handwrite the  
17 drug's name on the labels often do not write out the  
18 full generic names of the drug. Some providers may  
19 take shortcuts by writing drug's names with  
20 nickname, abbreviation or acronym, leading to  
21 dangerous medication errors compromising patient  
22 safety. When the injectable drugs are withdrawn  
23 from the vials and unlabeled syringes, many times  
24 these unlabeled syringes are administered to  
25 patients and the problematic area that these occur

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 are in ambulatory surgery, critical care and  
2 emergency department. This safety gap exists in  
3 many areas of the healthcare system.

4 In the FDA Patient Safety News website  
5 dated May 2003 the FDA issued a warning report  
6 titled Drug Errors Caused by Abbreviation. It  
7 documented the type of medication error caused by  
8 abbreviation and acronym. Another report dated  
9 December 2005 titled Preventing Errors with  
10 Neuromuscular Blocking Agent details the ISMP safety  
11 alert Paralyzed by a Mistake: Profiling Errors due  
12 to Look-alike Packaging and Labeling. In one case  
13 it described how pancuronium, a neuromuscular  
14 blocker, was administered by an emergency department  
15 nurse instead of a flu vaccine because the vial and  
16 label looked very similar. That patient recovered.

17 In Indiana, 16 patients received a thousand-fold  
18 overdoses of heparin. The nurse mistakenly  
19 administered 10,000 units per ml heparin instead of  
20 HepLock 10 units per ml. Three infants died and  
21 three survived.

22 The problem of unlabeled syringes is a  
23 widespread issue. How many more patients need to  
24 die or suffer harm before the implementation of  
25 removable and transferable labels? This label

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 requirement changes may help to reinforce patient  
2 safety. The pharmaceutical firm must step up to  
3 take a collaborative role in providing safer  
4 medication labeling option and the FDA should  
5 mandate removable and transferable labels. The 2006  
6 Institute of Medicine in July titled Preventing  
7 Medication Errors, Chapter 6 details that in four  
8 years from January 2000 to 2004 there were 32,000  
9 medication errors that were linked to look-alike,  
10 sound-alike drug names. Thirty-three percent of  
11 these errors were due to label and packaging issue  
12 and 30 percent of fatalities were due to these label  
13 and packaging issues.

14           The FDA had issued a statement on July  
15 20, 2006, that supports the Institute of Medicine  
16 2006 report Preventing Medication Errors. The FDA  
17 look, quote, "forward to using the occasion of this  
18 report to continue to work with stakeholder and  
19 partners to build on these efforts." It is my hope  
20 that the FDA will in the near future be able to  
21 mandate pharmaceutical firm to follow the IOM action  
22 agenda and that USP and ISMP support this innovative  
23 and unique system of removable and transferable  
24 labels on all injectable medication which will help  
25 to validate the proper identification of medication

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 and reach the larger goal of reducing errors and  
2 preventing fatalities. Due to my tragedy and the  
3 tragedy of these infant deaths, I wanted to take up  
4 the challenge to improve medication safety. My  
5 lifelong disability is the impetus that fuels my  
6 passion to helping others to avoid such errors.

7           The exciting label safety features that  
8 some European countries implement allow for simple  
9 label enhancement, that is a removable and  
10 transferable label for all injectable medication.  
11 The label that we wish to introduce to the United  
12 States is one that will address a critical area of  
13 patient safety. In the United States there are two  
14 products that have removable labels. On this side,  
15 this is Zemuron vial from Organon and the other side  
16 is Gardasil vaccine from Merck. Now, you notice how  
17 hard it is to remove that red label that's  
18 superimposed on top of the white one. This drug is  
19 used in the OR and all healthcare professionals use  
20 sterile disposable gloves and it's very hard to  
21 remove. You need long nails to remove it. On the  
22 other side, this has a pull cap that is very easy to  
23 remove and I find it the much more user-friendly  
24 system. By showcasing this label enhancement I  
25 would like to end with this line, better safe than

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1       sorry. Thank you.

2                       (Applause)

3                       MS. COUSINS: Thank you, Miriam. Our  
4       final speaker in this segment is Dr. Dennis Tribble  
5       of ForHealth Technologies Incorporated.

6                       DR. TRIBBLE: Thank you. I'm from out  
7       of town but I don't have slides so I guess I can't  
8       be an expert. ForHealth Technologies gives me the  
9       opportunity to get inside a lot of pharmacies. We  
10      do an IV robot. And so our interest in this  
11      particular subject has to do with a couple of  
12      observations, the first of which is we're seeing a  
13      change in practice some of you may not be aware of.

14      And that is with the increasing cost associated  
15      with compliance with USP 797 and some of the other  
16      requirements for IV production, we're starting to  
17      see a lot more centralization of IV admixture  
18      services to the point now where integrated health  
19      systems are actually building separate facilities to  
20      centralize that. The value to that process of  
21      course is that that means they can distribute the  
22      benefits of best practices to all of their member  
23      facilities and the patients served by them, even if  
24      those facilities would otherwise be economically  
25      unable to support those practices on their own.

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 What we're seeing as a byproduct of that is at least  
2 one we're aware of, and in fact there's someone here  
3 from this site, is already registered as a  
4 manufacturer by the FDA. And we're seeing a kind of  
5 dichotomy in the industry where some of these  
6 facilities are being governed as pharmacy practice  
7 under state boards of pharmacy and others are  
8 seeking licensure as manufacturers under the FDA.  
9 So the rules and ideas that we're considering today  
10 may ultimately wind up affecting the way we practice  
11 pharmacy in our pharmacies especially in these  
12 centralized facilities. So we probably need to keep  
13 that in mind.

14 The other thing that kind of came home  
15 as we were talking is we have the same problems  
16 producing labels for things we make in the pharmacy  
17 that the industry does. And one of the things that  
18 occurred to me as I was thinking about this, I have  
19 a number of customers who put clutter on their  
20 labels because that clutter is demanded by their  
21 state boards of pharmacy. Those state boards of  
22 pharmacy don't distinguish between an IV label  
23 produced for an inpatient pharmacy and a  
24 prescription label produced on a bottle of  
25 antibiotics going out the door at Walgreens. And

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 the result is that those labels have a tendency to  
2 be fairly full of things that most nurses would  
3 really rather not see. So there's probably some  
4 effort here that needs to occur to involve NABP and  
5 to get them to look seriously at some of their model  
6 practice acts in order to get them to do things with  
7 labeling requirements that are a little bit less  
8 arduous in this particular environment.

9           And finally, as a guy who's been playing  
10 with software for the last 15 years, there are some  
11 rules you see in medical device software that do in  
12 fact seem to be applicable here. This is the point  
13 I need to look at my notes so you'll forgive me if I  
14 too have to put on glasses. When you develop a  
15 medical device, you have to start with a hazard-  
16 based approach. You ask two questions, is it safe  
17 and is it effective. If it's effective it does what  
18 you want it to do. So to Diane's challenge to me  
19 earlier in the day, we must first decide what it is  
20 our labels are intended to do. Until we answer that  
21 question, we will not know what those labels ought  
22 to look like.

23           The second thing we have to look at is  
24 say what are the biggest hazards associated with our  
25 labels. We've had some good discussions about that

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 today. When you think about the hazards that we  
2 have, the first big hazard you have with any system  
3 is asking people to do things that they do poorly.  
4 And there are certain things that people do poorly,  
5 especially when they're in a hurry. One of the  
6 things that they do poorly is they don't read novels  
7 very well. People don't read labels like a John  
8 Grisham novel. They read labels the way they read a  
9 reference book. They look for key phrases. Why do  
10 reference books mostly have tables and figures in  
11 them? Because that's the easiest way to see the  
12 data. So we have to organize the data on our labels  
13 so that it's easy to read in a hurry. We saw some  
14 interesting examples of that today. Okay?

15           The other thing they don't do very well,  
16 and forgive me, but this is especially true of  
17 nurses. They don't do math in a hurry. Okay? When  
18 you present the data in a way that's ready for them  
19 to use so they don't have to do mental arithmetic,  
20 they usually do it right. But if they need to know  
21 that the concentration is 500mg per ml but you tell  
22 them that it's 5g - forgive me. In a 100ml. I  
23 probably just blew the calculation. But you get my  
24 point.

25           That means there isn't a one-size-fits-

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 all for this labeling because if the drug is dosed  
2 by frequency or administration rate, concentration  
3 is more important than the amount of drug in the  
4 bag. But if it's dosed as a single dose, I don't  
5 care what the concentration of clindamycin 600mg is  
6 in that pre-mixed bag. I want to give 600mg of  
7 clindamycin. The amount of the drug in the bag is  
8 important. But if I'm setting the infusion rate up  
9 and down based on a clinical response, what's the  
10 most important thing to me? The concentration in  
11 the bag. So one rule that works well in one  
12 instance is not always going to work well in others.

13 And finally, there's some other things I  
14 guess we've got to look at. ISMP has some really  
15 wonderful rules for expressing measurement. You  
16 know, you put commas, a thousand separator in there  
17 so people don't have trouble counting zeroes. You  
18 never put a trailing zero. We saw three bags up  
19 here where the concentration was 0.30 percent. I  
20 was waiting for Mike to come crawling over the  
21 table. Those rules have been out there for a long  
22 time. Why aren't those written into our pharmacy  
23 systems, our labeling systems? Why are they not  
24 part of the standards that we apply to labels that  
25 we make?

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1           Judicious use of white space. It turns  
2 out again if you look at well-written reference  
3 material, there's lots of white space. The  
4 information you're looking for is always in the same  
5 place. I know exactly where to go to read it. I  
6 develop habits around my confidence in the layout of  
7 that information and those habits actually make me  
8 more effective in reading that information. Those  
9 are all things I think I we need to think about  
10 here.

11           Finally, let's talk about special  
12 effects, tall man, color, whatever. I'm sorry, I've  
13 got to tell my grandmother story. I had a  
14 grandmother, God rest her soul, she's dead, that I  
15 learned quickly as a child never to tell her I like  
16 that. Right? I like that cookie. Because I would  
17 wind up with so many of them I could never stand  
18 looking at it again. I think we can do the same  
19 thing with these special effects. Tall man  
20 lettering makes sense in certain selected instances.

21       We should apply it judiciously. Color may make  
22 sense in certain instances. We should apply it  
23 judiciously. Warnings, when they are exceptional,  
24 when they really need to be seen are effective if  
25 they're applied judiciously. If there's a warning

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 on every label people stop reading it. We've had  
2 the same experience with software systems that do  
3 drug interaction checking. If I get a drug  
4 interaction check on absolutely every order I place,  
5 sooner or later I learn to hit the delete key before  
6 it even finished displaying. And we see the same  
7 effect on printed material that we put on the  
8 labels. If warnings are rare, they will be read.  
9 If warnings are common, they will be ignored.  
10 Anyhow, those were some thoughts from experience  
11 from the software industry I thought I would share.

12 Thank you for your time and attention.

13 (Applause)

14 MS. COUSINS: And they said I'd have a  
15 difficult job. Thank you all for staying on time, I  
16 really appreciate that. Thank you for the time you  
17 put into preparing your comments, I appreciate that.

18 Well, we're about to wrap up our meeting  
19 and we have two final folks to address you from the  
20 Food and Drug Administration. So let me turn the  
21 podium over to Carol Holquist, Pharmacist and  
22 Director of the Division of Medication Errors and  
23 Technical Support in CDER at the FDA.

24 MS. HOLQUIST: Well, thank you. First I  
25 think we can all agree that we had a very productive

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 meeting today. We really identified many of the  
2 challenges and constraints faced by all the  
3 stakeholders, whether it be industry, healthcare  
4 practitioners, regulators and even the public. When  
5 I was thinking about what really were the key issues  
6 addressed today, actually the last speaker did a  
7 very good job of summarizing many of them. But what  
8 I came up with too was a lot of the information that  
9 we came out of.

10 First was the clutter, the real estate  
11 that's available for these labels and really what  
12 really is considered clutter. It really depends on  
13 what stakeholder you're speaking with. Most of this  
14 clutter comes from a lot of the regs, some of the  
15 USP regulations that are put out in General Chapter  
16 Number 1, but also some of the legal considerations  
17 that we heard from industry. So I guess what's  
18 still really unclear to me at the end of today is  
19 you know what can we remove from the bag. You know,  
20 what can we remove, what can we de-clutter that will  
21 still be safe and everyone will feel confident that  
22 we're not going to go forward and make any more  
23 errors.

24 And in trying to do that came like the  
25 second thought of the day is can we standardize

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 these things and how best to do it. And I think we  
2 do have to be very careful in our considerations of  
3 standardization for some of the things just  
4 mentioned, that you know one size may not fit all  
5 areas. So we're going to need some testing in this  
6 area, whether it be with the human factors. I think  
7 also with label comprehension that's going to have  
8 to become more prevalent in the review process.  
9 We're going to need to look also at - when we talk  
10 about standardization we heard a lot on color  
11 differentiation today. We heard from manufacturers  
12 that it's very helpful for them to differentiate  
13 their strengths, but then we heard from some  
14 practitioners that when you look at everybody's  
15 together it may not be that helpful.

16 We're also going to need to look at  
17 where we put the bar code, do we put it in a  
18 standard place. You know, is there going to be a  
19 standard place for a pharmacy label that goes from  
20 an inpatient setting, can it cover that bar code so  
21 you don't end up with some of these errors where you  
22 have dual bar coding. Also tall man lettering was a  
23 huge issue here today. We heard that there is some  
24 need for standardization of that, but it shouldn't  
25 probably be used you know this willy-nilly approach

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 you know. Let's be proactive and make everything  
2 you know tall man lettering. I think we really have  
3 to - we heard today that we do have to reserve it  
4 and we have to have some gatekeeper for that.

5 And also I think in the end we heard  
6 about the timeliness, the timeliness that it takes  
7 for all these things to happen. If it is a  
8 regulation change and you all know it can take  
9 several years to do that. So what can we do in the  
10 interim? Do we do a guidance? We all know that  
11 guidance isn't regulation so it can be followed, it  
12 may or may not be followed. Is that the best  
13 approach? Is it something that we need to change in  
14 the USP general chapters? If it's changed there,  
15 FDA would have to follow it because we have to  
16 follow whatever's laid out in the official  
17 compendium. So I think all of these issues that  
18 we've heard today we're going to have to take back  
19 as a group and look to move forward so that we're  
20 not here 10 years from now discussing the same  
21 things that we heard 10 years previously. And I  
22 think you know the sponsors of this meeting, USP,  
23 ISMP and FDA, we're all very serious about trying to  
24 make some difference. And as everyone stated, the  
25 IOM report has given us all a great sort of thrust

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 there to move forward with these things and hope to  
2 give us some ability to really make a difference.  
3 So with that I'm going to turn it over to our  
4 director, Gerald Dal Pan.

5 (Applause)

6 DR. DAL PAN: Okay. Well, I first would  
7 like to thank everybody who participated, our  
8 organizers, our speakers, everybody who asked  
9 questions and everybody who came here to attend  
10 today. We certainly have our challenges set forth  
11 before us. I think that Carol and the other  
12 presenters clearly delineated what they are. The  
13 clutter issue I think is a straightforward issue.  
14 How to handle it might not be so straightforward.  
15 Other things are a little more complicated, like  
16 Carol say, tall man letter and coloring. But I look  
17 forward to our office, our agency working with ISMP  
18 and with USP to move this issue forward. We'll  
19 clearly need continued input from all the  
20 stakeholders and the fora that we do this, guidance  
21 development, regulation-writing, whatever one of  
22 those avenues we take does allow for public comment  
23 and we'll certainly be seeking that and looking  
24 forward to what different stakeholders have to say  
25 in that. And finally, I'd like to thank Mike Cohen

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 and his colleagues at ISMP, Diane Cousins and her  
2 colleagues at USP and my colleagues at FDA for  
3 organizing today's symposium, today's public  
4 workshop. And with that, thank you.

5 (Applause)

6 MS. HOLQUIST: I'd just like to add one  
7 more comment that I forgot to say, that you can - if  
8 today, if you didn't get your full say here that you  
9 still have the opportunity to submit comments to the  
10 public docket until mid-April. So if you have a  
11 burning desire to you know give added input in here  
12 it would be greatly appreciated. Thank you. Oh,  
13 the slides will be available as well on the web  
14 after today's meeting.

15 (Whereupon, the foregoing matter went  
16 off the record at 4:07 p.m.)

17  
18  
19  
20  
21  
22  
23  
24

**NEAL R. GROSS**

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701