

UNITED STATES OF AMERICA

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DRUG EVALUATION AND RESEARCH

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USE OF COLOR ON PHARMACEUTICAL PRODUCT

LABELS, LABELING AND PACKAGING

+ + + + +

PUBLIC HEARING

+ + + + +

MONDAY,

MARCH 7, 2005

+ + + + +

The public hearing was held at 8:00 a.m. in the Auditorium of the Lister Hill Center, Building 38A, National Institutes of Health Campus, Bethesda, Maryland, Dr. Paul Seligman, presiding.

PRESENT:

- MARY BAKER, Pharm.D.      Hospira, Inc.
- JAMES BROSELOW            Catawba County Medical Center, Hickory, NC
- MICHAEL COHEN            Institute for Safe Medication Practices
- JOSEPH CRANSTON         American Medical Association
- ALLAN JENSEN, M.D.        American Academy of Ophthalmology
- FRANK KYLE                American Dental Association
- MARY ANN McCELLIGOTT, Ph.D.    Novo Nordisk
- CHARLES MYERS            American Society of Health Systems
- ERIC SHEININ, Ph.D.        United States Pharmacopeia
- THOMAS WILLER, Ph.D.      Hospira, Inc.

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FDA REPRESENTATIVES:

PAUL SELIGMAN, M.D.      Presiding Officer

PETER CARSTENSEN

WILEY CHAMBERS, M.D.

CDR CAROL HOLQUIST, R.Ph.

ROBERT MEYER, M.D.

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

8:06 a.m.

DR. SELIGMAN: Good morning. Welcome to the FDA Part 15 hearing on the use of color on pharmaceutical labeling and packaging.

The objectives of today's hearing are to obtain public feedback regarding the advantages and disadvantages of using color to differentiate, identify, or classify drug products.

And to hear whether there are specific data to demonstrate whether the practice works in reducing medication errors or contributes to medication errors.

And finally to ascertain whether the use of color within certain classes of drugs improves or is a hindrance to patient safety.

Today we're going to have a panel of FDA experts who will be up here at the front as well as in the front row. And I'd like to introduce them briefly and then to talk about the ground rules for today's Part 15 hearing.

First of all, the members of the panel are going to be Dr. Robert Meyer, who is the Director of the Office of Drug Evaluation II in CDER. And he'll be joining us shortly, Dr. Wiley Chambers, who is the

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1 Deputy Director of the Division of Anti-Inflammatory,  
2 Analgesic, and Ophthalmologic Drug Products in CDER,  
3 Dr. Peter Carstensen, who is the Seniors Systems  
4 Engineer in the Division of Device Users Programs and  
5 Systems Analysis in the Center for Devices and  
6 Radiological Health, CDR. Carol Holquist, who is the  
7 Director of the Division of Medication Errors of  
8 Technical Support in the Center for Drugs, Drug  
9 Evaluation, and Research, and finally myself, Paul  
10 Seligman, and I'm the Director of the Office of  
11 Pharmacoepidemiology and Statistical Science, also in  
12 the Center for Drug Evaluation and Research.

13 Each speaker will be allocated a specified  
14 period of time. FDA panel members will question each  
15 speaker individually after each presentation. Please  
16 keep your talk focused on the hearing questions and  
17 limit your remarks to the time assigned.

18 The ground rules for a Part 15 hearing  
19 include the following:

20 The hearing is informal. The Rules of  
21 Evidence do not apply. No participant may interrupt  
22 the presentation of another participant. Only the  
23 presiding officer, namely myself, and the panel  
24 members may question any person during or at the  
25 conclusion of each presentation.

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1           And public hearings under Part 15 are  
2 subject to FDA's policy and procedures for electronic  
3 media coverage of FDA's public administrative  
4 proceedings. Representatives of the electronic media  
5 may be permitted, subject to certain limitations, to  
6 videotape, film, or otherwise record FDA's public  
7 administrative proceedings, including presentations by  
8 the participants.

9           Ths meeting will be transcribed and posted  
10 on the Internet within 30 days. We will also be  
11 accepting written comments to the FDA's Division of  
12 Dockets Management until April the 7th.

13           Finally, as we are guests of the National  
14 Library of Medicine's Lister Hill Center, there are a  
15 few housekeeping announcements that I want to make you  
16 aware of. First of all, no food or drink or beverages  
17 of any kind are allowed in the auditorium. If you  
18 have them at present, please remove them.

19           Please set your pagers and cell phones to  
20 vibrate.

21           To activate the audience microphone if you  
22 should need it, there's a button in front of the  
23 microphone and a red light will come on.

24           And finally, the message desk phone number  
25 here is 301-496-4062 if you need it.

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1           With that and without -- if there aren't  
2 any other questions or issues related to the beginning  
3 of this meeting, I'd like then to introduce CDR. Carol  
4 Holquist who is the Director of the Division of  
5 Medication Errors and Technical Support. And she will  
6 provide us an overview of the issue and present the  
7 questions as posed in the January 28th Federal  
8 Register announcement of the meeting.

9           Thank you. Carol?

10           CDR. HOLQUIST: Good morning. It is my  
11 pleasure to present an overview of the issues  
12 associated with the use of color on pharmaceutical  
13 labeling and packaging.

14           Over the years, several different color  
15 techniques have been used on device and pharmaceutical  
16 labels, labeling, and packaging to help identify,  
17 classify, or differentiate drug products and their  
18 respective strengths.

19           These color techniques can be briefly  
20 described as follows:

21           Color matching, the application of color  
22 in order to match one item with another. This is a  
23 color differentiation technique used with medical  
24 devices.

25           Color differentiation, this technique can

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1 be described as the use of color to enhance certain  
2 features on the label, labeling, and packaging to help  
3 distinguish or differentiate one item or product  
4 strength from another.

5 Color coding, this technique is described  
6 as a systematic application of color to aid in  
7 identifying, differentiating, or classifying a drug  
8 product generally within the same pharmacological  
9 class.

10 Color branding, this technique is similar  
11 to color coding. It has been described as a technique  
12 used to differentiate drug products within the same  
13 pharmacological class. However, a single sponsor  
14 manages the color.

15 As I stated earlier, a number of drug and  
16 device manufacturers already employ color in an effort  
17 to point out differences and to facilitate the  
18 selection and dispensing of medication and devices.  
19 Some examples include ophthalmologic, dental,  
20 anesthetic, and most recently, insulin drug products.

21 Many individual groups endorse the use of  
22 color in this way. Color use in such select  
23 environments as the operating room and dental suite  
24 provide quick identification of a specific  
25 pharmacological class by the color alone. Some state

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1 it is easier for their patients to remember the color  
2 of their drug product rather than the name.

3 Many patient safety and advocate groups do  
4 not support the use of color in this way and say the  
5 practice contributes to medication errors. Applying  
6 color across a pharmacological class of products may  
7 contribute to the similar appearance of drug products  
8 and lead to selection of the wrong drug.

9 We will hear from a number of speakers  
10 today who should address the following questions:

11 How and under what circumstances has the  
12 use of color on pharmaceutical packaging and/or  
13 labeling proven an improvement in patient care?

14 Is there no discernable improvement?

15 What are the deficiencies in the program?

16 Are there specific classes of drugs where  
17 use of color has demonstrated value?

18 Are there classes where use of color is a  
19 hindrance to public safety?

20 Are there drug products currently marketed  
21 that do not use color that should use color to aid in  
22 identification of the drug? If so, how should color  
23 be used?

24 How should the effectiveness of  
25 application of color on drug products be

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1 scientifically validated?

2 We are eager to hear from each presenter  
3 today. We plan to assess the data presented and  
4 carefully consider the next steps with regard to  
5 appropriate applicability of color on pharmaceutical  
6 labeling and packaging.

7 Thank you.

8 DR. SELIGMAN: Thank you, Carol.

9 Let me introduce then the first speaker of  
10 today. He is Mr. Charles Myers of the American  
11 Society of Health-System Pharmacists.

12 Mr. Myers? Do you have any slides? No?  
13 Okay.

14 MR. MYERS: No, I'm doing this without  
15 slides so no musical accompaniment.

16 Good morning to all of you. I am Charles  
17 Myers. I am a staff member of the American Society of  
18 Health-System Pharmacists. Those are pharmacists who  
19 practice in places like hospitals, organized settings  
20 like home care operations, HMO clinics, and other  
21 outpatient clinics, in long-term care facilities.

22 These are the pharmacists that are  
23 responsible on a daily basis for not only the  
24 logistics of drug use within those settings but also  
25 responsible for advising the medical staff and

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1 collaborating with the medical staff in terms of the  
2 therapeutic drug use policies that will exist in those  
3 facilities and in safeguarding the medication use  
4 process.

5 We would like to commend FDA for seeking  
6 public comments on this important issue. This is an  
7 issue on which our members have given considerable  
8 thought. I will tell you the punch line ahead of time  
9 and that is that our members think that color coding  
10 is not a good idea.

11 Most of my comments will address color  
12 coding. Our members have developed formal policy for  
13 ASHP about this matter and paraphrased, the policy  
14 that our members have developed for themselves and for  
15 our society is ASHP supports the reading of drug  
16 product labels as the most important means of  
17 identifying drug products and opposes reliance on  
18 color by health professionals and others to identify  
19 drug products.

20 You can back into the concept there that  
21 color coding then is not something that our members  
22 support because they believe that relying on color as  
23 a means to identify a product is not a good idea.

24 Let me ask you to think for a moment about  
25 a typical hospital. It could be, however, a home care

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1 operation or a long-term care facility if you prefer.

2 In terms of medication use, these are incredibly  
3 complex environments. There are so many drugs.  
4 Literally there a thousands of drugs that will be used  
5 in a given hospital every day.

6 There are so many of those drugs. There  
7 are so many strengths and concentrations, so many  
8 routes of administration, so many rates of  
9 administration, and only a few correct rates of  
10 administration.

11 There are so many ways that drugs could be  
12 categorized. We know, for example, that they could be  
13 categorized by pharmacologic class.  
14 Antihypertensives, anti-arrhythmics, glucogenic drugs,  
15 neuromuscular blocking agents, narcotics, pediatrics  
16 dosage forms and strengths, emergency medications,  
17 ophthalmologics, sterile and non-sterile products,  
18 internal and external products.

19 So we have great variety in the types of  
20 drugs that exist and the types of things that colors  
21 could be assigned to mean. And therein lies a  
22 potential problem. The matter of classification could  
23 become immensely complicated depending on potential  
24 conflicts and drugs that have multiple  
25 characteristics.

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1           For example, if a green label meant a drug  
2 was an antihypertensive and a red label meant that it  
3 was an anti-arrhythmic, how would a beta blocker drug  
4 that can be used for both purposes be labeled? How  
5 could colors be assigned in the case of combination  
6 products?

7           In hospitals and health systems, there are  
8 so many care providers to educate about medication  
9 uses and hazards. There are prescribers of all sorts,  
10 including specialists and nonspecialists, some  
11 employed on the premises, and some with only  
12 occasional contact with the facility through admission  
13 of their patients.

14           There are pharmacists, of course. There  
15 are nurses with varying levels of education and  
16 training. There are respiratory therapists, dialysis  
17 staff, emergency department staff, physician  
18 assistance, and students and, of course, trainees of  
19 all sorts in each of those disciplines. All these  
20 people would need to understand any color code schema  
21 developed.

22           There are also many potential colors and  
23 so many places and media on which the colors would  
24 have to be consistently applied. Paper labels,  
25 cardboard cartons, glass ampules, plastic syringes.

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1 There are so many manufacturers of the same or similar  
2 drug products. And product packages and appearances  
3 already change frequently, creating problems enough.

4 Color coding would be promptly destroyed  
5 unless colors were standardized. And yet in the face  
6 of all this complexity, there is little objective  
7 evidence about the safety effects of color coding in  
8 widespread use. And there are so many patients at  
9 risk.

10 Pharmacists in hospitals and health  
11 systems live in that complex world. And much of what  
12 they do is designed to ensure safety in the face of  
13 that complexity. To them, the issues of color coding  
14 and color in drug products are not new issues. They  
15 have thought this through.

16 And their short summary for you is this,  
17 color is a great differentiator. Actions to make  
18 different drug products stand out from one another are  
19 commendable and color can be very useful for that  
20 purpose. However, the safety of using color to  
21 transmit information, in other words, using color as  
22 a code, has not been sufficiently proven in the complex  
23 world of hospitals and health systems.

24 Those pharmacists believe that inducing  
25 even a partial reliance on color as a code to identify

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1 drugs or to denote specific aspects of drugs is a  
2 seriously bad idea until there is clear evidence to  
3 support such a practice.

4 Hospital and health system pharmacists are  
5 aware that in some limited cadres of practitioners,  
6 for example in ophthalmology and anesthesiology, there  
7 has been some experimentation with color coding.  
8 Health system pharmacists urge us all to understand  
9 that there are some crucial differences about those  
10 experiences compared to other more widespread use of  
11 drugs.

12 In those limited cadres, the number of  
13 drug products involved is small and the number of  
14 practitioners who have to be informed about the code  
15 meanings of colors is also small. Therefore, the  
16 transferability of their experiences to the larger  
17 world of the thousands of drug products and the  
18 hundreds of thousands of caregivers who have to  
19 understand the color meanings may not be sound.

20 We need evidence about the merits or  
21 dangers of color coding on a wide scale. FDA should  
22 insist upon that in large scale real world experience  
23 before endorsing color coding for anything other than  
24 limited cadres.

25 Further, we believe that objective

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1 evidence about the safety of color coding even in  
2 limited cadres should be sought through qualified  
3 researches in the human factors discipline.

4 If there are places in the world where  
5 color coding already is practiced on a large scale for  
6 drug products, those may be useful research arenas for  
7 assessing the safety impact of color coding.

8 Ultimately, we urge as well a commonsense,  
9 pragmatic distinction between whether color coding is  
10 feasible versus whether it is wise based on the  
11 evidence. Everything is technically feasible  
12 theoretically at a cost.

13 If sound research indicates that wide  
14 scale color coding enhances safety, then as a nation,  
15 we should adopt it even if it is difficult to achieve.

16 However, if the evidence turns out to be equivocal,  
17 and we believe that the evidence is equivocal at this  
18 point, then some commonsense thought must be given to  
19 whether we should invest in color coding.

20 We believe FDA has a social responsibility  
21 to consider what resources it would require to  
22 administer a color code schema on an ongoing basis.  
23 It seems logical to assume that legally assigned and  
24 protected colors would also launch inevitable  
25 litigated disputes. We believe the societal necessity

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1 and the wisdom of that expense should be considered,  
2 especially if the evidence about safety turns out to  
3 be equivocal.

4 The Federal Register notice of this  
5 discussion made some useful distinctions between color  
6 coding and some other aspects of using color. As I  
7 have said, health system pharmacists believe that  
8 color differentiation is useful. Color branding is a  
9 new term which we interpret as a type of color  
10 differentiation, not color coding.

11 Color matching is not a concept in which  
12 health system pharmacists have developed formal  
13 policy. Importantly and commendably, however, it  
14 appears that color matching would not require color  
15 coding so it is likely that health system pharmacists  
16 would find color matching useful.

17 Again, we commend the Agency for seeking  
18 comments on this important matter. Thank you.

19 DR. SELIGMAN: Do you have any questions  
20 from members of the panel for Mr. Myers? Wiley, do  
21 you want to come up to the microphone?

22 DR. CHAMBERS: Wiley Chambers. You  
23 mentioned that you would like to see proof before a  
24 color coding system was put into place. Have you  
25 given thought to what you would view as success in

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1 such a system before you would recommend its use?

2 MR. MYERS: It's a reasonable question,  
3 obviously. And human factors researchers would be  
4 careful to define success we are certain. We believe  
5 that ultimately the rate of errors would be the  
6 defining determinant for success or not success.

7 DR. CHAMBERS: Thank you.

8 DR. SELIGMAN: Any other questions from  
9 the members of the panel? Carol?

10 CDR. HOLQUIST: You said your position  
11 overall is that color coding is not a good idea. Can  
12 you describe how you guys came to that conclusion? Is  
13 it because of the errors that were reported amongst  
14 these agencies? Or, I mean within the hospital and  
15 retail as well? Or just hospitals?

16 MR. MYERS: Given the world of complexity  
17 in which our members practice and seeing the many  
18 close calls with medications that have been confused  
19 for whatever reasons and seeing occasional attempts,  
20 even at a local basis, for someone to decide that  
21 certain colors should mean certain things and then  
22 seeing errors happen, and we can find the errors  
23 documented within the USP's MEDMARX system and other  
24 places, given those realities, our members are  
25 skittish.

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1           And they are simply saying let's be  
2 careful about this. We ought to be able to find out  
3 the truth. When we know the truth, we ought to be  
4 able to do the right thing. Until we know for sure,  
5 let's do the safe thing. And let's ask people to read  
6 labels and not ask them to rely on something other  
7 than reading.

8           DR. CHAMBERS: Wiley Chambers again. Do  
9 you think there are any differences between within the  
10 hospital as opposed to as a general retail that would  
11 effect your opinion on this issue?

12           MR. MYERS: There probably are some  
13 differences. Certainly within hospital environments,  
14 there are many, many practitioners who will handle a  
15 drug product. In the case of a retail practice, you  
16 may be dealing with number one, the prescriber, and  
17 number two, the pharmacists, and number three, the  
18 patient. That's a fairly limited subset of people.

19           Hospitals are a very much more complex  
20 environment. So yes, there might be some differences.

21           DR. SELIGMAN: Mr. Myers, thank you very  
22 much.

23           MR. MYERS: Thank you.

24           DR. SELIGMAN: Carol? Carol? Carol?

25           Our next speakers, I guess, are Dr. Mary

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1 Baker and Dr. Thomas Willer from Hospira, Inc.  
2 Please.

3 DR. WILLER: First, I'm delighted to be  
4 here this morning. On behalf of Dr. Mary Baker and  
5 myself, Tom Willer, we'd like to present Hospira's  
6 position on the use of color in labeling. By the way,  
7 those who don't know us, Hospira was previously part  
8 of Abbott Laboratories and became an independent  
9 company in 2004.

10 In essence, we oppose the use of color  
11 coding for points listed on this slide. We note the  
12 limited number of colors. Lighting and proximity  
13 really have an effect on readability of labeling. We  
14 also believe, as the previous speaker, that color  
15 coding potentially or color use potentially  
16 discourages the reading of labels. And, again, that's  
17 a major issue.

18 The choice of the drug based on cap or  
19 label color, again, is an issue in color coding that  
20 presents some issues. Also, we believe that looking  
21 at color sort of makes you mentally a little lazy and  
22 you don't read it as you should.

23 The slide presents sort of the normal  
24 limits of color, at least for us, on a flip-top vial  
25 for injectable products. Please note the shades of

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1 color -- perhaps it does show up okay. Please note  
2 the shades of color and try to identify the number of  
3 distinct colors that could be assigned to drug  
4 products.

5 If you look at this cornucopia of colors,  
6 if you will, maybe you could get by with blue, green,  
7 yellow, red, possibly white. I counted 34 individual  
8 cap colors on this. But how many could we really use  
9 to color code drug products?

10 Again, the Pantone guide that we use for  
11 labeling or label and colors is sort of the full range  
12 of colors that are open to us for printed labeling.  
13 And, again, it seems a limitless number of colors for  
14 the labels and, again, the question is how many usable  
15 different colors are available? And I think you come  
16 up with a small number that you'd like.

17 While Hospira opposes color coding, we  
18 strongly support the use of color on labeling. The  
19 use of color on labels should be used to highlight and  
20 enhance label information, as noted here, product  
21 name, drug concentration, and key warnings.

22 As noted here, Hospira is constantly  
23 updating our labeling per year to the tune of about in  
24 excess of 3,000 labels. They are changes to our  
25 carton, our container, our package insert, trays, and

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1 corrugate labeling. So it's a very complex operation  
2 that we run.

3 As noted here, there are many stimuli for  
4 us to change our labeling. Some we're acting in  
5 response to letters from the Agency. Others changes  
6 in the reference list of drugs since many of our  
7 products are generic products. Next, new product  
8 labeling through ANDA submissions that we make.

9 We also do a periodic review of labeling  
10 systems or classes of drugs such as controlled drugs  
11 or the Carpuject, which is a syringe system.

12 Abbott, and now Hospira, has been active  
13 in acquisition of products from other companies or  
14 buying other companies. And that results in some  
15 labeling standardization from the old company to ours.

16 And lastly, we react to complaints in the complaint  
17 system.

18 We've dealt with the need to consider all  
19 of these label improvements, especially through a  
20 group that we call Label Enhancement Committee. I'd  
21 like to let Dr. Mary Baker continue at this point.  
22 Mary?

23 DR. BAKER: Thank you, Tom.

24 I'm Mary Baker. I'm with Global Medical  
25 Affairs. And I'd like to describe to you Hospira's

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1 efforts with label enhancement.

2 Hospira has about 130 drug products. Now  
3 we're talking all injectable drugs which constitutes  
4 over 600 list numbers, a list number being a different  
5 size, a different format, a Carpuject versus a flip-  
6 top vial, a tear-top vial, that sort of thing.

7 In 1992, our quality assurance group  
8 established a Label Enhancement Committee and we have  
9 met monthly ever since. The standing committee  
10 composition includes, medical, regulatory, label  
11 control, and product complaint, those two groups being  
12 part of our quality organization, and a very valuable  
13 part of our organization, the graphics group.

14 As Tom mentioned previously, we review  
15 complaints based on clinician complaint. Every single  
16 complaint that gets called into our product complaint  
17 group gets reviewed at the Label Enhancement meeting.

18 At the Label Enhancement meeting, our  
19 label editors provide color labeling to the Committee.

20 If we can obtain competitor's labeling because  
21 sometimes let's say that the Hospira product looks  
22 like a product from another manufacturer, we attempt  
23 to obtain that. The Internet has made it quite nice  
24 to take a look at what the competition does because  
25 some will put their catalog on the Internet.

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1           We also consider the storage area. Some  
2 hospitals store by brand. Some store by generic.  
3 Some store by both. It could be alphabetical in  
4 general distribution. We take into account whether  
5 this will be in a locked area such as in a controlled  
6 substances location or drug class because frequently  
7 in hospitals, you will have oncology products stored  
8 together or critical care products stored together as  
9 in a crash cart or PIXIS.

10           Taking a look at our labeling similarity  
11 complaints from 2000 to 2004, you will see a spike in  
12 the year 2001. That was based primarily on two  
13 products. Number one was the heparin Carpuject  
14 system. And the flip-top vial, which is FTV. That  
15 was based on a product called Nimbex which is now with  
16 Abbott Laboratories.

17           Nimbex had two issues. Number one, it  
18 went from a hexagonal-shaped vial to a round vial  
19 because of a change in the manufacturing location.  
20 And there also were a number of complaints regarding  
21 the labeling.

22           What we did regarding the Nimbex is we did  
23 do a label enhancement on the actual label and what we  
24 also did insofar as the shape of the vial is that a  
25 stop sign was put on the product for, I believe, about

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1 a six-month period to alert the clinician that the  
2 shape of the vial had changed because what  
3 anesthesiologists were doing is that they were  
4 reaching in back and grabbing the vial based on the  
5 shape of the vial. And they were grabbing by touch,  
6 not by reading the label.

7 And as you can see in the following year,  
8 the complaints have gone down. I also might want to  
9 add that the number of actual complaints is probably  
10 close to half this number because if somebody  
11 indicates that two of our products look alike, that  
12 generates two complaints, not one.

13 In the review process, if we feel that  
14 modification is required after the Committee reviews  
15 it, our graphics studio will put together a number of  
16 options for us to review, sometimes at the next  
17 meeting but usually they can get it done beforehand  
18 and we will decide which graphic to use.

19 Sometimes the clinician will complain  
20 about a product but the change has not made it into  
21 the general distribution. That is a common occurrence  
22 with products that are only made once or twice a year.

23 That we will make the change but the product was not  
24 scheduled to be made for another six months.

25 If there is no modification required, the

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1 clinician is notified. And we will continue to  
2 monitor for other complaints.

3 We use a very low tech system in some  
4 cases to see where a product is going to be stored.  
5 We use what's called a story board. And we'll take a  
6 large piece of cardboard, we'll put our label, the  
7 other company's label, if it's available.

8 And we will take a look and say okay, if  
9 you were looking at this, would you see that there is  
10 a similarity? That's been very helpful in helping us  
11 to choose colors to enhance the label.

12 Here is an example. Here this product is  
13 being transitioned to Hospira. It shows three  
14 products, Ketorolac in 15-, 30-, and 60-milligram  
15 concentrations, using a different color background,  
16 the reverse out labeling, and we tested these among  
17 pharmacists and nurses that were in the groups, the  
18 medical groups, and it was decided that this would  
19 provide sufficient differentiation.

20 To the Agency's questions regarding the  
21 use of color, as the previous speaker indicated color  
22 is a useful attribute but it is not a substitute for  
23 reading the label. Color can enhance but will not  
24 replace the primary identifier, which is the label.

25 And for an example, I'm going to show you

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1 our Carpuject syringe system cap color. This is how  
2 our current Carpuject product is being sold. It has a  
3 green cap color signifying a luer tip.

4 Previously, we marketed the product having  
5 different color caps on the end, which indicated the  
6 type of needle, or blunt cannula, or luer tip. What  
7 we found out when we went to the all luer tip, which  
8 is the green cap color, was that clinicians were  
9 purchasing the drugs based on the tip color.

10 So they would buy one particular product  
11 that had a blunt cannula. And they had another  
12 product that they would buy with the needle, which had  
13 a different color cap, and the philosophy was if I  
14 grab the one with the blue cap color, I know exactly  
15 what drug I have and I don't have to read the label.

16 Specific classes where color has effected  
17 public safety, we are not aware of major data that  
18 describes this. Drugs that do not use color that  
19 should use color, again, color is one attribute of the  
20 labeling. And the presentation of information is  
21 critical to accurately assess the identification of  
22 the product.

23 Scientifically validating the  
24 effectiveness of color on labeling, again rigorous  
25 market testing with different populations: color-

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1 blind, those of us over 40, and other populations as  
2 well. We realized that some of these products are  
3 used in the home care setting with patients and  
4 caregivers who are not medically trained.

5 There would have to be a transition plan  
6 from the current to the revised labeling. And there  
7 would have to be substantial education going across  
8 multiple disciplinary groups, nursing, pharmacy, and  
9 physicians.

10 And the other thing that has to be  
11 assessed is what would be the potential for risk of  
12 increased medication errors if somebody is used for a  
13 product being red and now it is green, when do you get  
14 the product that is actually turning green. Again,  
15 the distribution system does not allow for a product  
16 to instantaneously hit the market. So it may be six  
17 months after the ruling goes into effect that a  
18 clinician will see a change in the label.

19 Thank you.

20 DR. SELIGMAN: Thank you.

21 Dr. Baker either within your suite of  
22 products or when comparing your products to other  
23 products, you presented some data showing that there  
24 were, you know, I think some frequency data showing  
25 the number of similarities or reports of similarities.

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1 Do you know how often color may have contributed to  
2 some of those confusions?

3 You noted, you know, the hexagonal shape  
4 of a --

5 DR. BAKER: Right.

6 DR. SELIGMAN: -- particular bottle. I'm  
7 just curious as to knowing how often color may have  
8 been mentioned as a possible source of some of the  
9 problems.

10 DR. BAKER: Color is mentioned as a  
11 frequent look-alike. We get complaints over a wide  
12 variety of topics. As, for example, they will say  
13 that our product will look like a competitive product.

14 A lot of this has to do with the cap  
15 color. Tom showed the different cap colors and that  
16 say for example, we might use the same cap color for  
17 one of our electrolytes that some other company uses  
18 for one of theirs. That's happened some -- fairly  
19 regularly.

20 DR. SELIGMAN: What's the decision making  
21 or the thought process that goes on in your  
22 organization when it comes to the selection of colors  
23 either for caps or for luer tips or other kinds of  
24 products that you produce?

25 DR. BAKER: There are multiple

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1 considerations. As mentioned previously, we do look  
2 at where the product is being stored. If we are aware  
3 that a product that has a very similar name or it is  
4 close in the alphabet to the product either by brand  
5 name or generic name, we will avoid that particular  
6 color family. And go to something that is totally  
7 opposite.

8 DR. SELIGMAN: Yes.

9 DR. WILLER: If I could add on one point  
10 on to that, one of the things we do since most of our  
11 products are generic drugs, we try to adopt the same  
12 color scheme as the innovator. So if the innovator  
13 labeling is green, we'll generally follow with a green  
14 color for our labeling.

15 However, we'll also try to use the same --  
16 a green cap color if we can. Because of limitations  
17 on inventory and as I showed you, I think it was 47 or  
18 whatever number of caps, we're not going to keep five  
19 different shades of green. So we may just have green,  
20 however that's termed. And the innovator may be  
21 slightly darker or lighter than us. So we do try to  
22 have a similarity.

23 So to some extent for the generic products  
24 that we have, they will be color similar to the  
25 innovator.

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1 DR. CHAMBERS: How many different colors  
2 do you use?

3 DR. BAKER: Quite a few. We do use the  
4 Pantone. I can't -- we don't -- we do not limit  
5 ourselves to any number of colors, no.

6 DR. WILLER: In terms of the Pantone list  
7 which Mary brought -- I'm not sure if anybody has seen  
8 this, but there's just literally thousands of shades.  
9 And what we'll try to do is -- this is limitless to  
10 us. But we've got to make sure that it is a  
11 distinctive enough shade to use it.

12 In terms of the cap color, I think we're  
13 far more limited -- we're in the range of 10 to 20  
14 different cap colors.

15 DR. CHAMBERS: I guess more of what I was  
16 asking was if you had taken the time to go through and  
17 figure out just how many distinguishable colors you  
18 had options to use?

19 DR. WILLER: We've not done that.

20 CDR. HOLQUIST: Wiley just asked my  
21 question. But I have another question. Have you guys  
22 experimented not using color at all? And how would  
23 that effect the similarity in labeling? If you can't  
24 -- if, you know, if the color wheel is so small?

25 DR. BAKER: When we acquired products from

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1 Sanofi and the Carpuject line, they had all their  
2 products for the Carpujects had a green and blue  
3 stripe on the carton and they were black on white  
4 labeling.

5 So where we have not experimented with it,  
6 it was an expression from clinicians that they did not  
7 like all the products having black on white labeling.

8 And a green and blue stripe on the front of the  
9 carton.

10 DR. WILLER: We do use black and white on  
11 many of our trays for a product. If we have 25 vials  
12 or ampules that we put into a tray, we print a black  
13 and white tray online during the production process.  
14 So that's the only time we would have black on white.

15 But the actual color labels would still be on the  
16 individual products. So it's kind of a hybrid.

17 DR. MEYER: I'm Dr. Meyer from the FDA.  
18 Both you and the previous speaker I think made some  
19 very valid points about the downside of color coding.

20 But in terms of color differentiation where there is  
21 no coding, then the choice becomes somewhat  
22 extemporaneous, if you will. I mean it becomes the  
23 choice of the particular manufacturer.

24 I was curious when you're receiving  
25 complaints about your product looking alike another

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1 manufacturer's --

2 DR. BAKER: Yes?

3 DR. MEYER: -- product rather than your  
4 own, is there any attempt to coordinate your response  
5 to what the other manufacturer is doing? I guess it  
6 appears me that they might be out doing the same  
7 thing.

8 And, you know, with various colors you  
9 might both be changing in ways that continue to  
10 promulgate the problem or the other thing is whether  
11 your changes, in fact, make you look less like Drug A  
12 but more like Drug C. So I'm wondering how you  
13 grapple with those kinds of issues.

14 DR. BAKER: We have spoken with other  
15 manufacturers with certain products. Sometimes we've  
16 changed. Sometimes they've changed. Sometimes  
17 neither one of us has changed. But when feasible, we  
18 have talked to other manufacturers.

19 DR. WILLER: Mary is sort of our resident  
20 wizard on the Label Review Committee, our Label  
21 Enhancement Committee. We are cognizant of where  
22 products we're guessing would be stored in a pharmacy,  
23 whether it's alphabetical or by company or by product  
24 grouping. So we try to think of those limitations  
25 when we pick a new color or we make a change in color.

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1 DR. CHAMBERS: Wiley Chambers. You  
2 mentioned that at one point a vial was a hexagonal --

3 DR. BAKER: Correct.

4 DR. CHAMBERS: -- shape. Have you seen  
5 other configurations that -- well, let me back up. My  
6 assumption was that clinicians found that useful to  
7 have the differentiation. Was that what they were  
8 reporting to you?

9 DR. BAKER: This was a product we had  
10 purchased from another manufacturer. And the previous  
11 manufacturer had it in a particular location where  
12 they were able to manufacture a hexagonal vial. And  
13 we moved to our facility, which did not have that  
14 particular capability.

15 But the clinician indicated that they  
16 selected the product based on touch because they could  
17 reach in back, feel the hexagonal shape, and then  
18 choose the product based on the shape of the vial.

19 DR. CHAMBERS: I guess part of what I'm  
20 asking is if you had the option to remain with the  
21 hexagonal shape, would you have done so? Did you find  
22 that a good feature? It's one thing to say clinicians  
23 are using it as a feature. But it may not be the only  
24 feature. It may be in addition to reading the label,  
25 it may be a secondary safety factor. Or it may not.

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1 DR. BAKER: Well, again, they're selecting  
2 a product based on touch and not by reading the label.  
3 So we, at that time and still don't have the option  
4 to manufacture those particular types of vials.

5 Now what we did do is alert the clinician  
6 via use of the stop sign so they would be alerted to  
7 that particular fact that the vial shape had changed.

8 DR. WILLER: Just another example of that.  
9 I submitted the fentanyl citrate product as an ANDA  
10 in the mid-90s and that was also originally in a  
11 hexagonal container. And the innovator selected that,  
12 I'm sure, because it's a unique presentation. Also,  
13 it's a special order glass. And normally you can't  
14 get it unless you buy a special mold, et cetera.

15 So we and the other generic manufacturers  
16 subsequently just switched to a more normal, standard,  
17 round or circular vial or ampule. So we made no  
18 effort to imitate the innovator in that instance.

19 DR. CHAMBERS: I guess I'd still like to  
20 know if you had the option to go to the hexagonal,  
21 would you? I understand you don't. But if you didn't  
22 have that manufacturing limitation, do you think it  
23 was a good idea?

24 DR. WILLER: I can't respond.

25 DR. SELIGMAN: In terms of color

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1 differentiation, to what degree when you're producing  
2 a label and looking at issues relating to readability  
3 and legibility, do you test, you know, different  
4 either colors or fonts or layout schemes?

5 And I guess my question really goes  
6 towards the color, to the degree to which you look at  
7 different colors in order to determine which ones  
8 might, indeed, provide better differentiation in terms  
9 of legibility and readability?

10 DR. BAKER: We actually have several  
11 methods for testing. The color we have quite a number  
12 of pharmacists and nurses within Hospira which we will  
13 take it to them.

14 We will also take it to our customers and  
15 say in your institution, which one would be most  
16 suitable with the blue? With the green? Where do you  
17 store it? Is this a product that is only stored in a  
18 PIXIS machine? Is this a product that's only in the  
19 central pharmacy? So we will take it out to  
20 practitioners.

21 CDR. HOLQUIST: You mentioned that some of  
22 your products were used in home health care.

23 DR. BAKER: Yes.

24 CDR. HOLQUIST: Do you ever go to the  
25 patient level with those questions?

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1 DR. BAKER: We have not at this time.

2 CDR. HOLQUIST: Do you think it would be  
3 useful?

4 DR. BAKER: It may be. There's a fairly  
5 limited number of products that go directly to the  
6 patient.

7 DR. MEYER: If I heard you right, I  
8 understand that at time you try to at least match the  
9 general shade of the innovator product in terms of  
10 choosing the color for your product. And I was  
11 curious as to whether there are any instances you know  
12 of where the innovator's color scheme has been  
13 protected? Where it has prevented you from doing  
14 that?

15 DR. BAKER: Not that I'm aware of.

16 DR. SELIGMAN: Any other questions from  
17 the panel?

18 (No response.)

19 DR. SELIGMAN: If not, thank you both for  
20 your presentation.

21 Our next presenter is Dr. Eric Sheinin  
22 from the United States Pharmacopeia, USP. Dr.  
23 Sheinin?

24 DR. SHEININ: Thank you very much. Dr.  
25 Seligman and ladies and gentlemen, it's a pleasure to

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1 be here today to be able to talk about this very  
2 critical topic in terms of patient safety.

3 As USP has indicated in the past, we do  
4 not have a specific policy regarding the use of color  
5 coding on labeling and packaging of pharmaceutical  
6 products. However, the issue has been discussed and  
7 debated at various times by expert committees of our  
8 Council of Experts and by advisory panels to those  
9 committees.

10 The results have been consistent in that  
11 these experts acknowledge that there may be limited  
12 instances in which color coding may be helpful. Drug-  
13 specific color coding that spans the continuum of all  
14 drugs and dosage forms could be challenging and  
15 possibly increase medication errors rather than reduce  
16 them.

17 United States Pharmacopeia is a non-  
18 governmental organization that promotes the public  
19 health by establishing state-of-the-art standards to  
20 ensure the quality of medicines and other healthcare  
21 technologies. These legally enforceable standards of  
22 quality, strength, purity, packaging, labeling,  
23 storage, and nomenclature are developed by a unique  
24 process of public involvement and are accepted  
25 worldwide.

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1           Established in 1820, USP is a not-for-  
2 profit organization that achieves its goals through  
3 the contribution of volunteers representing pharmacy,  
4 medicine, nursing, and other healthcare professions as  
5 well as academia, U.S. and other governments, the  
6 pharmaceutical industry, and consumers organizations.

7           In addition to standards development,  
8 USP's other public health programs focus on promoting  
9 optimal healthcare delivery. USP's mission is to  
10 promote the public health through the safe use of  
11 medicines.

12           USP's Council of Experts generally has not  
13 supported color coding of pharmaceuticals for the  
14 following reasons.

15           Color coding can encourage healthcare  
16 professionals to rely solely on the color in selecting  
17 a product rather than actually reading the label to  
18 identify the product being administered.

19           There are only a limited number of colors  
20 in the spectrum. The shades of color would likely  
21 begin to look similar to many healthcare  
22 professionals, especially those who are color-blind to  
23 one degree or another.

24           Certain colors in poor lighting could  
25 begin to look like others, causing products to be

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1 confused.

2 As evidence of the potential for  
3 confusion, USP Medication Error Reporting Programs,  
4 MER and MEDMARX have received reports where color  
5 similarities in labeling and packaging have caused or  
6 contributed to medication errors.

7 For more than 35 years, USP has promoted  
8 the importance of collecting and sharing experiential  
9 data from healthcare professionals. USP currently  
10 operates two national reporting programs for  
11 medication errors, MER and MEDMARX.

12 USP Institute for Safe Medication Practice  
13 Medication Errors Reporting Program, or MER, is a  
14 voluntary, spontaneous reporting program for all  
15 healthcare professionals to report potential and  
16 actual medication errors.

17 As seen on this slide, some 9,000 reports  
18 have been received since 1991. There's an opportunity  
19 for interaction with the individual reporting the  
20 error. The information collected is shared with ISMP,  
21 FDA, and the pharmaceutical industry.

22 MEDMARX, an anonymous, Internet-based  
23 reporting system that has collected more than 840,000  
24 medication error records is used to disseminate  
25 patient safety information, including recommendations

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1 and practice standards, tips for consumers, annual  
2 reports, and articles published in peer-review  
3 journals.

4 Participating hospitals are able to review  
5 the data and determine how they measure against other  
6 hospitals in the program. Further, they also are able  
7 to track how widespread certain types of errors are  
8 throughout the nation.

9 The data presented today are from the MER  
10 Program, which has specific codes for errors related  
11 to color. Because there is no such code in MEDMARX,  
12 reports would require direct review and could be  
13 provided to the Agency at a later time if needed.

14 The USP Center for the Advancement of  
15 Patient Safety searched the MER database to measure  
16 the number of color coding errors over the time period  
17 of November 15th, 1994 through December 15th, 2004.

18 Three hundred and sixty medication errors  
19 related to color coding issues were reported during  
20 this ten year plus time frame. The reports were  
21 sorted according to the category index adopted by the  
22 National Coordinating Council for Medication Error  
23 Reporting and Prevention, which classifies an error  
24 according to the severity of the outcome.

25 Factors such as whether the error reached

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1 the patient and if the patient was harmed, and if so  
2 to what degree, were taken into consideration when the  
3 index was developed. As seen on this slide, the  
4 categories can be grouped according to potential  
5 versus actual error and whether or not the patient was  
6 harmed.

7 Slightly over 50 percent of the reports  
8 were potential errors while the majority of actual  
9 errors caused no harm to the patient. However, 4.7  
10 percent did cause harm, with four fatalities being  
11 reported.

12 Out of the 360 records, 50 indicated a  
13 mode or the phase of the medication use process where  
14 the error was initiated. The highest percentage of  
15 medication errors occurred in the dispensing mode.  
16 This is the phase in the medication use process where  
17 the medication is dispensed, normally by the  
18 pharmacist, to the patient or to a unit within the  
19 hospital.

20 Products involved in these harmful errors  
21 include the high alert drugs heparin, magnesium  
22 sulphate, and potassium chloride concentrate for  
23 injection.

24 This slide shows an example where there's  
25 two different strengths of Dopamine injection where

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1 the color and labeling on the two packages are  
2 identical. This is one type of packaging where color  
3 coding would not add to the differentiation of the two  
4 strengths and thus would not, on its own, prevent an  
5 error from occurring.

6 On this slide, two examples that led to  
7 fatalities are listed as well as a third example of a  
8 serious error. In the first example, the patient died  
9 when nitrous oxide gas was administered instead of  
10 oxygen partly due to the inability of a technician to  
11 distinguish between the adaptor colors.

12 The oxygen flow meter's index safety  
13 system, designed to assure connection only to oxygen  
14 wall outlets, had been broken when inserted.  
15 Additionally, the technician had difficulty  
16 distinguishing between the blue nitrous oxide and  
17 green oxygen adapter because the radiology suite where  
18 the medical gas was administered was dimly lit in  
19 preparation for a CT scan.

20 The patient died as the result of nitrous  
21 oxide poisoning.

22 A second patient died of heart failure as  
23 the result of a nurse flushing his IV line with  
24 potassium chloride instead of heparin. Both drugs  
25 were in the patient's medication drawer. The drugs

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1 were in similar-sized vials with similarly colored  
2 labels.

3 In the third case, a patient was  
4 administered anesthesia for a surgical procedure. The  
5 anesthesiologist administered sufentanyl 75 micrograms  
6 by mistake instead of 75 micrograms fentanyl. The  
7 patient experienced a temporary respiratory arrest and  
8 his oxygen saturation decreased to 80 percent.

9 Narcan 0.2 milligrams was administered and  
10 respiration was supported. Surgery was cancelled and  
11 the patient returned to the nursing unit. The patient  
12 was eventually discharged with no problems and the  
13 surgery was rescheduled.

14 The anesthesia section had this concern  
15 regarding the possibility of being unable to  
16 distinguish the red labeling of fentanyl from the  
17 green labeling of sufentanyl secondary to the high  
18 prevalence of red-green color blindness in the male  
19 population.

20 While the idea that standardizing the  
21 appearance of labeling and packaging would reduce  
22 errors has merit, in reality it is untested. However,  
23 there may be some value to such an approach if it is  
24 applied across the market rather than across drug  
25 classes.

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1           The concept of black and white labels for  
2 all prescription drugs also is worthy of discussion.  
3 At a 2003 USP-sponsored patient safety stakeholder  
4 forum, there was considerable discussion on the use of  
5 color coding. Ms. Diane Cousins, Vice President of  
6 the USP Center for the Advancement of Patient Safety,  
7 suggested the concept of black and white labels for  
8 all prescription drugs.

9           Black and white labels would include  
10 standard formats and placement of information similar  
11 to the format found on over-the-counter products.

12           Food products also have a standard format  
13 and placement. Black and white labels would create  
14 similarity among products that would force a patient  
15 or healthcare professional to read the label.  
16 Further, the information sought would be easier to  
17 locate in the standardized format as seen on the OTC  
18 and food products.

19           Anesthesiologists have used color coding  
20 by drug class for years in their practice. But this  
21 practice deals only with a limited number of products.

22           Considering the number of products in the  
23 marketplace, an array of distinctive colors would be  
24 next to impossible to achieve. Certain drugs within a  
25 class often have different characteristics,

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1 pharmacologic and pharmaceutic, that could be harmful  
2 based on the clinical condition of the patient.

3 For example, substituting or selecting one  
4 statin for another could result in the administration  
5 of a higher dosing profile and lead to liver toxicity.

6 In closing, USP supports the suggestion  
7 that caution is needed regarding the use of color  
8 coding for pharmaceutical products to prevent  
9 medication errors. And if used, it should be on a  
10 case-by-case basis.

11 USP is very interested in working with  
12 stakeholders to examine how changes in product  
13 labeling, packaging, including colors, and/or  
14 nomenclature could have a positive impact on  
15 medication error prevention.

16 The 2005 UPS Convention will be held later  
17 this week. Among other responsibilities, the  
18 convention members will consider a number of  
19 resolutions that will direct much of USP's activities  
20 from 2005 to 2010. One of the resolutions that will  
21 be considered relates to this issue.

22 If adopted by the convention, two of USP's  
23 expert committees, which consist of scientific experts  
24 in drug packaging and medication error reduction,  
25 along with our staff, would address this issue.

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1 I think you for the opportunity to  
2 participate in this hearing and for your attention.  
3 Thank you.

4 DR. SELIGMAN: Thank you, Dr. Sheinin.

5 Any questions from members of the panel?

6 Carol?

7 CDR. HOLQUIST: You stated that in your  
8 USP forum, that you proposed that black and white  
9 labels be used with a standard format. What data was  
10 used to support that recommendation?

11 DR. SHEININ: I'm not aware if there were  
12 any data. No, there were none. It was just an idea,  
13 a thought that as I indicated, would force people to  
14 look at the labels. I mean personally, from what I  
15 have seen through my career at FDA and now at USP,  
16 many of the errors are caused because the dispenser or  
17 the administrator of the medication is too rushed and  
18 just doesn't look at the label. They rely on other  
19 things.

20 To me the solution is to train them you  
21 have to look at the label and check it. I'm just  
22 speaking for myself now. This is not USP. But  
23 doesn't a nurse, when they come in, check the  
24 patient's band to make sure they have the right  
25 patient? Well, I think it is equally important to

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1 check that they're administering the right drug.

2 DR. CHAMBERS: Of the medication errors  
3 that you mentioned that caused death, one of them was  
4 a difference between oxygen and nitrous oxide. And  
5 that was a plug in. I'm not sure -- unless you can  
6 help me -- where would you put a label in such a case?

7 DR. SHEININ: I guess there could be a  
8 label on the adapter. That situation obviously was  
9 complicated by the fact that the connector was broken.  
10 As you know, the medication gases, medical gases,  
11 when delivered, the connectors are designed so that  
12 only certain male fits a certain female. But it  
13 doesn't always work that way.

14 And I know you've heard and I've heard  
15 over the years of situations where something is  
16 broken or a technician actually forces something in  
17 because they think it's the right connector. But the  
18 connectors certainly could have a label on them as  
19 well as the container has a label.

20 DR. CHAMBERS: I'm just thinking since  
21 most of the errors tend to occur because multiple  
22 safety factors break down and that sounds like what  
23 was going on. I mean not only did it not fit in the  
24 right size, there was a color coding to try and help  
25 it. My guess is there's also a marking of what each

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1 of the two things were on the containers.

2 But in spite of that --

3 DR. SHEININ: Right.

4 DR. CHAMBERS: -- it still wasn't.

5 DR. SHEININ: Exactly.

6 DR. CHAMBERS: But to take away some of  
7 those, I'm not sure would be -- if you were to go to  
8 say all black and white, then we've only got two  
9 safety features as opposed to three. And yet we saw  
10 an error occur even with three.

11 DR. SHEININ: Right. And as I indicated,  
12 there could be color coding on a case-by-case basis.  
13 One of the things that I mentioned was  
14 anesthesiologists using color coding but yet there was  
15 a mixup there with the sufentanyl and the fentanyl.

16 So nothing is failsafe. I think we have  
17 to do everything we can do to try to prevent errors.  
18 I don't think there is any system that will totally  
19 prevent medication errors.

20 DR. CHAMBERS: But do I understand  
21 correctly it's USP's position that some color coding  
22 in limited areas is helpful just not widespread?

23 DR. SHEININ: Right. Yes, we did support  
24 the color coding of the ferrule on concentrated  
25 potassium chloride injection with a black ferrule.

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1 DR. CHAMBERS: Was that the error that you  
2 mentioned that the cause of death was that not the  
3 label of those were -- let me back up. Sorry. The  
4 potassium was not with a black cap at that point in  
5 time?

6 DR. SHEININ: It probably did have a black  
7 cap.

8 Yes, Bob?

9 DR. MEYER: Just following up on that last  
10 comment about the specific sort of, I guess well  
11 demarcated areas where the color coding might be  
12 helpful. Are there any circumstances or other means  
13 that the USP sees that where such instances can be  
14 identified where perhaps some area of practice or some  
15 particular kinds of drugs are sort of ripe for color  
16 coding.

17 DR. SHEININ: Nothing that I can report at  
18 this time. But if that resolution is passed, and I  
19 have every reason to believe it will be, we have a  
20 Safe Medication Use Committee and a Packaging and  
21 Storage Expert Committee that will take that issue up  
22 over the next five years and hopefully make some  
23 recommendations.

24 And we do have the ability to sponsor open  
25 conferences where we can solicit input from the

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1 public, from interested parties. And I would think  
2 that would be one mechanism that we would use to go  
3 forward with that.

4 DR. CHAMBERS: The proposed resolution is  
5 in favor of using color or not in favor of using color  
6 or it looks to examine it?

7 DR. SHEININ: I don't know the exact  
8 language but I believe it goes something along the  
9 lines of USP resolves to look into the situation.  
10 Very few of our resolutions are so pro or con.

11 We did have one which you probably would  
12 be interested in -- maybe not you Wiley, but Bob --  
13 Robert, for this current cycle, there was one  
14 suggesting that we look into the advisability and  
15 feasibility of developing a standardized imprint code  
16 for solid oral dosage forms for poison control centers  
17 and physicians when an elderly patient comes in with a  
18 bottle and dumps it on their desks and says what are  
19 all these things?

20 And it was very heated discussions in a  
21 group that we put together to discuss it with industry  
22 on one side and practitioners on the other side. And  
23 no consensus was ever reached.

24 So I would hope if we go forward with the  
25 color coding issue we could come to some sort of a

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1 consensus.

2 DR. SELIGMAN: Of the 360 cases that you  
3 presented over ten years where color appeared to have  
4 played a role in the medication errors, were there  
5 particular types of drugs or classes of drugs or  
6 features related to the use of color that accounted  
7 for those errors?

8 DR. SHEININ: Not that I'm aware of.  
9 Shawn?

10 MS. BECKER: I think you listed the most  
11 significant drugs that we were seeing, you know the  
12 high alert drugs seemed to be causing the most  
13 problems but I'm not aware of any other color issues.

14 DR. SELIGMAN: Other than the drugs, there  
15 was no particular types of colors or certain features  
16 related to the use of color that may have accounted  
17 for or contributed to the errors?

18 MS. BECKER: I think it's just the  
19 similarity of the colors when products look the same.

20 DR. SELIGMAN: Okay.

21 DR. SHEININ: I'd like to just add one  
22 thing in response to one of your questions to Dr.  
23 Baker previously about matching the presentation of  
24 the innovator. I personally think that's critical.  
25 If at all possible, any generic product should have

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1 packaging and labeling that looks like the innovator's  
2 to avoid medication errors or confusion among the  
3 patients.

4 DR. SELIGMAN: Thank you, Dr. Sheinin.

5 DR. SHEININ: Thank you.

6 DR. SELIGMAN: We are running a little bit  
7 ahead of schedule which is just fine. We'll take a  
8 30-minute break and reconvene at about 9:40. Thank  
9 you.

10 (Whereupon, the foregoing matter  
11 went off the record at 9:13 a.m.  
12 and went back on the record at  
13 9:43 a.m.)

14 DR. SELIGMAN: If you all take a moment  
15 and return to your seats, I'd like to begin again.

16 Our next speaker is Dr. Michael Cohen.  
17 He's the President of the Institute for Safe  
18 Medication Practices. Dr. Cohen?

19 DR. COHEN: Thanks very much. Good  
20 morning everyone. I thought the speakers so far have  
21 done a great job and I appreciate their input  
22 personally as well as for FDA.

23 This is something that's been of interest  
24 to me for quite some time. And I thought what might  
25 be helpful is to perhaps demonstrate some of the

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1 problems that we've have with the application of  
2 color. So I'm going to take the opportunity this  
3 morning to not just answer the questions that have  
4 been posed but also to show, you know, some of the  
5 issues that have arisen over the last 30 years with  
6 the Medication Errors Reporting Program.

7 We work with USP and the Medication Errors  
8 Reporting Program, as Dr. Sheinin mentioned. We also  
9 work with the Pennsylvania Patient Safety Reporting  
10 System in the Commonwealth of Pennsylvania, the  
11 hospitals, surgery centers, and birthing centers.

12 Under Act 13 in our state, it's mandatory  
13 for them to report medication errors to our  
14 organization on behalf of -- which we collect on  
15 behalf of the state's Patient Safety Authority. We  
16 also share our information with FDA and under a  
17 Freedom of Information Act request, we are able to  
18 obtain reports of medication errors as necessary.

19 I just want to define again -- go through  
20 -- I know it was defined a little bit earlier by Dr.  
21 Holquist in the beginning the differences between  
22 color differentiation, color coding, color branding,  
23 and color matching. And I just thought it might be  
24 helpful to say a few words about that and also give an  
25 example of each so that you truly understood.

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1           I have to say that to my knowledge, we  
2 really haven't seen much in the way of color coding of  
3 commercial pharmaceuticals. I suppose that the  
4 potassium chloride concentrate for injection with the  
5 black cap would be considered color coding although  
6 I'm not sure everyone actually knows that when you see  
7 black, that means potassium chloride concentrate  
8 because that's the only parenteral product that is  
9 allowed to have that color or lack of color I should  
10 say.

11           But I'm not familiar with too many other  
12 products. Possibly the dopamine strengths -- at one  
13 time one was orange, one was red, and one was green.  
14 And I believe there was a requirement for dopamine to  
15 identify the strength. I'm not sure how helpful that  
16 was.

17           Outside of that, I'm not real sure if  
18 we're really talking about color coding today or color  
19 differentiation because there really hasn't been much  
20 use of color coding.

21           Color differentiation, I think that can be  
22 very helpful. And I'm going to show you an example or  
23 two. And as we go along, you'll see additional ones.

24           This is to differentiate features, different features  
25 with specific products. It can be used over a long

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1 range of products and some companies have attempted to  
2 do that.

3 But as Dr. Meyers mentioned in his talk,  
4 it becomes very difficult because over a period of  
5 time, additional companies will also come out with  
6 products in similar sized containers, et cetera, which  
7 will have similar colors. And there's really no  
8 controls over that at this point.

9 So color differentiation over a wide array  
10 of products within a manufacturer's line can  
11 occasionally present problems. And I want to show you  
12 some good examples of that.

13 Nevertheless, it can also be helpful in  
14 drawing attention. That is color can draw your eyes  
15 towards important label information. And I'll show  
16 you some examples of that as well as the use of color  
17 to help to differentiate two drugs names that are  
18 similar.

19 This is color differentiation. All the  
20 way over on the right, the pair of products there are  
21 both adrenalin chloride solution. I think when you  
22 look at this carefully, you may be able to see that  
23 there is actually a difference between these two  
24 containers. However, this was not evident to people  
25 working within a hospital when they had to store these

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1 drugs on a crash cart for the emergency room or for  
2 other areas of the hospital.

3 One is for topical application. And the  
4 other one is for injection. And every once in a  
5 while, we would get a report of somebody placing this  
6 in the crash cart instead of the hypodermic. And at  
7 the time, there was widespread use of high-dose  
8 epinephrin, which was the reason for the presence of  
9 these 30 milliliter vials.

10 And so during the code, someone would open  
11 the cart and open the vial. And unfortunately it had  
12 a screw cap and it just delayed application of the  
13 drug.

14 And so many of us communicated with the  
15 manufacturer at the time, Parke-Davis, and they agreed  
16 to help by differentiating the products -- oh, there's  
17 a better one here -- there we go -- by using this  
18 background color. And so immediately people were able  
19 to see the difference.

20 Although I would have liked to have seen  
21 something that would have also drawn attention to the  
22 fact that this was topical because you still couldn't  
23 see the vial inside. However, this really did help.  
24 And I don't recall getting repeated reports of  
25 medication errors once these new drug vials with the

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1 color differentiation reached the user environment.

2 Color matching is a little bit different.

3 This is kind of a blue plug goes into a blue socket.

4 And I know of -- this is a good example of something  
5 that works pretty well in the area of color matching.

6 This is Dr. Jim Broselow who, I notice, is going to  
7 be a speakers later on today, and he has the Broselow  
8 Tape, which is widely used in emergency care.

9 You put a baby, for example, you lay them  
10 out on the tape and you actually measure what color  
11 they are. Once you have that color, you can have a  
12 crash cart, for example, that has drawers that takes  
13 you right to the proper size airway, the proper size  
14 for endotracheal tube, the drugs that would be used in  
15 that length child, et cetera, et cetera. So this is  
16 color matching.

17 You could also use this type of color  
18 matching on a drug label. So you could put the doses  
19 of different drugs for different ages on a drug label.

20 And you'd be able to do that as well. And there's  
21 other ways like dose packs, et cetera, that would  
22 actually match the color.

23 This has been very successful in many  
24 ways. And it's being improved as time goes on and new  
25 applications will be developed.

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1           As far as color coding, this is, as Dr.  
2 Holquist said in the beginning, a very systematic  
3 application of color that really identifies specific  
4 information about the product. The one that I do  
5 know, and I forgot to mention this at first, that was  
6 supposed to be a color coding scheme is the  
7 ophthalmics.

8           And, you know, I think what you'll see and  
9 what you'll hear is what works well in one environment  
10 may not work well in other environments. I know Dr.  
11 Meyers said that as well. And that's really true with  
12 the ophthalmics.

13           As far as the ophthalmologist's office,  
14 great. Tan means an anti-infective, pink anti-  
15 inflammatories, yellow means beta blockers, et cetera,  
16 et cetera. And they're able to take a look at this  
17 color and then use that medication.

18           Probably in the patient's environment, in  
19 their home, that's helpful in differentiating the  
20 different types of ophthalmic products.

21           Take those same products, not just one or  
22 two but scores of specific color within a range and  
23 put that in an ambulatory procedure unit, short  
24 procedure unit, or in a pharmacy, community pharmacy,  
25 where often they may store by drug name, either

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1 generic or brand, or even by drug company, and you  
2 would begin to see that you have dispensing errors,  
3 which is exactly the experience that we've had with  
4 the ophthalmics.

5 And I was unaware that this was going to  
6 happen when these products first reached the market.  
7 We were quite surprised, and we did, in fact, receive  
8 a number of reports of mix-ups.

9 Color coding, research-based evidence  
10 regarding the use of color and reduction of medication  
11 errors, I'm not familiar with. I know there is, in  
12 fact, research going on in two centers right now  
13 looking at color, one in the U.K., one that we're  
14 sponsoring in Texas.

15 And some of the early results do show  
16 that, you know, color coding actually does not help to  
17 prevent medication errors. We'll have to take a look  
18 at that as time goes on.

19 Although color coding may help to  
20 differentiate drug classes, as I said with the  
21 ophthalmics, it may increase intra-class medication  
22 errors.

23 And two I have here, Example 1, color code  
24 by drug class and various drugs within a class may be  
25 confused with one another or a color code by drug and

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1 various strengths or concentrations for that drug may  
2 be confused.

3 This is a color code scheme that is in  
4 wide use in operating rooms. It's kind of faded. The  
5 neuromuscular blockers or muscle relaxants are a much  
6 different color red. They look kind of pink here.  
7 But this is actually used in operating rooms really  
8 around the world, not just in the United States. U.K.  
9 has implemented a process like this as well.

10 And actually we support the use of these  
11 user-applied color-coded labels. You're working  
12 again, as Dr. Myers said, in a small environment  
13 within the OR with people who truly understand the  
14 meanings.

15 I would shudder to think what would happen  
16 if somebody applied these to the critical care drugs  
17 that might be used in the OR environment but are also  
18 used in the intensive care unit, the emergency room,  
19 and out on the med-surg units at the same time without  
20 a true understanding on the part of the health  
21 professional what the meaning of these colors actually  
22 are.

23 And I think that's a big problem We have  
24 not been trained in our nation to identify the  
25 ophthalmic color codes, those of us in pharmacy

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1 school, those of us in medical school.

2 And I think one of the lessons that we  
3 have from that is -- and nursing school -- and I think  
4 one of the lessons that we have from is if you're  
5 going to do anything at all with color coding  
6 commercially, you have an educational campaign to  
7 conduct. People have to really understand what these  
8 colors mean.

9 And they have to understand some of the  
10 problems that are associated with this. You cannot  
11 just do this wholesale without some type of education  
12 being provided. And unfortunately, that is not a real  
13 high-level strategy as far as preventing medication  
14 errors. Education that is.

15 Too often people somehow miss that  
16 education or they don't understand. Or they lose the  
17 knowledge over time.

18 But this is useful in the OR with a small  
19 number of individuals and a small number of drugs in  
20 an enclosed environment. I'd worry about it being  
21 used outside.

22 One of the things that we had hoped  
23 actually to happen, similar to the potassium chloride  
24 concentrate, which has the black cap, and which early  
25 on I actually believed that although it certainly

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1 didn't prevent the errors and people would draw it up  
2 in a syringe and not label the syringe and then, you  
3 know, inject it directly intravenously into a patient  
4 and cause an arrest, it did help to differentiate the  
5 potassium product from all other products.

6 And I do believe that there was a decrease  
7 at least in the number of voluntary reports that we  
8 were receiving. Certainly not scientific by any  
9 means. I'll talk about that later using a voluntary  
10 program to even, you know, indicate in any way what  
11 actually might be happening is very misleading. And  
12 it should never be done in that way.

13 But we did hope that at least we would  
14 have been able to use what we call anesthesia red.  
15 This was an ASTM standard but it would have been used  
16 sparingly on a drug vial. The cap perhaps, a border  
17 around the drug name, but along with other  
18 enhancements like the drug name itself, the strength,  
19 et cetera, et cetera.

20 And I do think because this is a drug that  
21 if it is accidentally mixed up with any other parenteral  
22 product and accidentally given to someone who isn't  
23 intubated, who isn't receiving artificial ventilation  
24 of some type, they're going to stop breathing.  
25 They're going to be totally paralyzed. They're not

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1 even going to be able to tell you that there is a  
2 problem. So it is a real danger.

3 We thought that, you know, applying this  
4 color code which would indicate neuromuscular blockers  
5 would be very valuable. Unfortunately it did not make  
6 it through the entire process over at USP. And at  
7 this point, I understand that it is only going to be  
8 the warning "paralyzing agent." But that might have  
9 been a use for color coding.

10 We know we're supposed to read labels  
11 three times. All healthcare practitioners learn this  
12 when they're dealing with medical products. Certainly  
13 nurses, and pharmacists, and physicians.

14 But unfortunately from time to time, we  
15 have our eyes drawn away by other material. And I use  
16 this slide to show you it ain't just about the color.

17 And, you know, you can test all you want the color.  
18 That is only one variable. And a couple of our  
19 speakers have already mentioned that. It is a single  
20 variable.

21 There are other variables that absolutely  
22 require consideration. On this label, which I think  
23 is very poorly designed and has caused medication  
24 errors, you will see most prominent the drug company  
25 name at the top of the label within a blue band. I

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1 think your eye is drawn to that immediately.

2 You will see possibly in some cases an eye  
3 instead of, you know, well, not instead of anything --  
4 that also, I think, catches your attention. You will  
5 see very small fonts, which are not Helvetica-type  
6 fonts or Sans Serif-type fonts, which are a little bit  
7 more difficult to read.

8 You will see a lot of wording. I think  
9 you will see similar colors within a class and you  
10 would begin to understand how easy it would be for a  
11 nurse or a pharmacist to mix these up in their  
12 practice. And that's exactly what has happened with  
13 these products.

14 So I think an important lesson is to never  
15 rely on a single variable such as color. One must  
16 always take into account the amount and size of text,  
17 the "corporate dress" we call it, including the fonts,  
18 the shape, the size, the logo, the backgrounds that  
19 are used, the manner in which corporate identity is  
20 expressed. Similar strengths is also something that  
21 can be very misleading. And all of this is extremely  
22 important.

23 And we have found in our experience anyway  
24 that the more highly stylized these labels are with  
25 that corporate look, and some of the designs that we

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1 have seen now are just so distracting to me, it's  
2 going to draw attention away from the real purpose and  
3 that is reading the label.

4 And to better understand, this little  
5 experiment is useful. This shows how just one  
6 variable can really confuse things. Nobody would  
7 misunderstand the meaning of each of these words. And  
8 if you were playing cards and somebody said clubs,  
9 diamonds, you'd know exactly what we're talking about.

10 And likewise, I don't think anybody would  
11 misunderstanding this. But what happens is when you  
12 distract people and put two of these variables  
13 together, it becomes very difficult, I think, to read  
14 the label or understand. And it is very misleading.

15 It leads the practitioner in the wrong  
16 direction. It makes it very easy for a medication  
17 error to occur.

18 There's a potential considerations with  
19 color for label, the potential for mix-ups within the  
20 class must be considered. And just to focus a little  
21 bit more on the ophthalmics, this is a category that  
22 has a single antibiotic, a single sulfonamide, and  
23 antibiotic combination with steroid added, and this is  
24 an ophthalmic ointment, this is a solution.

25 Here's the differentiator right there, the

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1 one word and the one word, which is very difficult to  
2 see. And sometimes these are not opened in a  
3 community pharmacy. That's one difference between  
4 community and a hospital. The labeling would be  
5 applied to the outer carton so it might not even be  
6 recognized and the patient would get the wrong dosage  
7 form.

8 This is a combination of just antibiotics.

9 This is a combination of antibiotics in an eye  
10 ointment. And this is another combination of  
11 antibiotics along with a steroid. The combination of  
12 antibiotics and steroid are a little bit darker in  
13 color than the other.

14 This is pretty close to the real world, by  
15 the way. So you can see how easy this color code  
16 scheme would have been mixed up.

17 These are three different beta blockers  
18 that are color coded by the ophthalmic color code  
19 scheme. And I think you can really see here how each  
20 is 0.5 percent. Your eyes are immediately attracted  
21 to the 0.5. That's what you see.

22 You see the drug company name superior to  
23 anything else on the label at the top. You see the  
24 logos, this corporate dress that I speak of. And it's  
25 very difficult immediately to tell the difference

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1 between these.

2 And here's what happens. These do get  
3 stored together by accident sometimes. A technician,  
4 a nurse, will take the container, think she has the  
5 right thing, and then throw it in with all the other  
6 products that, you know, and even though they're not  
7 the same product.

8 When someone else comes by in the pharmacy  
9 and chooses one of those items, they're going by the  
10 drug name but it might be on the outside of a bin that  
11 it is stored in. So they see the name there, they put  
12 their hand in, and it's assured that this is the right  
13 drug. And never actually see the drug name because  
14 they're so misled by the similarity.

15 Here's another example of the ophthalmic  
16 confusion. Again, with very, very highly stylized  
17 labels that probably communicate Ciba Vision better  
18 than vasocidin. And I don't know if that's still on  
19 the market or any of these are. But these are from my  
20 library.

21 So considerations with color on labels,  
22 first of all, I think you absolutely -- if you're  
23 going to do this, I don't care what it is, you have to  
24 have practitioner testing with prototypes. These are  
25 the people that use these. They know their

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1 environments. And it should be tested within their  
2 environment using a failure mode and effects analysis  
3 process.

4 And that can be done fairly easily with  
5 graphics and a questionnaire that drives them to  
6 answer. Will it be 100 percent? Is it scientific?  
7 No. But I don't know that you have to be scientific  
8 with something like this or that you could even be  
9 scientific. There are just so many variables as Dr.  
10 Myers talked about in his opening speech.

11 So you have to consider the environment of  
12 use and work processes. What works well in an  
13 ophthalmologist's office may not in other areas. What  
14 works well in the OR may not. What will it be stored  
15 next to?

16 It depends on how the storage is  
17 accomplished, which is a variable. What other drugs  
18 within the color class might it be confused with? And  
19 many, many questions would have to be asked if this  
20 was done.

21 Most of us are familiar with this process  
22 of failure analysis. How you literally would set up a  
23 process flow diagram and determine what might go  
24 wrong. Now this has been applied to testing products  
25 in the user environment. And it should be something

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1 that's required by FDA.

2 Consider the process flow -- well, I'll  
3 just bypass this because this is -- these are the  
4 kinds of things that you would look at. Not all of  
5 them -- this is not all inclusive. But how things are  
6 ordered, how they reach the inventory, how they're  
7 stored, the light in that environment, you know will  
8 it make one color look like another color, space,  
9 relation to other items, drug delivery, who are the  
10 users going to be, where is this going to be sent, and  
11 so on and so forth.

12 And when I say user environment, what just  
13 looks so perfect on a two-fold blow up of a label on a  
14 flat, you know, table on a piece of paper, when you  
15 put it into the user environment, it can look very,  
16 very different.

17 So here we have on the product on -- a  
18 whole sleeve of products on the left of cefazolin 1  
19 gram and on the right, we have cefazolin 10 gram. And  
20 I turned the vial around so that you could see that.

21 But this is how it might actually be  
22 stored in the user environment. And then name of the  
23 drug is almost cut off. And depending on the height  
24 of the shelf, it would be cut off. And these are the  
25 kinds of considerations that practitioners would need

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1 to make.

2           You have a cover here -- I'm not sure if  
3 this is on the market anymore -- but basically they're  
4 sealed. It says sealed for safety almost obliterates  
5 the readability of this product label. So imagine  
6 that in addition, we also had similar color caps and  
7 labeling, et cetera, et cetera. It would be a  
8 disaster.

9           Here's another problem that we run into  
10 especially with parenterals. The caps pop off. And  
11 they may not stay on. So it can make one product look  
12 like another even if one of them does remain with a  
13 color-coded cap. So that has to be taken into  
14 consideration as well.

15           The Carpuject syringes, they're all green.  
16 How many people would know, taking a look at this  
17 quickly, that on the left is demerol, in the middle is  
18 morphine, on the right is hydromorphone. And there's  
19 quite a difference in the potency of these agents.

20           So, again, you need the practitioners to  
21 put these in the environment in which they're going to  
22 be used. And think about what might be confused. And  
23 it's a very, very useful experiment to see this  
24 happen.

25           People are pretty clever. And they will

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1 show you how you might err -- or what misleading path  
2 you might take.

3 Here's an ophthalmic container that looks  
4 like glucose control solution. For some time, we had  
5 problems with ophthalmic containers that looked like  
6 the Hemocult or Seracult that was used as a guaiac  
7 stool test.

8 And this is a hydrogen peroxide solution  
9 that's rather potent and would be placed in patient's  
10 eyes along with alcohol and it was a very, very  
11 painful experience for the patient. So that has to be  
12 considered as well.

13 You don't know what it's going to be mixed  
14 up with essentially. Here's two other drug vials.  
15 They certainly look alike and one of these gets thrown  
16 in the other bin, I really doubt that a nurse or an  
17 anesthesiologist would pick this up. If it says that  
18 it's enalapril or Vasotec injection is the brand name  
19 for Merck's enalapril, not this one, that it also  
20 looks like pancuronium.

21 I think that would be history.  
22 Pancuronium is a paralyzing agent and probably would  
23 cause someone's death if they weren't intubated. So,  
24 again, you know, we have this situation where the user  
25 environment is a little bit different.

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1                   Here's           partially           turned           vials.  
2           Azatheioptine on the left inamrinone on the right.  
3           Vecuronium,           another           neuromuscular           blocker,  
4           acetazolamide on the right.   Quite frankly, this goes  
5           beyond color coding, color differentiation.   This  
6           should be done, in my opinion, for all products that  
7           are going to be marketed.

8                   I think manufacturers should conduct user  
9           testing.   And be able to present that information to  
10          FDA.

11                   Very specific, unusual colors sometimes  
12          are misleading.   We don't see this color purple very  
13          much.   And we got reports of some mix-ups here because  
14          people got used to that color and thought it was  
15          unusual and that it specified a specific drug.

16                   A similar situation here with these  
17          products.   So you can see what I'm talking about.

18                   Here's one the Department of Defense had a  
19          problem but we had problems all over the country with  
20          this.   This is a different type of color coding.   It's  
21          for a syringe.   And basically I can get a better  
22          picture of this.   Same problem here, different brands.

23                   For many, many years, insulin syringes  
24          were color coded orange.   And then the International  
25          Standards Organization told all the syringe

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1 manufacturers if they want to market their syringes  
2 worldwide, they have to meet their color code  
3 standard. And the color code was by needle gauge, not  
4 what type of syringe.

5 And the needle gauge for 25-gauge was  
6 orange. And what happened was we had this rash of  
7 events that were getting reported to us where the  
8 nurses were confusing tuberculin syringes with insulin  
9 syringes.

10 And what would happen the tuberculin  
11 syringe is a 1-mL syringe and the scale is in tenths  
12 of a milliliter. Except there was no zero in front of  
13 the decimal point. It just said .6. And the nurses  
14 would take a quick look at this and if they needed to  
15 give six units or eight units of insulin, they would  
16 draw it up to the .8 without realizing there was a  
17 decimal point there or a period there.

18 And instead of the patient getting six  
19 units, they would get 60 or eight units, they would  
20 get 80. So this is color coding and the way that it  
21 was applied was just a total shock to the  
22 practitioners. They were never taught about this.  
23 And we had this rash of very, very serious errors.

24 So this is not the way that products  
25 should be introduced if color coding is going to be

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1 used. Please.

2 Now since then, one of the companies at  
3 least has changed the color scheme and it does seem to  
4 -- they have about 80 percent of the market. And it  
5 does seem to have been -- the problem does seem to  
6 have subsided.

7 Consideration with color on labels again,  
8 haphazard application of multiple colors to  
9 differentiate products must be avoided. Again, take  
10 into account the amount and size of text, the  
11 corporate dress, the fonts, the logos, and so on and  
12 so forth.

13 This has been a real disaster, this  
14 particular problem here because it has effected  
15 hundreds of patients. And I'm not sure but I believe  
16 it's still on the market and additionally causing  
17 problems. CDC wrote about this in Morbidity and  
18 Mortality Weekly Report. Several of the state health  
19 departments wrote about this as well.

20 And the problem very simply is nobody  
21 knows what these colors mean. They have no meaning.  
22 And they're very, very difficult to follow or even  
23 differentiate because they're very unusual colors and  
24 not just one but two and three different colors on the  
25 same label in some cases.

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1                   And also, within the circle, total  
2 inconsistency. Here the five means tuberculin units.  
3 Here it means milliliters. Here the number is the  
4 number of doses. I think you can see the problem.

5                   We had over a 100 patients in California  
6 alone that received instead of PPD injected  
7 intradermally, received TD, tetanus and diphtheria  
8 toxoid vaccine because of the mix-up. So when you're  
9 talking 100 patients, that's a lot of different  
10 healthcare practitioners that have made this mix-up.  
11 Then we had flu vaccine given instead of PPD.

12                   We've had these others mixed up. The DoD  
13 actually did send out a warning to their entire -- all  
14 the military hospitals to warn them about this.

15                   Polio virus vaccine confused. Tetanus  
16 toxoid vaccine confused, et cetera. This is bad use  
17 of color coding. And it's exactly what you want to  
18 prevent.

19                   Rocket stripes on -- one manufacturer's  
20 products were very misleading. They all had these  
21 green and blue rocket stripes. And people's eyes were  
22 attracted to that. And if you go back into the data,  
23 you'll see mix-ups between different critical care  
24 drugs.

25                   So this is -- it's very important how this

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1 color is applied. But again, it is not just the  
2 color. There is a lot more that it involves. And as  
3 I said, the fonts, and the position of the color, and  
4 what it draws attention to, and so on and so forth.

5 It should primarily draw attention, in my  
6 opinion, to the drug name and it shouldn't say dose.  
7 It should say strength. But also the amount in the  
8 container, the total amount in the container. And I  
9 think that has occasionally misled people and caused  
10 medication errors.

11 So I think -- this is an example of what  
12 I'm talking about. Here at one point Merck had unit  
13 dose packaging that was black and white. And, you  
14 know, people would read the label and hopefully  
15 differentiate. But a lot of people didn't read the  
16 label. And I think they were fooled by the bar code  
17 and the similarity on the two unit dose packages, et  
18 cetera.

19 One fix was to place a yellow -- color  
20 bands for the different types of drugs. But  
21 unfortunately what they decided to do was color code  
22 it by strength. So your eyes were drawn to the  
23 strength. And it didn't take long for the two 20-  
24 milligram products to be confused.

25 One of the other manufacturers used the

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1 color band to draw attention to whether it was, I  
2 think, sustained-release product or a delayed-release  
3 product in this case. That was Astra Merck.

4 More recently this product was changed to  
5 this product which is now this designation. Not the  
6 same product. This is Singulair.

7 And now we have a problem because the  
8 attention is drawn to the drug name but they don't do  
9 a good job drawing attention to the strength. This is  
10 a four milligram and this is a five milligram. Again,  
11 I think practitioner testing absolutely would have  
12 picked this up before it became a widespread problem.

13 And I know the company is concerned enough to be  
14 working on a third revision now for the unit dose  
15 package.

16 Here's others. Hydroxyzine gentamicin,  
17 thorazine suppositories, compazine suppositories,  
18 compazine pediatric, compazine adult.

19 Here's one of the companies, they actually  
20 used these color code bands internally to identify  
21 products in production before they had the label on  
22 it. And, unfortunately, when these get out on the  
23 nursing units, they make things look exactly alike.  
24 And it's self-serving. It doesn't help the  
25 practitioners avoid errors.

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1           Here's the use of color to draw attention  
2 to only a portion of the important information. That  
3 is the strength per milliliter. What they overlook is  
4 that it is a five-milliliter product or actually 500  
5 milligrams.

6           They did this with other strengths as  
7 well. And I have to say we published an article in  
8 Annals of Emergency Medicine about some deaths with  
9 Ketalar as the result of drawing attention to the  
10 wrong portion of the label. And people thinking the  
11 entire container had 100 milligrams when it didn't.  
12 The entire container had fivefold more than that.

13           This is one that we've had a lot of  
14 problems with. Fortunately one of the manufacturers  
15 decided to eliminate this presentation and has gone to  
16 a drug vial instead. On the left, Methergine, which  
17 is an ergot derivative. On the right -- I'm sorry, on  
18 the top, Brethine (terbutaline), used for totally  
19 opposite purposes in obstetrics.

20           You would find these products in the  
21 delivery room. And if you had somebody that was  
22 having uterine contractions prematurely, they would  
23 probably get Brethine or terbutaline as a tocolytic.  
24 It's an off-label use, I understand, for that.

25           Unfortunately, people were getting

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1 injected with Methergine, which causes uterine  
2 contractions. And this has gone on for quite some  
3 time. And fortunately one of the manufacturers, as I  
4 said, has eliminated.

5 This is color in the packaging, though.  
6 And those little color bands that I talked to you  
7 about that mislead people.

8 Here's color on an OTC product. You  
9 totally overlook the fact that this is benzocaine,  
10 which some patients might be allergic to because you  
11 can certainly see everything else is very, very  
12 similar. So here's they're not drawing attention to  
13 important information.

14 It can be used successfully to  
15 differentiate products, to draw attention to important  
16 information, to enhance recognition of unique letter  
17 characters. So let me show you that.

18 I already did show you this. That  
19 certainly helped to eliminate this problem.

20 We had a problem. This actually was  
21 attacked in a couple of ways. This is a long-standing  
22 problem in medicine where people would order or  
23 dispense the wrong drug. Hydralazine instead of  
24 hydroxyzine. Both are 50-milligram strength.

25 And you can see when a company puts

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1 everything together in the same color patterns  
2 exactly, including the strengths, how easy it would be  
3 to mix these products up especially when other  
4 products within their line are different colors. So  
5 you would certainly think these two blue and orange  
6 ones must be the same thing. This is old though.

7 And this was addressed with "tall man"  
8 letters to differentiate the characters in the drug  
9 name that are unique. We actually have some studies  
10 completed now that show the value of "tall man"  
11 letters in preventing mix-ups between two look-alike  
12 drug names.

13 And the other thing that was done is  
14 reverse print and the use of color to help  
15 differentiate these products. And frankly, I think  
16 this is working pretty well. So that's a good use of  
17 color.

18 Here is another good use of color. On the  
19 left, Doxil. This is a liposomal form of doxorubicin.

20 And the does of this product can be much lower than  
21 the typical doxorubicin product. It should be much  
22 lower. Unfortunately, people didn't know that.

23 And if they would get an order for  
24 doxorubicin and not recognize that this is quite  
25 different as a liposomal injection, and requires a

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1 lower dose, unfortunately they would give this drug  
2 but use the higher dose of the conventional product.

3 And I think one of the things that helped  
4 prevent this was to have a red color band to draw  
5 attention that it must not be substituted and that it  
6 is a lipid-based formulation or a liposomal  
7 formulation.

8 I think they could have done even more  
9 than that but I think that this, along with a lot of  
10 feedback to the field on medication errors that have  
11 happened, has, in fact -- it's been a while since we  
12 actually had an error reported.

13 Here's another great redesign of a  
14 product. They had mix-ups between cisplatin and  
15 carboplatin. And here is the use of color and a stop  
16 sign. It says, stop, verify the dose, drug name and  
17 dose. And this is cisplatin, using color and elevated  
18 font to differentiate this from carboplatin, which the  
19 dose is very, very different. Carboplatin is a much  
20 higher dose than cisplatin.

21 And here as well. And there were other  
22 features for this product as well. And this has  
23 really helped to eliminate this confusion between the  
24 two drugs. So this is another good use of color.

25 Here's the use of color to draw out the

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1 letter characters that are unique. There is  
2 acetazolamide and acetoexamide, an anti-diabetic drug  
3 not used very much any more but still around to my  
4 understanding. And a mix-up there could be fatal, has  
5 been fatal. We know that we had a case in New Jersey  
6 several years ago.

7 And so more recently "tall man" letters  
8 have been applied by FDA but this is an example of how  
9 one of the companies took color to help differentiate  
10 the letter characters. I think that was helpful and  
11 could be used in combination.

12 And has been used in combination for other  
13 trademark issues where we have lookalikes like  
14 Zyprexa, Zyrtec. If you take a look, they use a color  
15 background. They use italics. They use a different  
16 font than the rest of the word.

17 The same thing with Lamictal to reduce  
18 confusion with Lamizol. And I think this can be very  
19 helpful.

20 So final recommendations, practitioner  
21 input, expert analysis also. It's not just  
22 practitioner input. It's gathering the data from the  
23 practitioners and then having an expert panel take a  
24 look at that and perform their own failure analysis  
25 using failure mode and effects analysis methods.

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1 I don't believe that large-scale  
2 scientific studies are needed or would be very  
3 fruitful, you know, in testing these. I don't know  
4 how the heck you'd ever do it as a matter of fact  
5 because of all the variables that you've heard this  
6 morning.

7 I don't think just the practitioner input  
8 or expert analysis alone is going to be enough. I  
9 think the Office of Drug Safety in the Division of  
10 Medication Error and Technical Support must have a  
11 role in this. And they should have the final say as a  
12 matter of fact.

13 I'm a little concerned that some of the  
14 things that get approved by FDA in the divisions  
15 absolutely make no sense. You've seen some of this.

16 And I think it has to go through people  
17 that pay attention to this, that are doing this every  
18 day. And really have a good knowledge. They keep up  
19 with the literature. They see the problems every day.

20 They have the experience. They need to be the ones  
21 that pass judgment on these products before they're  
22 approved.

23 Label consults with ODS I think is  
24 important. Support for error reporting and more rapid  
25 response by FDA for serious problems. We have an

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1 awful lot of good stuff that comes through the  
2 Medication Errors Reporting Program and the FED  
3 MedWatch Program and other programs that are out  
4 there.

5 And people need to be paying attention to  
6 this, looking at it constantly. And I know they are.

7 But then they have to be able to react to it. And I  
8 think they've got to react a little bit quicker.

9 That Methergine/Brethine to me was a  
10 disaster. It's been five or six years until the vials  
11 were available. And people were hurt. And it  
12 continued and continued despite the knowledge that  
13 this was hurting people.

14 I can't understand why it would take so  
15 long for a change like that to be made. And I think  
16 it's an atrocity actually.

17 Support for error reporting is very, very  
18 important. Reserve color coding for high alert drugs  
19 such as insulin, neuromuscular blockers, concentrated  
20 electrolytes but only after testing and feedback about  
21 prototypes.

22 But I have to say, this has to be used  
23 very sparingly. If it's going to be used at all, only  
24 a portion of the package for the color scheme. And it  
25 should not be associated with label information such

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1 that it draws attention away from identifying the drug  
2 and the strength.

3 I would not want to see more than one  
4 product like the neuromuscular blockers using a  
5 specific color that indicates something. And it has  
6 to be associated, again, with education. And I think  
7 the same is true with the other drugs as well.

8 It must be uniform throughout the industry  
9 and not just one company brand although I admit I'm  
10 not really familiar with color branding and what the  
11 implications are.

12 I would hope that's not a situation where  
13 other companies would have to pay a fee to the holder  
14 of the copyright or trademark, whatever it is, and  
15 that they couldn't use it freely or else they couldn't  
16 use it at all. That doesn't make any sense.

17 So I'm not sure about color branding. So  
18 maybe we'll hear a little bit more about that this  
19 afternoon.

20 Understand that actual color code schemes  
21 require simultaneous and ongoing education of health  
22 professionals. Color code for user-applied labels in  
23 anesthesia is well-known to anesthesia. Ophthalmics  
24 to ophthalmologists but not by staff outside the OR.  
25 I think I made that point earlier.

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1 Bar-coding will help. Again, support for  
2 scientific research for the use of color but only when  
3 it's one of several different variables, not by itself  
4 in an isolated healthcare environment.

5 Finally, you know, there is always this  
6 question. I'm on that Drug Safety and Risk Management  
7 Committee and I know that questions came up when we  
8 talked about trademarks. And is there a scientific  
9 way to study whether or not a drug name might be  
10 problematic, et cetera.

11 And I guess some of the components of the  
12 tests that are being used right now like  
13 computerization of the name and matching it with  
14 others in the database are somewhat helpful and  
15 scientific. But keep in mind, too, that something  
16 like this I'm not sure if it could be completely  
17 scientific.

18 I think it's much more related to how  
19 users react with these products in their environment.

20 And they're the experts. They are the ones that are  
21 going to give you the good feedback.

22 And I'm always reminded of this particular  
23 article which appeared in British Medical Journal a  
24 couple of years ago, which the headline was -- or the  
25 title "Parachute use to prevent death and major trauma

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1 related to gravitational challenge -- systematic  
2 review of randomized control trials." And the whole  
3 point here was obviously that nobody has ever required  
4 a scientific study to determine whether or not  
5 parachutes work in preventing death from free-fall yet  
6 it certainly does work and we certainly do use it.

7 And then finally the article by Leape,  
8 Berwick and Bates which discusses what practices will  
9 most improve safety. And they talk about the need --  
10 for patient safety topics specifically, is evidence-  
11 based medicine always required in order to determine  
12 what strategies need to apply?

13 And basically their conclusion was no.  
14 And I think this is a very important article because  
15 they compared it to aviation safety and anesthesia  
16 where small changes have been made all along to  
17 improve the system. And we have had a dramatic  
18 decrease in the number of people that have died in  
19 airplane crashes or from anesthesia incidents yet  
20 there really haven't been scientific studies to  
21 support those changes.

22 And I think that's a very, very similar  
23 situation here with color coding. I think it's  
24 potentially dangerous if it's not done very, very  
25 carefully and reserved very, very carefully for a very

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1 small number of products within a line. I wouldn't do  
2 it across a whole line.

3 Thank you very much.

4 DR. SELIGMAN: Thank you, Dr. Cohen.

5 Do we have questions from the panel?  
6 Wiley?

7 DR. CHAMBERS: Wiley Chambers. Can you  
8 give us an idea of how many colors you think are  
9 potentially usable to distinguish? You put up a slide  
10 of Bausch & Lomb's products at one point and said they  
11 all look the same. They probably have about 300  
12 products.

13 How many colors do you think could  
14 potentially be used to separate those?

15 DR. COHEN: Well, I would absolutely have  
16 been against color coding the ophthalmic products and  
17 using a color code scheme if that's what they believe  
18 it to be. To me it's not a color code scheme.

19 I couldn't tell you what all the different  
20 colors even mean. And there are so many. You see the  
21 problems where colors start to run into one another  
22 and look very similar.

23 DR. CHAMBERS: Well, the other alternative  
24 would be that it is all black and white. Is that what  
25 --

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1 DR. COHEN: I don't think that's the  
2 answer either. I heard that comment a little bit  
3 earlier. And I would respectfully disagree that you  
4 could still have all the labels black and white but  
5 unless you make everything else absolutely identical -  
6 - so in other words, if some had different fonts, and  
7 some had different backgrounds for the strength, and  
8 some had corporate labels, they could all be black and  
9 white.

10 But these are other variables. It's just  
11 as I've shown. Whether it's red or green or black, it  
12 doesn't matter. You're still going to have the same  
13 problem.

14 I have seen lack of color as an effective  
15 way to prevent errors. And I'll tell you how. The  
16 Baxter for many years manufactured and distributed  
17 what they called the Baxter ATC-212 machine. And we  
18 put the tablets and capsules in a wrapper in a machine  
19 and you would get out a whole strip that were printed  
20 exactly the same as one another. They all looked the  
21 same.

22 And the nurses became very, very aware  
23 that the only way to identify this was to look at  
24 color -- to look at the drug name. It was the only  
25 way they could. And so they got used to that. But

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1 everything about those was exactly the same. If a  
2 different manufacturer, a different size, different  
3 fonts, et cetera, et cetera, came in, you know, it  
4 might cause additional problems.

5 DR. CHAMBERS: I guess I'm having trouble  
6 understanding. If you don't think you should be using  
7 color to distinguish between them, you're suggesting  
8 just the words that are used --

9 DR. COHEN: Where I think color is useful  
10 is to differentiate products. So, for example, the  
11 epinephrine vials that I showed you, I thought that  
12 was a very effective use of color to differentiate  
13 products.

14 I also think that, you know, some of the  
15 manufacturers are going to have colors for  
16 differentiating vials. They don't have any meaning.  
17 Unfortunately, without practitioner testing  
18 occasionally, you're going to have one vial look like  
19 another manufacturer's vial of something else.

20 That's the kind of thing that I think  
21 mostly could be picked up by practitioner testing if  
22 it is done right.

23 But on the other hand, I can see, you  
24 know, when you have a wide array of colors, how that  
25 could be problematic with -- not on the other hand,

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1 but, you know, mixing it up with other drugs as well.

2 DR. CHAMBERS: Let me take a step back on  
3 -- you talked about different groups using the package  
4 or having to look at the labels for different reasons.

5 And I'm going to come back to the area of  
6 ophthalmology. If the patients can't read the label  
7 because they can't see well enough to read the label,  
8 why is applying a color cap not a useful endeavor?

9 DR. COHEN: There are reasons. For one  
10 thing, sometimes the color caps are removed and  
11 replaced with another color cap. So if that's what  
12 they're going on, you could have like a green-colored  
13 cap for, I guess, a miotic and a red-colored cap for a  
14 mydriatic and they could get switched.

15 So obviously there could be a container  
16 mix-up. And we've actually had things like that that  
17 have been reported over the years.

18 I suppose that, you know, like I said  
19 color does have some usefulness within the  
20 ophthalmologist's office and within a patient's home.

21 But it is simultaneously causing problems in the  
22 pharmacy and elsewhere.

23 And I think one of the reasons in this  
24 case is that you also didn't take into account -- I  
25 don't mean you but FDA and the manufacturers, the way

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1 that those drug names appear. They're very hard to  
2 read. There's a lot of words.

3 You could have used elevated fonts to make  
4 the drug name, for example. The way that the company  
5 is superior. It's on the top of the container above  
6 anything else. The first thing on that container  
7 should be the drug name. The way the strengths appear  
8 within a red border.

9 What I'm saying is if you gave  
10 practitioners -- or if the company gave practitioners  
11 and experts a chance to look at that, they could point  
12 out these potential problems and suggest changes that  
13 would have prevented problems with the color code  
14 scheme.

15 And that's why I said at the end I don't  
16 know that I could tell you that color coding should  
17 never be used. I found it helpful with potassium  
18 chloride. I think it would have been very helpful in  
19 preventing neuromuscular blocker accidents and that  
20 didn't happen.

21 They're the only -- that and the  
22 ophthalmics are really -- and maybe the dopamine are  
23 the only ones that I know of that have actually been  
24 color coding where they indicate something. The rest  
25 of them are color differentiation.

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1 DR. CHAMBERS: Do you think a patient  
2 safety problem or even efficacy problem would occur if  
3 there was a mix-up between -- you put up timolol,  
4 levobutanol, and betaxolol.

5 DR. COHEN: Yes.

6 DR. CHAMBERS: Would that cause any  
7 difference in patient safety?

8 DR. COHEN: Well, it would to the  
9 pharmacist that dispensed the wrong thing. And that's  
10 the -- see, here's the problem -- and that's another  
11 thing that's not being taken into account.

12 A pharmacist that dispenses the wrong  
13 medication is embarrassed at the least because the  
14 patient comes back and tells him he has the wrong  
15 thing. At the most, they get sued for giving them the  
16 wrong medication.

17 This is a very important thing to  
18 pharmacists and nurses when they make a medication  
19 error. They could lose their job in some states. So  
20 that's the kind of thing, I think, that you have to  
21 also consider when you're -- with the ophthalmic line.

22 That actually can happen.

23 I mean some states are very punitive. And  
24 if an error is reported, or three errors -- we know  
25 that in some states, you could lose your license.

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1 DR. CHAMBERS: Is it --

2 DR. COHEN: And in fact, there are subtle  
3 differences between these drugs perhaps but if you  
4 take it to the extent of neuromuscular blockers,  
5 there's different amounts of histamine released with  
6 these products, there's different durations of  
7 activity, I mean you could have potentially disastrous  
8 results if you mix up the neuromuscular blockers  
9 within that same particular class if it's not done  
10 right.

11 DR. CHAMBERS: Yes, no, and I understand.  
12 And I picked that particular example because I know  
13 those three medications have been tested against one  
14 another and have been shown to be the same in safety  
15 and efficacy.

16 DR. COHEN: So you --

17 DR. CHAMBERS: Now that was a particular  
18 grouping that you happened to have up there that we  
19 have testing on.

20 DR. COHEN: So the ophthalmologists and  
21 possibly to the patients but not to the people who  
22 make the errors.

23 DR. CHAMBERS: Right. And the question  
24 comes down to if the scheme as you were suggesting it  
25 goes through different expert groups to go and figure

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1 out which way to differentiate them, if there are  
2 conflicts between that testing, in other words one may  
3 be more confusing to the pharmacists but less  
4 confusing to the patients, or the other way around, I  
5 guess the question is which way should the FDA be  
6 erring on?

7           Should they be erring on that it is more  
8 important for the patients to be able to  
9 differentiate? Is it more important -- the ideal  
10 situation is that everybody can use it for their  
11 useful purposes.

12           DR. COHEN: Yes.

13           DR. CHAMBERS: But in some cases, we're  
14 going to run into conflicts because we just have too  
15 many and we have to make a choice one way or the  
16 other.

17           DR. COHEN: Yes.

18           DR. CHAMBERS: And I guess I'm asking  
19 which way do we make that choice?

20           DR. COHEN: Well, I can't give you that  
21 answer. Again, without taking into account -- and I  
22 hate to repeat -- but you possibly could use color but  
23 not in the same way that you see it applied right now.

24           And not without considering the corporate  
25 dress, the logos, the fonts, how the drug name is

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1 expressed, the strengths, three of them exactly the  
2 same. All of that has to be taken into account.

3 And if you wanted to keep this color code  
4 scheme, then the rest of that has to be redesigned  
5 because I think that's always going to be a problem  
6 the way it is right now.

7 I've talked to the ophthalmologist group,  
8 I've talked to people at FDA. And they're still out  
9 there. I think they could still cause a problem.

10 CDR. HOLQUIST: You stated earlier that  
11 there have been some studies that show the tall man  
12 letters have been effective.

13 DR. COHEN: Yes.

14 CDR. HOLQUIST: Are you aware of any  
15 studies that have been done to test all these  
16 different variables like the trade dress, the color to  
17 try to pinpoint which is the prime, you know, offender  
18 of the confusion?

19 DR. COHEN: No, I'm not. Not for  
20 appearance. There is this one color code -- a color  
21 study right now that's being completed in the U.K. It  
22 was sent to me by David Cousins from the National  
23 Health Service there. And, you know, it's not  
24 published yet so unfortunately I can't give you a  
25 reference but it does indicate that it's not going to

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1 be that helpful to color differentiate.

2 But that's only one study. I mean there  
3 are others that need to be done. And they only looked  
4 at the use of color itself. They didn't look at all  
5 the other variables. That's important to recognize.

6 CDR. HOLQUIST: You also stated that there  
7 should be experts analysis of this done before it  
8 comes to the Agency. Who would you envision being on  
9 such an expert analysis from the outside?

10 DR. COHEN: I think it is a very similar  
11 thing to the current situation with trademark  
12 analysis. That there are groups that do this type of  
13 work. I suppose, you know, if a company wanted to do  
14 it, they could.

15 But I don't think an internal review like  
16 this would be useful without working with  
17 practitioners that are actually using these products.

18 I think that that has to be a part of it.

19 So I know there are groups that do this  
20 type of testing obviously. That's been going on for  
21 some time.

22 CDR. HOLQUIST: You spoke briefly that  
23 color coding might be helpful with insulin drug  
24 products. And we've seen a number of errors among the  
25 insulin product line. Could you just elaborate a

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1 little bit on that, especially when it comes to  
2 mixtures of insulin products that are coming out now?

3 DR. COHEN: Well, we see a lot of errors  
4 with insulin. And it is a problem. And some of it is  
5 due to the nomenclature. There is some appearance  
6 similarity and the way that, again, the fonts appear  
7 on the label.

8 The mix-ups for the most part seem to be  
9 with the combination insulins. We're getting the  
10 70/30, especially the ones with the very similar name  
11 Humalog -- I'm sorry, NovoLog, Novolin, 70/30, 70/30.

12 With the other manufacturer that we see, Humulin,  
13 Humalog, one is 70/25, the other is 70/30.

14 Mix-ups might be -- and I don't have a way  
15 to, you know, scientifically tell you which has more  
16 errors associated with it. But we do seem to see  
17 confusion between that.

18 And now we're seeing a whole array of new  
19 insulin products reaching the market. It's very, very  
20 difficult for the practitioners to keep up with these.

21 I do note, however, that there has been some  
22 application of color to some of the newer products  
23 like Lantis is a little like a light blue. I don't  
24 know the exact Pantone. And I believe the Humalog  
25 product is a red color, et cetera.

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1           It just that it seems to be the neck of  
2 the vial, the closure, the ferrule, and the cap. And  
3 that's what I meant about very sparing use of the  
4 color.

5           And I'm not sure how far beyond that would  
6 be worthwhile. There are just so many other insulin  
7 products. And a lot of similar names. I don't know.  
8 It would have to be tested.

9           DR. MEYER: I guess just to press that  
10 then, it sounds like what you're asking -- or what  
11 you're perhaps advocating there is more color  
12 differentiation than color coding because the slide  
13 you actually -- I think it referred specifically to  
14 color coding of insulin.

15           DR. COHEN: It is color differentiation  
16 absolutely. You know again, if you asked health care  
17 practitioners, for the most part, I bet you if you  
18 did a little test right now, what does the light blue  
19 mean?

20           They wouldn't be able to tell you. We  
21 haven't done a good job educating people. If we are  
22 color coding, we haven't done a good job with  
23 educating people as to the meanings.

24           CDR. HOLQUIST: Yes, that was another  
25 question I had is that education, you said, was a big

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1 component of this. How would we test to ensure that  
2 the education was an effective campaign?

3 DR. COHEN: Well, it's very difficult. I  
4 mean it has to start at the level of academia.  
5 People need to understand that when they're in school.  
6 And we're not teaching that now. We don't even teach  
7 medication error prevention at this point.

8 So, you know, practitioners come out and  
9 they go into practice, if you're going to have a bunch  
10 of color coding schemes and they don't know what they  
11 mean, that's going to cause more errors than it will  
12 prevent them.

13 So I think it does start with academia.  
14 And, you know, we all have a job to do. We reach the  
15 healthcare practitioners, you do as well. If you were  
16 going to do it, you would have to make that part of a  
17 campaign. Like if you were going to start color  
18 coding the insulins, for example, nurses darn well  
19 better know what these different colors mean if you  
20 really expect it to be color coding and not just color  
21 differentiation.

22 DR. SELIGMAN: Any other questions?  
23 Peter?

24 DR. CARSTENSEN: Dr. Cohen, you mentioned  
25 practitioner testing, I have a background in human

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1 factors but in the device world. And I was wondering  
2 if you could elaborate a bit on what you mean by  
3 practitioner testing. And just to make it a little  
4 easier on you, you know --

5 DR. COHEN: We've done -- at ISMP  
6 personally, we have a division called Med Errors that  
7 does practitioner testing a lot more than I do. The  
8 reason I would do it is if somebody reported a  
9 medication error and they were seeking help, we don't  
10 charge. We will go to the nth degree to help them to  
11 solve a problem with a medication error.

12 And so we have occasionally done them. We  
13 have a large database of healthcare practitioners.  
14 Most of the list of the work that we've done has been  
15 with trademarks and not with graphics although we've  
16 done some graphics as well.

17 We would actually use a process, a failure  
18 mode and effects analysis where we would actually try  
19 to set up where we believe this product might be used  
20 based on the proposed labeling if it was a new drugs  
21 before it was approved. We would work with the  
22 manufacturer and actually scan the product, different  
23 presentations, et cetera.

24 And we would actually send it out to the  
25 field. There would be a questionnaire where we'd ask

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1 a number of questions about who would use it and how  
2 this would be used and in what environment, et cetera,  
3 besides where we thought it would be used.

4 And all this information would be received  
5 back after they would take a look at the label, they  
6 could take it out to the pharmacy and look at the  
7 shelves, all those kinds of things they would be  
8 actually directed to do. What other products might it  
9 be stored near? You know all those kinds of things  
10 would be asked.

11 All that data is received back. You would  
12 have an expert panel that does this kind of stuff all  
13 the time actually look at these responses and come up  
14 with recommendations that would then go back to the  
15 company.

16 And that could be presented to FDA, at  
17 least something there to start with.

18 DR. CARSTENSEN: So it sounds like it is a  
19 controlled study. And you're careful how you -- you  
20 select a range of typical practitioners I would --

21 DR. COHEN: Correct. We've long felt that  
22 this is something, along with the trademark,  
23 practitioner input is critical to, you know, help  
24 guide whether or not that name --

25 DR. CARSTENSEN: Right.

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1 DR. COHEN: -- might be a problem.

2 DR. CARSTENSEN: Well, that's certainly  
3 true in the device world. We call that usability  
4 testing --

5 DR. COHEN: Yes.

6 DR. CARSTENSEN: -- and validation. But  
7 it's a very structured kind of testing done. It  
8 sounds like that's what you have in mind.

9 DR. COHEN: It is. You're under a little  
10 bit different situation, though, that we would be in  
11 that, you know, it's a lot more difficult to change  
12 things post-marketing than it would be for the drug  
13 products.

14 DR. CARSTENSEN: Oh, yes.

15 DR. COHEN: You're encumbered by that  
16 situation. They can't just change a device because  
17 it's been reported as being involved in an error.  
18 They can't force the manufacturer -- you know, if they  
19 did it voluntarily, I guess.

20 But, you know, if we -- and there will be  
21 things that will get through. I don't know that  
22 you're ever going to be -- you've heard other speakers  
23 say that, too -- 100 percent perfect in preventing all  
24 errors. But when they do happen --

25 DR. CARSTENSEN: Yes.

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1 DR. COHEN: -- you have to have a system  
2 to be constantly monitoring that. It probably belongs  
3 in DMETS. And you need to be able to react a little  
4 sooner. That Methergine/Brethine thing is something  
5 that we should all be ashamed of in my mind.

6 DR. CARSTENSEN: I had one other question.  
7 When you mentioned FEMA, I would put that, myself, in  
8 a larger context of risk analysis. FEMA is just one  
9 tool --

10 DR. COHEN: Oh, sure.

11 DR. CARSTENSEN: -- for accomplishing  
12 that.

13 DR. COHEN: I tend to use that. There are  
14 about five or six methods that could be used --

15 DR. CARSTENSEN: Right.

16 DR. COHEN: -- for proactive risk analysis  
17 other than FEMA. And I am aware of that. And one  
18 technique or another would be --

19 DR. CARSTENSEN: Okay.

20 DR. COHEN: -- you know the technique that  
21 I'm most familiar with is FEMA. And it's worked  
22 pretty well.

23 DR. CARSTENSEN: Sure. And I noticed when  
24 you flashed up the ophthalmic containers in the  
25 pastels, I don't know if people are aware but when you

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1 project pastels on a screen like this --

2 DR. COHEN: Right.

3 DR. CARSTENSEN: -- that's not the true  
4 color. They tend to wash out --

5 DR. COHEN: I did mention that --

6 DR. CARSTENSEN: -- on that screen.

7 DR. COHEN: -- with the --

8 DR. CARSTENSEN: Did you?

9 DR. COHEN: -- neuromuscular --

10 DR. CARSTENSEN: Okay.

11 DR. COHEN: -- blocker. Yes, that is  
12 absolutely the case. It's very hard to make it look  
13 like it is.

14 DR. CARSTENSEN: Yes, but I think what I'm  
15 saying is if you see it, the same labeling in real  
16 life, there will be a clearer distinction, I think,  
17 than what happens. What happens when you project  
18 those kinds of --

19 DR. COHEN: Yes.

20 DR. CARSTENSEN: -- pastel colors, they do  
21 tend to wash out.

22 DR. COHEN: Yes. Thank you.

23 DR. SELIGMAN: Our next speaker is Dr.  
24 Mary Ann McElligott. She's from the Regulatory  
25 Affairs from Novo Nordisk. Dr. McElligott?

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1 DR. McELLIGOTT: Okay. Good morning.

2 I would like to begin by identifying  
3 ourselves, our company, as the company that Carol  
4 Holquist discussed this morning. It was the company  
5 that applied for color branding on our insulin analog  
6 products. So maybe we precipitated this meeting, I  
7 don't know.

8 We live in a colorful world. And until  
9 2004 when we received approval to put a color branding  
10 color on our insulin analogs, our insulin analog  
11 labels, as the insulin labels, were not very colorful  
12 at all.

13 And so what I would like to do this  
14 morning is to express our viewpoint on the importance  
15 of the use of color on labels of the class of drugs,  
16 the insulin and insulin analogs. And also to discuss  
17 a little bit about how and why we feel color should be  
18 used.

19 There was discussions early on about color  
20 coding for insulin products that I think some people  
21 this morning alluded to. But still we were in 2004  
22 with no color on those insulin products. So I'll get  
23 into that a little bit and also describe our  
24 experience and why we wanted to put color on our  
25 labeling.

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1 I'll also cover our proposal for using  
2 color branding on the insulin analogs and what we  
3 discussed with FDA in trying to bring this to  
4 approval. And also discuss a little bit about the  
5 potential risks and benefits that we thought about for  
6 use of color in the labeling and packaging of these  
7 insulin analogs.

8 So what was the history of the color for  
9 the insulin products? In the 1990s, and mainly in the  
10 latter half of the 1990s, the International Diabetes  
11 Federation has an insulin task force that was rather  
12 active in discussing with industry, and FDA came to  
13 the table, too, but discussing a code for the human  
14 insulin products and also for the upcoming analogs  
15 that were being developed, the insulin analogs that  
16 were being developed.

17 Several meetings were held and out of  
18 those meetings, there was agreement on -- a color  
19 coding agreement for the human insulins.

20 And that what meant is that the agreement  
21 was for human insulin R, human insulin N, and human  
22 insulin 70/30, each of them would have the same color  
23 no matter what the manufacturer. So if there were  
24 several manufacturers, R would have the same color  
25 across manufacturers.

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1           The color coding scheme was also discussed  
2 for the analog insulins and the first insulin analogs  
3 that were developed were the rapid-acting insulin  
4 analogs.

5           The color schemes that were discussed at  
6 those early meetings in the late 1990s were that the  
7 analogs would have their own separate colors. So a  
8 rapid-acting analog of one company would have one  
9 color. A rapid-acting analog of another company would  
10 have another color. However, IDF had a whole code  
11 listing of the different colors that were being  
12 developed.

13           There were no discussions on any color for  
14 the analog mixtures, which were later developed. But  
15 there were some colors assigned for the human insulin  
16 mixtures.

17           So in 2004 when we started to think about  
18 wanting color on our labels for reasons which I'll get  
19 into in the next few slides, there was no defined plan  
20 or role in ownership of the color code for insulins.  
21 IDF was not actively hosting meetings to determine  
22 color codes for the coming products. And industry and  
23 FDA, we were all sort of on our own.

24           So before I get to what we proposed for  
25 color branding, I would just like to say the

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1 definition of color coding. However, it's been  
2 covered several times before. So I will just sort of  
3 indicate how our proposal for using a brand color on  
4 our insulin analog products is not color coding.

5 So color coding is a systematic standard  
6 of an application of color to aid in the  
7 classification and identification where a color would  
8 be memorized to the function.

9 The color branding that we're talking  
10 about is not the systematic standard application of  
11 color. And the color should not be memorized for that  
12 product. It should just be an aid.

13 Organizational ownership of the standard  
14 code, an example with the human insulins being  
15 discussed, IDF was going to be the organizational  
16 ownership and the color branding that we're talking  
17 about, each manufacturer would just determine on their  
18 own what color they would want to put on their  
19 product.

20 Also with color coding, for it to be  
21 applied properly, there has to be industry-wide  
22 participation and the colors need to be preassigned.  
23 And with color branding, we're not talking about any  
24 such standardized code with preassigned colors that  
25 industry would have to all participate in.

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1           So why in 2004, by the time we got  
2 approval, was there no color on the insulin labels and  
3 packaging? Well, early on, there were insulin  
4 certification regulations in the CFR. And there was a  
5 special Regulation 429.12 that required that black and  
6 white packaging be applied in the case of U-100  
7 insulin.

8           So in May of 1998, there was a Federal  
9 Register notice put out. And in that Federal Register  
10 notice where they were discussing repeal of the  
11 insulin certification requirements, FDA acknowledged  
12 the 429.12 requirement for black and white packaging  
13 and indicated that it did have limited use.

14           And so by September 1998, they did indeed  
15 repeal the 21 CFR 429.12. And so then there was no  
16 further requirement in the CFR for black and white  
17 labeling of the insulin. So that's where we began our  
18 thoughts in our company about how we could go about  
19 trying to get color on our labeling for our insulin  
20 analogs.

21           So we had experience outside the United  
22 States. We sell insulin all around the world for many  
23 years, the human insulins and the insulin analogs.  
24 And the human insulin and the analogs all have colors,  
25 a branding color associated with them. And there were

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1 no issues with the use of color in selling that  
2 insulin all over the world.

3 So based on that experience and in the  
4 United States we had a growing family of Novo Nordisk  
5 insulin products, we had our rapid-acting insulin,  
6 analog-approved, and also a premixed mixture was  
7 approved, and we had more coming on the horizon. And  
8 all of these would be looking pretty similar with the  
9 lack of color.

10 So with these similarities in look, there  
11 is potential for product confusion. And if there is  
12 product confusion, if the wrong medication gets  
13 dispensed, safety concerns are of utmost importance.  
14 And we were experiencing medication errors mainly at  
15 the pharmacy-dispensing level and also package mix-  
16 ups.

17 So this is an example of what we were  
18 dealing with when we sought to apply for use of a  
19 brand color on the label. On the right-hand side is  
20 our rapid-acting analog. It's the packaging for a  
21 pre-filled syringe. It's in a FlexPen, which is a  
22 pre-filled syringe. And on the left we have the  
23 NovoLog Mix 70/30, which is the pre-mixed analog  
24 mixture. It's also in a FlexPen pre-filled syringe.

25 And you also should note the similarity in

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1 brand name, NovoLog and NovoLog Mix 70/30. In initial  
2 discussions with FDA when we were going for approval  
3 of our pre-mixed product, we were interested in  
4 changing the name of the product and FDA was  
5 interested in keeping the parent name of the product  
6 in that mixture. So the names are very similar.

7 And not only are the names very similar,  
8 but when it's in our corporate trade dress, the look  
9 of the labels are extremely similar. So you can sort  
10 of visually see why mix-ups may be occurring.

11 So what we were interested in moving  
12 towards was this type of look, which is our labeling  
13 in the rest of the world. So on the right-hand side,  
14 we have the FlexPen pre-filled syringe labeling for  
15 our NovoLog, which is called NovoRapid in the rest of  
16 the world. And on the left, we have the NovoMix 30,  
17 which is our NovoLog Mix 70/30 product.

18 And both of them you can see are  
19 associated with a brand color. So the NovoRapid has  
20 orange around the name and the NovoMix 30 has blue  
21 around the name. So this was the basic corporate  
22 trade dress that we were interested in trying to  
23 secure in the United States for our products.

24 And this is just an example of how color  
25 can aid in differentiating two similar products. This

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1 is our labeling in Japan. And if you can't read  
2 Japanese like I can't, you can still see that, you  
3 know, seeing the color could help you match it up even  
4 if you can't tell, you know, what words you are  
5 reading.

6 So what was our basic proposal for color  
7 branding of the insulin analogs in our application to  
8 FDA? We basically said that we wanted to just use  
9 color to aid in distinguishing one item from another.

10 We did not want this color to be a substitution for  
11 reading the actual name on the label because that is  
12 the definitive requirement that you really need.

13 We were not seeking a code that would be  
14 systematically applied across the industry to classify  
15 and identify each insulin type. We just wanted to be  
16 able to chose a color for the brand similar to any  
17 other product in any other class. Or even to use it  
18 to distinguish dosage strength. And that color would  
19 be chosen and managed by each manufacturer.

20 And currently color is used in the  
21 industry to aid in brand and dosage strength  
22 differentiation for many products and across many  
23 product types.

24 And this is an example of in our trade  
25 dress, this is our oral anti-diabetic agent mealtime

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1 Prandin. And we have a 2-milligram, 1-milligram, and  
2 a .5-milligram. And we use color on that labeling to  
3 help in distinguishing these dosage strengths.

4 So when we were proceeding to submit an  
5 application to FDA to allow for color on our insulin  
6 analog labeling, we thought about what were the  
7 potential risks of using a color on the packaging.

8 And in the survey of the literature --  
9 that you really can't find too much about the risks of  
10 just the use of color -- however we did come across  
11 discussions on -- that the use of risks are mainly  
12 associated with the application of color coding and  
13 drill down to the inability to distinguish colors or  
14 the colors then become too similar that the different  
15 dosages across the class of drugs are confused.

16 So the other thing that jumped out at us  
17 about color coding is it is not proven to reduce  
18 medication errors as many people have covered this  
19 morning. So a risk may be if several manufacturers  
20 use similar colors.

21 And in the case of insulin analogs, we  
22 felt that if two manufacturers used similar colors,  
23 that use would be mitigated by the obvious differences  
24 in the different corporate trade dress of each --  
25 across the manufacturers. And also there would be

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1 differences in name. So there would be multiple  
2 levels of ways to differentiate these products, not  
3 just on color alone.

4 But one thing we did need to acknowledge  
5 was it is unknown if the use of color branding can  
6 cause errors. And there was really no way to study  
7 it.

8 So what were the potential benefits of  
9 color branding? Color differentiation is favored by  
10 practitioners to help reduce product selection errors  
11 within a manufacturer's product line. And that has  
12 been well discussed by ISMP. However, the biggest  
13 benefit for color branding, we felt, was the potential  
14 to reduce medication errors, although not proven.

15 So what was the essence of why we were  
16 trying to get color branding on the insulin analogs?  
17 We had insulin analog labels without color branding.  
18 There was no color on the label to distinguish the  
19 brand. And we had documented dispensing medication  
20 errors.

21 Along with these documented dispensing  
22 medication errors, we were having an increasing number  
23 of patient safety issues. And they were associated  
24 with this label confusion. So if the patient went  
25 home and was supposed to get NovoLog and got NovoLog

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1 Mix 70/30 instead, with the different pharmacologic  
2 action, there is going to be safety issues.

3 We had marketed Novo Nordisk insulin  
4 labeling with color in 178 countries. And some of  
5 them for many years. So we felt -- and with almost no  
6 issues -- so we felt that we had a good base from  
7 which to propose it for use in the United States.

8 And at the time when we submitted the  
9 supplement in 2003, there was no prohibition in the  
10 CFR to say that you couldn't use color on the insulin  
11 labels. And we did anticipate that the use of color  
12 for the reasons summarized previously would give a  
13 favorable risk/benefit profile for this specific  
14 issue.

15 And on October 8th, after many discussions  
16 with FDA and exchanges of information, we were  
17 approved to use color on the NovoLog Mix 70/30 and  
18 NovoLog labeling and packaging.

19 And this is the visual of what we ended up  
20 with. And as you can see, we did get the use of color  
21 on the label and we also added some differentiation in  
22 the name to help distinguish these two very similar  
23 products. And as somebody mentioned this morning, if  
24 they're on the pharmacy shelves in alphabetical order,  
25 these are definitely going to be next to each other.

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1           So we were very happy that we got the  
2 color on the labeling. And we would like to express  
3 that our position on color on product packaging for  
4 insulins and insulin analogs, we support it to aid in  
5 the identification of insulin and insulin analogs.

6           And further we say that color should be  
7 proposed by each manufacturer and approved as one  
8 variable in -- and as a component of FDA looking at  
9 what the trade dress looks like, distinguishing it,  
10 name, look, and everything else that goes into looking  
11 at how a label differs from a competitor. And what  
12 should be approved when the product is approved.

13           So thank you. And any questions?

14           DR. SELIGMAN: In looking at what you  
15 ultimately were approved to use versus some of the  
16 earlier slides where there were much sort of bolder  
17 graphics to distinguish them, I was curious as to why  
18 you ended up with the latter as opposed to the former.

19           DR. McELLIGOTT: I think it was the basis  
20 of our negotiations. We did try for the initial one  
21 but I think maybe with all good negotiations, you come  
22 to somewhere in between. And that is what we ended up  
23 with. And maybe that's just a first step in maybe  
24 getting to what we have in the rest of the world to  
25 help distinguish.

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1           But we did succeed in getting color to  
2 help aid in the differentiations. So that's a good  
3 first step.

4           DR. SELIGMAN: Other questions? Wiley?

5           DR. CHAMBERS: If you do additional  
6 insulin products, are you looking to add different  
7 colors to additional products?

8           DR. McELLAGOTT: Yes, with each new  
9 product coming, we would -- when we submit our new  
10 drug application, we would put our color proposal in  
11 there for that product.

12          DR. CHAMBERS: Have you looked forward to  
13 try and plan how many colors you think you ultimately  
14 can use and still be able to distinguish?

15          DR. McELLAGOTT: Well, some of the newer  
16 products wouldn't have the same name. So they  
17 wouldn't be as confused. They would maybe be further  
18 away on the pharmacy shelves. So we wouldn't  
19 necessarily have to distinguish so carefully with each  
20 new product.

21           But we would just be looking to using a  
22 color just like with any other drug product and drug  
23 brand, as you're developing your brand, you think  
24 about a color that embodies your brand and you use  
25 that on your labeling.

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1 DR. CHAMBERS: So potentially you would  
2 use that same stripe for an entirely different  
3 product?

4 DR. McELLIGOTT: Well, that would be part  
5 of the discussion since that was the initial approval  
6 for just that stripe with the different colors. So  
7 the third product we would have, the discussion would  
8 have to be the color could either go as that stripe or  
9 could we then move to what we proposed similar to the  
10 European labeling.

11 DR. CHAMBERS: Ultimately you believe that  
12 your European configuration is a more distinguishable  
13 configuration than what you're currently using in the  
14 United States?

15 DR. McELLIGOTT: It appears to us and also  
16 that's our trade dress all around the world for each  
17 product, we have the same dress. And then we use the  
18 color to help distinguish our products within our  
19 product range.

20 DR. CHAMBERS: have you thought of a  
21 scientific way to show that one is necessarily better  
22 than the other? I mean you basically have the  
23 opportunity of having two different formats. You  
24 could potentially compare them and collect information  
25 about whether one is better than another.

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1           Although it's different parts of the  
2 world, but I'm wondering if you've ever tried doing  
3 that kind of comparison to provide that type of  
4 information?

5           DR. McELLIGOTT: Well, early on when we  
6 were proposing that we wanted to utilize color on the  
7 labeling to help with the NovoLog/NovoLog Mix mix-ups,  
8 we did look at our error rates in the rest of the  
9 world compared to the United States for dispensing  
10 errors and package mix-ups.

11           And if you consider that we sell more in  
12 the rest of the world than here, we had extremely rare  
13 any of those reports compared to the United States  
14 where the reports were mounting.

15           CDR. HOLQUIST: Do you think that limited  
16 number of reports is attributed to the fact that not  
17 most of the rest of the world actually collects data  
18 on medication errors at this point in time? And that  
19 it is just becoming a new thing in Europe?

20           DR. McELLIGOTT: That is one of the  
21 factors. But we did restrict it to not way far back  
22 in history but much more current reporting numbers.

23           CDR. HOLQUIST: You stated that with the  
24 color branding, it's going to be something that's  
25 company specific. What agreements do you have in

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1 place that will help alleviate similar colors being  
2 used from another manufacturer for the same type of  
3 drug product when they want to introduce color  
4 branding on their products?

5 DR. McELLIGOTT: Well, we weren't  
6 suggesting that there needed to be that kind of  
7 control over it. Just as we saw earlier this morning,  
8 that there are several manufacturers come up with  
9 similar colors for other type drugs.

10 And then when they see that it is out on  
11 the market that way, they analyze should they change  
12 the color. And that sometimes even contact the  
13 manufacturer and discuss changing the color. That was  
14 all we would be interested in doing. Nothing further.

15 CDR. HOLQUIST: Do you have plans on  
16 introducing the IDF color scheme into the United  
17 States for your Humulin products? And do you see that  
18 as posing a risk for something that has a definite  
19 meaning with a particular color to what you're trying  
20 to use with color branding?

21 DR. McELLIGOTT: Well, at this point, we  
22 haven't thought about the color on the insulin labels  
23 itself. That may come in due time. But, you know, I  
24 just can't comment at this time because we haven't  
25 made a proposal to put the colors on those insulin

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1 products.

2 DR. SELIGMAN: Any more questions?

3 DR. CARSTENSEN: I'd be interested in  
4 hearing -- what you did in terms of validating the  
5 scheme, did you use pharmacists outside your own  
6 company to help validate your scheme?

7 DR. McELLIGOTT: For -- when we --

8 DR. CARSTENSEN: When you added --

9 DR. McELLIGOTT: -- developed --

10 DR. CARSTENSEN: -- color.

11 DR. McELLIGOTT: -- our corporate trade  
12 dress?

13 DR. CARSTENSEN: Right.

14 DR. McELLIGOTT: We did do focus groups to  
15 see how our trade dress played with the various  
16 customer groups.

17 DR. CARSTENSEN: And how do you define a  
18 focus group?

19 DR. McELLIGOTT: I think we had many  
20 different focus groups, the different levels, the  
21 customers, the nurses, the doctors.

22 DR. CARSTENSEN: You had a bunch of people  
23 in a room simultaneously and you queried them? Is  
24 that what you mean by a focus group?

25 DR. McELLIGOTT: I don't remember how the

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1 -- I think our trade dress has been in play about  
2 three or four years and I don't remember how we went  
3 about doing the focus groups exactly.

4 But I do remember that as the new look was  
5 being developed, there were definite focus groups to  
6 see which new look -- how the new look played against  
7 other looks. And that's why this look was selected.

8 DR. CARSTENSEN: Okay.

9 DR. SELIGMAN: Thank you very much.

10 CDR. HOLQUIST: When you showed your slide  
11 with the insulin pen, both the pens were actually blue  
12 in color and the color at the tip were the only like  
13 differentiating factors.

14 Have you experienced, like they do in the  
15 ophthalmologic world where patients will just refer to  
16 the color of like the pen that they're using? Like I  
17 use the blue insulin pen?

18 And if so, do you envision if another  
19 company uses that particular color for some other  
20 branding, do you anticipate confusion among different  
21 product lines that use the same type of device?

22 DR. McELLIGOTT: Are you saying that the  
23 people are confusing the navy blue of the pen or the  
24 color of the --

25 CDR. HOLQUIST: The navy blue of the pen

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1 because often times those things will be taken out of  
2 the carton that has more color on it and they'll just  
3 rely on what's on the actual container label, which  
4 would be the pen in that case.

5 DR. McELLIGOTT: Yes, well I think on the  
6 pen label, as I showed with that stripe on the outside  
7 of the box, that stripe is also on the label on the  
8 pen. Right.

9 DR. SELIGMAN: Thank you very much.

10 DR. McELLIGOTT: Thank you.

11 DR. SELIGMAN: Our next speaker is Dr.  
12 Joseph Cranston from the American Medication  
13 Association. Dr. Cranston?

14 DR. CRANSTON: Good morning. My name is  
15 Joseph Cranston. And I'm a pharmacologist by  
16 training. And I currently serve as the Director of  
17 Science, Research, and Technology at the American  
18 Medical Association. And I'm speaking here today at  
19 this Part 15 hearing as an official representative of  
20 the AMA.

21 First of all, the AMA commends the FDA for  
22 holding this hearing to determine the benefits and  
23 potential drawbacks of applying color to drug  
24 packaging and labeling as a means to identify,  
25 classify, or differentiate drug products, and to

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1 prevent medication errors.

2 The AMA's Council on Scientific Affairs,  
3 hereafter to be referred to as the Council, presented  
4 a report at the AMA's annual meeting in June 2004  
5 titled "The Role of Color Coding in Medication Error  
6 Reduction."

7 The recommendations of that report were  
8 adopted by our House of Delegates, which is our  
9 policymaking body. I was the staff author of the  
10 report.

11 The FDA cited this Council report in the  
12 Federal Register notice for today's meeting. And my  
13 comments today will discuss the major findings of the  
14 report and its recommendations.

15 The Council report only addresses color  
16 coding, which has been defined earlier today and in  
17 our report we use the ISMP definition as the  
18 systematic standard application of a color system to  
19 aid in the classification and identification of drug  
20 products. A color coding system allows people to  
21 memorize a color and match it to its function.

22 The Council report evaluates current  
23 evidence on whether color coding reduces medication  
24 errors. The report includes results of a literature  
25 review and discussions with experts in the field.

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1           The Council found that currently there are  
2 three widely-used color coding systems for  
3 pharmaceutical products that are intended to reduce  
4 medication errors.

5           First, as already mentioned today, the USP  
6 black-cap packaging requirements for potassium  
7 chloride for injection concentrate.

8           Second, also as already mentioned today,  
9 the American Academy of Ophthalmology's uniform color  
10 coding system for caps and labels of commercially-  
11 available topical ocular medications, a color coding  
12 system that is supported by the FDA, at least in one  
13 of its Agency guidance documents.

14           And thirdly, the ASTM Standard D4774-94  
15 for color coding of user applied, not commercially  
16 available, user-applied syringe labels in  
17 anesthesiology. This ASTM standard, which is  
18 supported by the anesthesiology community, assigns a  
19 specific color to each class of anesthetic drugs. For  
20 example, induction agents.

21           Anesthesiologists affix the appropriate  
22 colored labels to syringes containing the appropriate  
23 medication prior to surgery. These user-applied color  
24 labels on syringes are intended to provide visual  
25 queues during surgery so there will be a reduced risk

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1 of inter-class drug errors due to accidental syringe  
2 swapping.

3 Each of these color coding systems appears  
4 to enjoy strong support from health professionals such  
5 as ophthalmologists and anesthesiologists. However,  
6 based on the Council's literature review, published  
7 scientific evidence that shows that color coding  
8 reduces medication errors is extremely limited. And  
9 for the most part, anecdotal.

10 Based on volunteer reports to the UPS-ISMP  
11 Medication Error Reporting Program, elimination of  
12 fatalities due to mix-ups between sodium chloride 0.9  
13 percent injection and potassium chloride for injection  
14 concentrate were observed after black caps were  
15 required on the vials of the latter product. This  
16 observation suggested the color coding had a positive  
17 effect on reducing medication errors with these  
18 products.

19 However, deaths due to accidental  
20 concentrated potassium chloride injections still  
21 occur. Thus medication safety experts such as the  
22 ISMP also recommend restricting the availability of  
23 potassium chloride for injection concentrate products  
24 in clinical areas.

25 Prior to the implementation of the AAO's

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1 color coding system for commercially-available topical  
2 ophthalmics, there were documented cases of serious  
3 adverse events resulting from patient difficulty in  
4 distinguishing between various ocular medications.

5 However, the Council could not identify  
6 any published scientific studies that evaluated  
7 whether this color coding system has led to a  
8 reduction in medication errors.

9 On the other hand, as Dr. Cohen already  
10 pointed out this morning, the USP-ISMP Medication  
11 Error Reporting Program has received reports of intra-  
12 class medication errors with topical ocular  
13 medications. For example, mix-ups between  
14 cyclopentolate hydrochloride 1 percent and tropicamide  
15 1 percent solutions have been reported.

16 And as Mike suggested earlier today, while  
17 the AAO's color coding system may work well in  
18 physician offices and in patients' homes, the  
19 potential for error could increase in pharmacies and  
20 in nursing units where product packages with similar  
21 colors, logos, fonts, and sizes are placed next to one  
22 another.

23 The Council identified one reasonably well  
24 designed scientific study that attempted to determine  
25 whether the color coding system for user-applied

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1 syringe drug labels in anesthesiology actually reduces  
2 medication errors. Fasting and Gisvold analyzed  
3 inter-operative problems related to anesthesia,  
4 including medication errors, that were prospectively  
5 recorded for over 55,000 procedures during a 36-month  
6 period in a 970-bed hospital in Norway.

7 After the first 18 months, the  
8 anesthesiology department implemented color-coded  
9 syringe labels according to ASTM Standard D4774-94 and  
10 also had educational meetings and audits that focused  
11 on medication errors.

12 The investigators observed a 37 percent  
13 decrease in medication errors after the intervention.

14 However, this was not statistically significant  
15 because the total number of medication errors in the  
16 study was extremely small, about 0.1 percent. Also,  
17 differences in the number of syringe swaps before and  
18 after the introduction of color-coded syringes was not  
19 statistically significant.

20 The authors concluded that syringe swaps  
21 were not eliminated by color coding and suggested  
22 color alone may not be sufficiently strong as a visual  
23 queue to eliminate errors.

24 Thus, based on the Council's literature  
25 review, there clearly is a lack of published evidence

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1 that proves color coding reduces medication errors.

2 The Council also contacted individual  
3 experts from a number of key organizations involved in  
4 medication error prevention, including the American  
5 Society of Health System Pharmacists, the ISMP, USP,  
6 FDA, and PhRMA.

7 All recommended caution in the application  
8 of color coding systems in some organizations. As was  
9 pointed out by Dr. Myers earlier today, the AHP  
10 opposes reliance on color coding to identify drug  
11 products.

12 Some of the potential problems with color  
13 coding that were identified included the following.  
14 And some of these have already been shown today.

15 There's a limit in the number of  
16 discernible colors available for commercial use.

17 Subtle distinctions in color are poorly  
18 discernible unless products are truly adjacent to one  
19 another.

20 As previously noted, color coding of drug  
21 classes can increase the chance of intra-class  
22 medication errors.

23 Colors may fade when exposed to light.

24 It is not always possible to exactly  
25 reproduce Pantone colors from batch to batch.

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1                   Approximately eight percent of men and  
2 less than one percent of women have some difficulty  
3 with color vision.

4                   Color coding can be error-prone if it is  
5 not applied consistently across the industry or within  
6 a single manufacturer's product line.

7                   Physician and other health professionals  
8 may be unable to remember large or multiple color  
9 coding systems.

10                  And finally, color coding may offer a  
11 false sense of security and in some instances, result  
12 in failure of the physician or other health  
13 professionals to, in fact, read the label.

14                  So based on its literature review and  
15 discussions with experts in the field, the Council put  
16 forth two key recommendations in its report that were  
17 adopted by the AMA's House of Delegates.

18                  First, the AMA recommends that the FDA,  
19 and the USP, and the pharmaceutical industry that  
20 color coding of commercially-available pharmaceutical  
21 products for the purpose of preventing medication  
22 errors be considered cautiously and on a case-by-case  
23 basis.

24                  And secondly, the AMA encourages further  
25 research on the effectiveness or lack thereof of color

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1 coding of pharmaceutical products to reduce medication  
2 errors.

3 Thank you.

4 DR. SELIGMAN: Thank you, Dr. Cranston.

5 Do we have any questions? Members of the  
6 panel?

7 DR. CHAMBERS: Wiley Chambers. Does the  
8 AMA have suggestions on how the research would be  
9 conducted?

10 DR. CRANSTON: No, frankly.

11 (Laughter.)

12 DR. CRANSTON: On a personal note, I mean  
13 I would agree with Dr. Cohen that the more important  
14 thing, I think, is at least with color differentiation  
15 and even with color coding is to do the studies up  
16 front, you know, failure mode and effects analysis and  
17 so forth, to ensure before the product is ever  
18 marketed, you know, that there is some comfort that  
19 what's been selected is going to work.

20 DR. CHAMBERS: I think the question comes  
21 down to there are a number of different constituent  
22 groups and there's no immediately obvious way to  
23 conduct that either prior to or after approval. And  
24 there is -- if there are conflicting results between  
25 the different groups, deciding which groups carries

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1 more weight is not an easy thing.

2 DR. CRANSTON: I appreciate your problem.

3 (Laughter.)

4 DR. CRANSTON: I don't know how to solve  
5 it. I mean we may get calls tomorrow, you know, from  
6 the ophthalmologists and the anesthesiologists that  
7 they didn't like our presentation. I mean this is the  
8 evidence we came up with.

9 DR. CHAMBERS: Thank you.

10 DR. SELIGMAN: Thank you very much, Dr.  
11 Cranston.

12 Our next presenter is Dr. James Broselow.  
13 Dr. Broselow, are you here? If he is not, we'll move  
14 on to the next presentation and come back to Dr.  
15 Broselow when he returns.

16 Dr. Frank Kyle from the American Dental  
17 Association. And I believe I have your presentation  
18 here.

19 DR. KYLE: Thank you.

20 My name is Frank Kyle. I'm a dentist. I  
21 work for the American Dental Association in the  
22 Washington, D.C. office. I'm a Manager of Legislative  
23 and Regulatory Affairs.

24 And I'm here this morning representing our  
25 Council on Scientific Affairs, pretty much at the

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1 invitation of the Food and Drug Administration, to  
2 talk about our limited experience with color coding  
3 for dental anesthetic cartridges.

4 I think if any of you have been to a  
5 dental office, you're very familiar with the dental  
6 anesthetic cartridge. I think it is a fairly unique  
7 delivery system for dentistry. I'm not sure of other  
8 practitioners that use that particular mode of  
9 administering anesthetic.

10 Let me just say a little bit about the  
11 American Dental Association to start with and our Seal  
12 of Acceptance. The ADA is a member organization. It  
13 has about 152,000 members. That represents about 72  
14 percent of the dentists in the United States.

15 We have long sought to promote dental  
16 product safety and effectiveness and our Seal of  
17 Acceptance has become well recognized among consumers  
18 and the dental professionals as a measure of that  
19 safety and effectiveness.

20 We -- the ADA that is -- issued the first  
21 Seal of Acceptance in 1931. It is strictly voluntary,  
22 however, there are more than 300 countries that  
23 participate in the Seal Program. There are about  
24 1,100 products that carry the Seal of Acceptance. And  
25 I'm sure if you've been to any grocery store or

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1 pharmacy, you've seen the Seal on toothpaste,  
2 mouthwashes, et cetera.

3 About 40 percent of the Seal of Acceptance  
4 programs are consumer products such as toothpaste and  
5 so on. The rest are, of course, materials that are  
6 basically marketed or provided to the profession such  
7 as restoratives, antibiotics, and dental anesthetic  
8 cartridges.

9 In the early 1990s, the ADA House of  
10 Delegates, again our governing body, passed several  
11 resolutions directing that the Association help  
12 develop a uniform color coding system for local  
13 anesthetic cartridges.

14 The idea behind this was to provide an  
15 extra safety factor complementing the need to read the  
16 cartridge label, which could be difficult because of  
17 the size. I'm sure you're familiar with that small  
18 1.0 cc cartridge. Furthermore, it was found that in  
19 some instances, the cartridge label could become worn  
20 off from handling.

21 So to further this process, the Council on  
22 Scientific Affairs held several meetings with  
23 manufacturers of ADA-accepted local anesthetics to  
24 develop and finalize a code. In addition, there is a  
25 Standards Committee on dental products that provided

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1 input into this process.

2 The manufacturers, in general, were very  
3 supportive of the ADA's efforts in developing the  
4 color coding system due to their concern about  
5 possible confusion due to conflicting color schemes  
6 and agreed on a format for a color code: a color band  
7 a specific distance from the plunger-end of the  
8 cartridge, black lettering for all labeling on the  
9 cartridge, and a time period for implementation.

10 This is basically the color code scheme or  
11 the labeling scheme that is used on the dental  
12 cartridges. As you can see, there is a color code  
13 band specified a specific distance from the end.  
14 There is a specific color scheme given to the  
15 particular type of anesthetic and I'll show you that  
16 in just a moment.

17 There's the stopper -- the stopper is an  
18 orange rubber stopper and it's not designed to be used  
19 as an indicator of color code. The lettering is  
20 spelled out. And it should be durable so that it is  
21 not easily worn off in handling.

22 Basically there are three types of  
23 lidocaine that are used in dentistry. And these are  
24 the three color codes that are assigned to the  
25 lidocaine. A couple of mepivacaine concentrations

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1 that are commonly used. A couple of prilocaine  
2 concentrations that are commonly used. And then two  
3 other additional long-lasting anesthetics that are  
4 frequently used.

5 The color coding format, as agreed to by  
6 manufacturers, was approved by the Council on  
7 Scientific Affairs in 2002. And became part of our  
8 ADA Seal Program in 2003. So we just have a few years  
9 experience with it.

10 All of the participants, that is,  
11 manufacturing participants in the ADA Seal Program  
12 currently comply with this system. That includes  
13 about 80 percent of the market for local anesthetic in  
14 the United States.

15 The Association is not aware of any  
16 reports of error as the result of the implementation  
17 of this color code system. I must say, however, that  
18 I don't know that the Association had any particular  
19 experience with error reporting prior to the  
20 initiation of this color coding system.

21 And finally, the ADA color coding system  
22 has been presented to the ISO for inclusion as an  
23 international standard for dental and local  
24 anesthetics and that was done in 2003.

25 And that completes my comments.

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1 DR. SELIGMAN: Thank you, Dr. Kyle.

2 Any questions, comments from the panel?

3 Carol?

4 CDR. HOLQUIST: Just one comment. We  
5 actually did get a report of confusion of someone  
6 picking out the wrong syringe. And I think it was the  
7 blue color that's used for the mepivacaine because  
8 it's like two blues that you use in that same color  
9 scheme.

10 I don't think it was administered to the  
11 patient. It was caught prior to administration.

12 DR. KYLE: Again, I don't know that we  
13 would necessarily get that kind of information. You  
14 would probably be the recipient of that information  
15 more than we would be.

16 Let me just also add -- I forgot to  
17 mention in my comments that one side effect, if you  
18 will, or one benefit of this system is it does assist  
19 the support staff of the dentist to order cartridges.

20 Like they can easily when they're running low on a  
21 particular concentration or branding or whatever that  
22 they might want to keep in supply.

23 DR. CHAMBERS: Does the ADA have any plans  
24 to either conduct a response or any kind of testing to  
25 look at the utility of this system?

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1 DR. KYLE: None that I am aware of.

2 CDR. HOLQUIST: And do you foresee the  
3 introduction of many other products within that color  
4 scheme?

5 DR. KYLE: You know that's a good  
6 question. And I'm afraid I don't know the answer to  
7 that. I would basically assume that these were the  
8 products in place in the early 2000s when the system  
9 was put into place. I don't know of any new advances  
10 in local anesthetic.

11 My guess is that if such a new product  
12 were developed, they would again meet with the  
13 standards group and determine a color code for that  
14 new class or new category of anesthetic. But I'm not  
15 aware of any that have been introduced. And I don't  
16 know exactly the procedure that will be done.

17 CDR. HOLQUIST: In your practice setting,  
18 is it that all of these cartridges are just laid out  
19 on the tray? Or are they already loaded into the --

20 DR. KYLE: In my experience, and I suspect  
21 this is true for most practitioners, they have a  
22 limited assortment. They wouldn't necessarily have  
23 all eight or ten in their own offices. They would  
24 have their favorite ones, probably two or three maybe  
25 with some short-acting and some long-acting and that

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1 sort of thing.

2 Generally speaking, depending on the  
3 procedure set up for that or that patient's particular  
4 treatment diagnosis, they would know whether they  
5 would want a short-, or a medium-, or a long-acting  
6 anesthetic.

7 And probably the doctor's preference is  
8 well known to the assistant and she just puts -- he or  
9 she puts out the cartridge appropriate to that, maybe  
10 a couple of them, that sort of thing.

11 So there's probably only one or two on the  
12 treatment tray at any given time. If you needed, you  
13 know again, for instance an oral surgery procedure,  
14 they might do moderately acting anesthetic to start  
15 the procedure, to do say the extraction, and then give  
16 a long-acting anesthetic at the end of the procedure  
17 to tide the patient over until the full effect of  
18 their analgesics might kick in.

19 So there might be two different ones. But  
20 you wouldn't have probably more than a couple on a  
21 tray at any one time.

22 DR. CHAMBERS: Are there any other color  
23 schemes used for any other ADA --

24 DR. KYLE: None that I'm aware of. And  
25 none that the Council of Scientific Affairs identified

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1 for me.

2 DR. CHAMBERS: Okay. And I take it from  
3 your earlier statement, there are no plans to expand  
4 beyond the anesthetic?

5 DR. KYLE: None that I'm aware of. Again,  
6 this is -- we're very much a provider-driven  
7 organization. So if the dentists came to us and said  
8 we would really like to see a restorative material  
9 color system, then they would probably take a look at  
10 that. But I don't think there are any plans to do  
11 that.

12 DR. CHAMBERS: Thank you.

13 DR. SELIGMAN: Thank you, Dr. Kyle.

14 Dr. Jensen, Dr. Allan Jensen from the  
15 American Academy of Ophthalmology.

16 DR. JENSEN: Thanks. Thank you very much.  
17 I am Allan Jensen. I'm a practicing ophthalmologist.  
18 I actually see patients in the City of Baltimore.  
19 And I'm past President of the American Academy of  
20 Ophthalmology. And I appreciate all of the previous  
21 references. We also appreciate the invitation to  
22 address the hearing.

23 A number of points, first of all, we've  
24 been successfully using a color coding system for over  
25 20 years. We have no science to prove that it is

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1 helpful. We do think it's been a safety feature for  
2 our patients and for our doctors. But again, we have  
3 no science and I don't know of any scientific studies  
4 that show that.

5 I would like to agree with the previous  
6 speakers that color coding is not the major answer.  
7 It is certainly necessary to read the label.

8 And as someone seeing patients mostly of  
9 Medicare age, some with poor vision, I certainly  
10 agree, again, that we should have large labels  
11 although it is hard to put a large label on an eyedrop  
12 bottle. We should use good contrast. Black and white  
13 is much better than gray on maroon or maroon on gray.

14 And there should be some uniformity in the labeling  
15 of these drugs.

16 In ophthalmology, we are unique because  
17 all the drops look the same. We don't have different  
18 colored pills and different shaped pills. All the  
19 drops are tiny and round and either clear or usually  
20 white.

21 We continue to endorse a system -- a  
22 uniform color coding system for topical ocular  
23 medications, again, as we have for over 20 years.  
24 Many of our patients are partially sighted and  
25 elderly. And they are especially susceptible to

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1 accidental installation of the incorrect eyedrops.  
2 The uniform color coding system will help patients and  
3 doctors distinguish amongst eye medications.

4           You should be aware, and I know you are,  
5 many of our patients after surgery are taking three or  
6 four different drops. And to be perfectly honest,  
7 they don't say I'm taking my Ocuflox and my  
8 prednisolone, and my levalbuterol.

9           They say -- and we ask are you taking the  
10 tan drop and the red drop and the pink drop. And even  
11 very intelligent patients, if they're only taking them  
12 for three or four weeks, find it much more easy to  
13 talk about the color of the bottle rather than the  
14 exact name of the drop.

15           And when I start my practice each day, I  
16 have five or six bottles lined up. And some are  
17 dilating drops. Some are anesthetics. Some are  
18 glaucoma drops. And I'll certainly identify them at  
19 the beginning of the day.

20           But when I see 30 patients a day, I don't  
21 look at the label each time I put the drop in. I've  
22 done that at the beginning of the day. And after  
23 that, I identify them by the color of the bottle.

24           This system was originally initiated after  
25 we, at the Academy, received reports and we received

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1 reports from the National Registry of Ocular-Induced  
2 Drug Side Effects, saying that there indeed had been  
3 errors because people had confused their medications.

4 And we've developed this system in  
5 cooperation not only with the FDA but with the  
6 pharmaceutical industry, which has been very helpful.

7 Twenty years ago, it was one of my first jobs in the  
8 Academy.

9 And one of the things I learned,  
10 interestingly, it's very expensive for the drug  
11 companies to put these tints on the bottles and on the  
12 caps. They have to make sure they're not toxic. Have  
13 to make sure they don't degrade the drug and so forth.

14 We chose the colors and some of this is  
15 lost in history. I don't know why we used red for one  
16 and green for others. But we choose them by classes  
17 of drugs, not by exact drugs, which we'll talk about a  
18 little later, but according to the nature of the  
19 disease, the produce side effect profile, and the risk  
20 of serious sequella if they should be mixed up.

21 As I say, we've done this in cooperation  
22 with the pharmaceutical industry. And we still work  
23 with them. We certainly will not have 100 percent  
24 consensus because of limited colors. And this system  
25 has been based upon primarily patient safety,

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1       prescribing patterns, and the available color options.

2                 Here is indeed our system.    And I would  
3       like to respond a bit to Dr. Cohen's remarks.    When he  
4       did show the three drops all with yellow tops with  
5       different names, the fact is they were all the same  
6       class of drugs.    They were beta-blockers.

7                 The color of the cap, the color of the  
8       bottle is not meant to tell exactly what the name of  
9       the drug is but it is to tell which class it is in.  
10       And you still do indeed have to read the label.

11                Likewise, when he was throwing out Bausch  
12       & Lomb bottles that looked similar in color, the fact  
13       is they were all antibiotics.    And they all were the  
14       same color tan because they were antibiotics.    And the  
15       purpose is not to identify the precise drug but just  
16       the class of drug.    And it certainly is true there can  
17       be intra-class errors.

18                It was mentioned on the slides the colors  
19       got washed out.    So I actually brought some real  
20       examples.    And the red is for dilating drops or  
21       cycloplegics.       Orange is carbonic anhydrase  
22       inhibitors.    Green are miotics.    And that can be  
23       pilocarpine or it could be carbachol.    We don't know.

24       You have to read the label.

25                One of the points that was also brought

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1 out was that the labels can be -- or the tops can be  
2 mixed up. And I certainly agree.

3 Our policy just says that top and the  
4 label should be the same color. It's very helpful,  
5 though, and this company has done it, that also the  
6 top of the bottle be colored. So if you do mix up  
7 that cap, the patient can still tell the difference.  
8 Not all companies do that.

9 So I would say if you are going to have a  
10 policy or change the policy, besides having the cap  
11 and the label be color coded, the top of the bottle  
12 should also be color coded.

13 We do have the two ongoing concerns.  
14 Number one, as we see more and more generics, they're  
15 not all following the rules. And I get some drops now  
16 that all have white tops and white labels. And indeed  
17 those I do have to read the label every time I use it.

18 And it makes it a little difficult for me and the  
19 patient.

20 To me one of the most major problems we  
21 have is not color coding but -- and this was mentioned  
22 also before -- we see a lot of accidents, once a week  
23 in the emergency room, patients who have non-drugs, we  
24 talked about guaiac testing materials, we see the  
25 glue, we see Super Glue in bottles that look exactly

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1 like eyedrops. And I don't know who should regulate  
2 that.

3 But I think a major problem we should try  
4 to address is how to avoid confusion for the patients  
5 when non-ophthalmological are put in bottles that just  
6 look like eyedrops and cause significant injury.

7 In summary, the Academy of Ophthalmology  
8 continues to recommend this uniform color-coding  
9 system for the caps, labels, and ideally the bottle  
10 tops of all topical ocular medications. We don't have  
11 science. But it has been very useful to us. And we  
12 think it has been a safety measure for our patients.

13 I'm certainly glad to answer any  
14 questions.

15 DR. SELIGMAN: Thank you, Dr. Jensen.

16 Any questions from members of the panel?

17 CDR. HOLQUIST: You mentioned that within  
18 a product class, like within the same class, errors  
19 wouldn't necessarily be a problem for you. What about  
20 if somebody had an allergy to one of the antibiotics  
21 or there was like a steroid used in one of the  
22 combinations, do you see a lot of that type of  
23 confusion? Or is it just --

24 DR. JENSEN: Well, certainly if it's in  
25 the antibiotic class, people can be allergic to one

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1 antibiotic and not another. You have to take the  
2 history and look at the label. The color coding is  
3 not to eliminate that. It's just so you know if it is  
4 an antibiotic.

5 And you're right. It becomes very  
6 complicated when people have combination drugs. There  
7 are drugs that are a combination of antibiotics,  
8 steroids, and frankly I don't know how we code those.  
9 It does become a problem.

10 Dr. Chambers may know the answer to some  
11 of those things.

12 CDR. HOLQUIST: Are you running out of  
13 colors?

14 DR. JENSEN: Yes.

15 (Laughter.)

16 DR. MEYER: Who do you see as the primary  
17 target for this color? For your particular color  
18 coding? Is it for the patients? Is it for the  
19 practitioner? Presumably not so much the pharmacists.

20 DR. JENSEN: I was interested in the  
21 discussion that the pharmacists might be confused  
22 about the colors and give the wrong drug. Now the  
23 pharmacists job is to read the label and give out the  
24 right drug no matter what the color is.

25 Number one, it is for the patient. We

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1 have 80-year-old patients who have bad vision, who are  
2 getting feeble, and it's hard for them to recognize.  
3 I think it helps them tremendously to have a color on  
4 the top of their bottle. And clearly it helps us,  
5 too.

6 DR. CHAMBERS: This is Wiley Chambers.  
7 Let me just make -- take the opportunity to make one  
8 comment. The slide that was shown with the  
9 combination steroid/anti-infective are not following  
10 the scheme.

11 The steroid/anti-infective combinations  
12 are approved as steroids. They have labels that say  
13 they are for steroid indications. And they are  
14 supposed to have pink caps. They were not supposed to  
15 have tan caps. That's an error with the manufacturer.  
16 That's not reflective of the color coding system.

17 DR. JENSEN: Thanks. Thank you.

18 DR. SELIGMAN: Thank you, Dr. Jensen.

19 Has Dr. Broselow arrived yet?

20 Why don't we take a few minutes then and  
21 ask if there are any questions or comments from  
22 members of the audience, either for any of the  
23 speakers or anything that anyone would like to add or  
24 say.

25 We're going to give Dr. Broselow another

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1 15 or 20 minutes to show up since we were ahead of  
2 schedule.

3 Are there any comments? Thoughts?  
4 Questions? Anecdotes? Good stories?

5 Yes, sir? Please identify yourself.

6 MR. NEWMAN: Yes, Rick Newman, R&D  
7 Services.

8 Just a thought, you know, as I'm searching  
9 for consensus and seeing where folks are going with  
10 all of this and trying to understand some of the next  
11 steps, it seems like color coding in one specific area  
12 that, especially with user applied or in the  
13 ophthalmic situation, but then as I look at the area  
14 of color differentiation, using differentiation, which  
15 a lot of people are using both from a manufacturing  
16 standpoint, it's starting to be used by some pharmacy  
17 compounders for use in hospitals when there are  
18 specific needs and issues.

19 And I got to thinking that really it's  
20 almost like talking about what we use for a  
21 highlighter, with a highlighter pen when we're looking  
22 at our notes or reading a book. That if we highlight  
23 the key information, as Dr. Cohen was talking about,  
24 for the dosage or the strength, and just use it to  
25 highlight those key points that we want to be sure we

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1 get across to whoever might be using the product, that  
2 might be a good way to look at the limited use of  
3 color. Just a thought.

4 DR. SELIGMAN: I think that would probably  
5 fall in sort of the class of what we call  
6 differentiation, I presume, highlight.

7 Any other comments from members of the  
8 audience? Any questions for the speakers?

9 Mary, do we have any information or status  
10 on the one remaining speaker? Okay. Well, our final  
11 speaker is coming from some distance. So he may be  
12 stuck.

13 So I think what we'll do then, if you  
14 don't mind, rather than keep you all waiting, is let's  
15 take a 30-minute break. We'll reconvene at 12:15 when  
16 he is scheduled to speak. And hopefully he'll be  
17 here. And that will be the final presentation.

18 So let's all take a 30-minute break then,  
19 okay?

20 (Whereupon, the foregoing matter  
21 went off the record at 11:43  
22 a.m. and went back on the record  
23 at 12:14 p.m.)

24 DR. SELIGMAN: Our final speaker has  
25 indeed arrived. So Mary if you just grab folks. For

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1 any of you who has ever come from a large family, I'm  
2 sure you'll be very interested in this one, "Color  
3 Coding Kids." I never could figure out how my mom  
4 kept all of us apart. So please be seated and we'll  
5 begin in just a moment.

6 Our final speaker of this morning is Dr.  
7 James Broselow. Dr. Broselow?

8 DR. BROSELOW: Thank you very much. It's  
9 a pleasure to be here. And I'm sorry I was late. I  
10 went to an awful lot of trouble to be late. I got up  
11 at five o'clock in North Carolina.

12 Anyway, this is called Color Coding Kids.  
13 And when I say we, it's Dr. Bob Luten, I've worked  
14 with Dr. Luten since back in the 80s. And I'm going  
15 to give you a little bit of background on this idea so  
16 it won't look like it's coming out of the middle of  
17 nowhere.

18 This is me and this is -- that's my claim  
19 to fame. That's the Broselow Tape. And it's a  
20 length-based device. I was in family practice in  
21 Frankenmuth, Michigan, and I moved to Hickory, North  
22 Carolina, and I switched over to emergency medicine.

23 And when I did that, I started  
24 moonlighting in emergency department and go fairly  
25 comfortable with adults but recognized fairly early on

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1 that in a rural ER in the United States, when children  
2 came in, it was a nightmare.

3 First of all, everything was size related,  
4 all their equipment, their drug dosages. You'd have  
5 to look at the child, guess their weight. A lot of  
6 times they were unconscious or in a lot of distress.  
7 They couldn't move or talk. So you didn't really know  
8 how big they were. Sometimes you didn't have an age.

9 Then you had to estimate from your  
10 estimate of their age what their weight was. Using a  
11 complex formula, you'd come up with a weight  
12 estimation. You would try and round it out to  
13 kilograms.

14 Then you would start to try to pull from  
15 memory or a card all the doses of the various drugs  
16 that were nightmarishly close, milligrams of atrophine  
17 .1, so-and-so .01, so-and-so .2. And you were doing  
18 all these drug dosing and then telling the nurse the  
19 dose. If you happened to figure out, they didn't know  
20 if it was correct. And then they would have to  
21 translate that to mLs, of course, to give it to the  
22 patient.

23 Meanwhile, you were treating things that  
24 people never saw, rare emergencies. Everybody was  
25 nervous. You couldn't find the equipment. And so it

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1 was really a mess.

2           And I had the idea to get something more  
3 objective. And so I did some studies of just rural  
4 North Carolina on the relationship between children's  
5 length and their weight. And as you would guess,  
6 length was a good predictor of weight. And we knew it  
7 would work.

8           We didn't know if it was close enough to  
9 be useful but the studies that I did did show a good  
10 correlation. It was repeated by the group that put  
11 the PALS course together. And they did a national  
12 study. And it showed that length was the best  
13 predictor of weight.

14           Well, once you had this relationship here  
15 with weight and length, you can make little kilogram  
16 boxes. And in those boxes were calculated the dosage  
17 of all those drugs. So you were actually measuring  
18 the dose from the child. It was a direct measurement.

19           And so this has been well accepted. Once  
20 we started looking at length and weight, it was  
21 interesting to look at what else might correlate with  
22 length.

23           And I was most interested in equipment  
24 because the pediatric equipment for resuscitation was  
25 very critical, especially the endotracheal tubes so

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1 that they would fit snugly because you can't blow them  
2 up and make them fit like you can an adult's that have  
3 balloons on them.

4 So a number of studies were done in some  
5 children's hospitals and other hospitals' operating  
6 suite, and it showed that length was the best  
7 predictor of endotracheal tube sizes.

8 Well, once we had those critical pieces of  
9 equipment, we related the other equipment for children  
10 and put them in length zones. And so this little part  
11 of the tape over here that is colored had the name of  
12 about 20 pieces of equipment. Well, we thought if we  
13 color coded it, you wouldn't have to read all the  
14 equipment.

15 And it led to a storage system in which  
16 you could measure a child, get their length, and then  
17 you could open a drawer like this crash cart that has  
18 color-coded equipment that matches. Or you could just  
19 store your own equipment by color. But it was a way  
20 of getting the proper size equipment.

21 This is just another way of doing this.  
22 This is a soft bag. This is velcroed off so in a  
23 hospital, if the child were a purple, you could take  
24 that purple bag off that has their critical equipment  
25 and send them in the stretcher if they go to Trauma

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1 for a CT. And also that, you know, could be used by  
2 EMS. It rolls up.

3 So that was a system that we developed.  
4 This is just to show you a time frame. These worried-  
5 looking guys are EMTs. That's a Broselow Tape.  
6 That's that bag I showed you.

7 This is Dunblane, Scotland, in one of  
8 those early tragedies when a crazy person came in and  
9 shot a bunch of children in the same classroom. They  
10 had just put the system in. This says yellow boxes  
11 were lifesavers. Why were they yellow? Because most  
12 of the kids were the same size because they were in  
13 the same class.

14 So what I'm showing this for is to show  
15 that this has been fairly widely used and also it  
16 wasn't just me in a rural ER in North Carolina that  
17 had a problem. I had addressed pretty much a  
18 universal problem with children in the sizing issue.

19 And when I tell this story -- I'm going to  
20 get into the system but my daughter is getting her  
21 Ph.D. in German literature next month. She can't do  
22 math. She had no interest in medicine. But when she  
23 was about 15 years old, she could take a "Broselow  
24 Tape" and come up with the dose of every drug for a  
25 pediatric emergency, every piece of equipment, and she

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1 had no medical training.

2 So the implications were if I could take  
3 one of the hardest things for me to learn as a  
4 physician and take it so my daughter could do it,  
5 there were strong implications in that.

6 So Dr. Luten and I have spent a long  
7 period of time trying to develop a system related on  
8 those concepts. And, you know, basically what we want  
9 to do, we call this Color Coding Kids but what we want  
10 to do is we want to color code kilograms. And we want  
11 to put them into zones because medications have  
12 ranges.

13 As you all know, amoxicillin 500, 50 to  
14 100 is the range. So a drug has a range. So we  
15 revised the ranges so the color ranges were within the  
16 therapeutic ranges of drugs. And with that in mind,  
17 we could actually have a universal system.

18 Now you could call the range 2-3, like 2-3  
19 kilograms, 4, 5, 6, 7, 8, 9, but they're numbers.  
20 They're confusing because milligrams are numbers, mLs  
21 are numbers, weight is a number, the time is a number.

22 So we wanted to call the zones something different.

23 So what you could think well, let's call  
24 them a name. You could call them an apple and a pear  
25 and a peach. We elected to call them a color. Why do

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1 I mean call them a color? Because if somebody called  
2 an emergency department and measured a kid and got  
3 their length color, they could say their color is  
4 blue. But you don't see the color blue, right? It's  
5 a word that indexes a zone.

6 But also because it is color coded, you  
7 can see it. So it has that added dimension on top of  
8 the name.

9 So this is just to show some information  
10 that this has become widely accepted. It's in PALS  
11 and Apples and most of the major textbooks because  
12 length was the best predictor of weight.

13 Interestingly, it does a couple things.  
14 One, is it predicts weight because it's the best  
15 predictor and we have a bunch of studies. Two, it  
16 defines ideal body weight in the sense that many acute  
17 drugs just go into the water part of the body anyway.

18 So it's not a bad place to start. And third, it's  
19 the best correlation with equipment which you're doing  
20 at the same time.

21 Now we talked about length, but this is  
22 clearly a weight-based system in the sense if you want  
23 to color code a child and you know that they're 41 to  
24 51 pounds or 19 to 23 kilograms, you have a weight.  
25 There's no reason to length them to get the weight.

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1 So they would be a blue.

2 But we had the added feature that if you  
3 don't have a weight, you can always get in your  
4 information system. You can get a color that gets you  
5 into your tools.

6 So in this scenario, it's a "Broselow  
7 Tape" with nothing written on it. Picture a  
8 carpenter's tape, or later we'll show you a wall  
9 chart, but it's the relationship between length, lean  
10 body mass, and weight. So it indexes a system.

11 I'm not going to go into this but we're  
12 building a hospital system and a system for physicians  
13 and people that treat children. And the easiest way  
14 to see how this would work is this is a pocket book.  
15 That's the weight range.

16 So in this scenario, you go to that  
17 section of the book. You're in the blue section. And  
18 everything is related to those weights in kilograms.  
19 And it shows you -- we can do analgesics and  
20 antibiotics. And you'll see that there are a bunch of  
21 antibiotics.

22 We tend to use keywords to identify these  
23 zones like we call this amoxicillin high dose. The  
24 dose is 12 mLs every 12 hours. So it really just  
25 calculates for you. But it takes care of size-related

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1 things. If the kid is a blue, then we know what size  
2 of cefaclor we want to use because we know his size.  
3 So we can give some recommendations.

4 And I can go into this later. I'm not  
5 really going to go into the system. But we're trying  
6 to do is develop a system for hospitals that reduces  
7 errors.

8 In this scenario, these doses tend to be  
9 the dose the doctor would order like milligrams or  
10 mLs. In our hospital system, we're trying to get the  
11 color actually to give the dose in mLs, what the nurse  
12 would pull out at the scene.

13 An example of how we could do this -- and  
14 this gets more related to labeling, this is what I  
15 call a mLs rainbow. It's for epinephrine. The one on  
16 the left is the 1/10,000 concentration. The one on  
17 the right is 1/1,000.

18 Now what could you do with that label?  
19 Well, if you take that one on the right and you put it  
20 on that box of epinephrine, then your Broselow pull-  
21 out tape, your color, or the weight color tells you  
22 the mLs that you pull out of the bottle.

23 See, all the steps are eliminated. You go  
24 directly from your thought process to what you want to  
25 give the child. When you think of how many steps

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1 people go through to calculate, to estimate, and then  
2 they can make errors in any of those stages but some  
3 of the bigger errors are time delays and also that  
4 people get very nervous, especially if you're working  
5 with a team.

6 In a way, this is very similar to amps in  
7 adults. You know the old amp thing where you open an  
8 amp, you screw it in, and you give it. Well, in kids,  
9 we don't want to be cute and put every medicine in an  
10 amp. But we want to put information in amps.

11 In other words, once you know the child is  
12 a blue, then what you want to perform here is you just  
13 go into the color.

14 You'll notice in our system that we never  
15 give a color without the name. So that's how we  
16 handle color blind. People have asked us that. It  
17 will be a fixed sequence. But also we always have the  
18 name.

19 This is over-the-counter medications and  
20 the approach to that. Again, it's a weight-based  
21 system. We would recommend that people use weights if  
22 they have it to get the color. But this is the idea  
23 of a wall chart to get the color. So you get into a  
24 color information system.

25 Now this is an example of how a color, a

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1 length color, could relate to a line on a syringe.  
2 Now you'll notice that you don't really have to speak  
3 much English to do that, do you, once you kind of  
4 understand how it works.

5 If you know your child's color or weight,  
6 then you use that color to go directly to the syringe.

7 If you don't, you can length them and use a wall  
8 chart.

9 And why would you want to use length for  
10 over-the-counter medicines? Well, weight is fine.  
11 But if you want a safety system, think about length.  
12 It's almost impossible to overdose anybody by length.

13 Any normal child.

14 Now how can I say that? Well, first of  
15 all, if the child is normal, the length predicts their  
16 ideal body weight. So it's the right color. If the  
17 child is obese, a lot of us don't necessarily want to  
18 dose the heavy dose. So this is less. You're not  
19 going to overdose anybody.

20 Well, how about the small child? Well,  
21 we've got a range of, like Tylenol or acetaminophen  
22 has a range so you put it in the middle of the range,  
23 you've got almost 20 percent before you get out of the  
24 range that the child has to be underweight. In  
25 addition, you're using length which is ideal body

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1 weight. And real thin kids tend to have more water  
2 relative to their size so you have a little bit of a  
3 buffer there.

4 So think about how far a child would have  
5 to fall off of the scale to overdose with this. And  
6 they would be an outlier. That's not a normal child.

7 They've got some kind of illness. They're 30 percent  
8 below ideal weight. So outside of those children, you  
9 really could not overdose anybody with this system.

10 This is, again, the idea -- not a syringe  
11 to make it simpler but, you know, this might work for  
12 acetaminophen and Motrin which are the same dose per  
13 mLs. And so the child would be a yellow and you fill  
14 it up to yellow and you pour it in a cup or you could  
15 pour it in a spoon. And you've given an accurate  
16 dose.

17 This, to me, I've been talking about  
18 color-coded tools, like a color-coded syringe. You  
19 could see a color-coded cup or measuring device. But  
20 this is really the concept we're getting at. We're  
21 talking about color-coded information. That mLs label  
22 that is on there is the same mLs label that would be  
23 on a box of epinephrine for a code.

24 In other words, you get the color and you  
25 look in the color. And as an international system, it

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1 could always be mLs. So you're in Belgium. And you  
2 look at the box of medicine. And you look in the  
3 rainbow and your kid is a yellow. And you look in the  
4 number and that's mLs. You do not have to speak  
5 English to do that.

6 And if you're too poor to have a scale at  
7 home, you can always have a paper wall chart.

8 And you can learn it in your own language.

9 You could be Hmong and come into America and they can  
10 explain to you that we use a color-coded system here.

11 Or you people that may not be fluent in  
12 French, you could be in Belgium or in France and your  
13 kid has a fever and you pick up a bottle of medicine.

14 And you look in your child's color and that has the  
15 dose in mLs.

16 If it were tablets, it could have the  
17 number of tablets just as easily.

18 But it is an international way of giving  
19 information. And here's a cup. And that's the four  
20 mL line. So a person that does not speak English  
21 could walk up to a wall chart, look in the color, see  
22 the number, recognize the number on whatever cup was  
23 in it and give the dose.

24 Is this too easy? Is this too  
25 unimportant? You know people don't feel like treating

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1 fevers is all that important. And doctors know that  
2 it doesn't matter. And we know that the public panics  
3 over it. But at the very least, there's probably 10  
4 percent of emergency department visit occur strictly  
5 because the fever is not adequately treated.

6 It certainly would be cost-effective, it  
7 would pay for itself. How much anxiety to those poor  
8 people that do think it matters when the kid has 104  
9 fever? How about if they're Spanish? And in the  
10 middle of the night, they're struggling with a fever.

11 Why not give them a way to do it?

12 This is just -- you all know this probably  
13 -- published studies. They never give it right. When  
14 I talk in front of ER audiences, I always ask them if  
15 they have ever had two or three kids in a row with the  
16 right dose of Tylenol because you can almost write it  
17 up. Somehow the public never seems to get the dose  
18 right.

19 And so these are just a summary here of  
20 some of the studies that have been done. They all  
21 show less than 50 percent adequate treatment of fevers  
22 with acetaminophen.

23 Evidence-based, Duke actually did three  
24 studies on this. The first two were not published  
25 because they did not have historical details. In one

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1 of the studies, 20 percent of the people did not speak  
2 English. They found the same thing.

3 This is the one that was published in the  
4 Archives of Pediatrics. And it showed that, again,  
5 the very poor performance by the public of dosing  
6 over-the-counter medications and there was very close  
7 to 100 percent correct dosing in this particular  
8 formula.

9 The conclusion of the authors, "This study  
10 suggests a marked improvement in the caregiver's  
11 ability to correctly determine and measure an over-  
12 the-counter medication for their child using a color-  
13 coded method compared with conventional methods."

14 There was an editorial review of this and  
15 this is a copy of that. And the conclusion there  
16 speaks for itself. "Using a simple color-coded  
17 syringe with instructions for measuring acetaminophen  
18 doses makes it less likely for parents to underdose  
19 and overdose their child with the medicine."

20 Again, the implications of this are broad.  
21 We're talking about Tylenol. But you're actually  
22 talking about any kind of an over-the-counter  
23 medication. You're talking about every language that  
24 it could be done. You're talking about color coding  
25 so that the public knows their child's color. It's

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1 easier to remember. It's easier to track even if it's  
2 a weight color.

3           You're talking about building on  
4 prevention systems where a child has a color for  
5 Tylenol or Motrin and then is in the hospital and a  
6 drug comes from the pharmacy, a chemotherapeutic agent  
7 that's potentially toxic. It has the color of that  
8 kid on the drug. The child says, "Whoa, I'm not a  
9 blue. I'm a red." The parent who doesn't speak  
10 English.

11           The ability to tie this into infusion  
12 devices, defibrillators, equipment, anything that has  
13 sizing associated with it.

14           You know why does it make sense to color  
15 code children because they change. And they change --  
16 if you're an ER doc like me, if you're a first  
17 responder taking a kid out of a swimming pool, if  
18 you're an ICU nurse who is struggling with how to mix  
19 up an infusion, or you are a parent who doesn't speak  
20 English in the middle night, and they're color coded  
21 because they come in different colors. And color is  
22 truly a universal language.

23           Thank you.

24           DR. SELIGMAN: Thank you very much.

25 Panelists, do you have some questions?

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1 CDR. HOLQUIST: This concept is pretty  
2 intriguing to me. I guess I have some questions with  
3 its use in OTC products where -- maybe I'm just  
4 understanding the concept correctly.

5 Each one of these products that will be  
6 coming from the manufacturer, whether -- like with the  
7 case of Tylenol, it comes in a concentrated  
8 formulation and it comes in the regular elixir. So  
9 each one of those products would have their own color  
10 for that particular product?

11 DR. BROSELOW: No, no. That is a rainbow.  
12 That's a colored rainbow you saw up there. It has  
13 all colors. And the rainbow is a way of giving  
14 information. And it is concentration-specific.

15 In other words, the mLs in that rainbow  
16 are fixed to the drug that it is in. In other words,  
17 the way you recognize concentration is at the level  
18 where you apply that to the container. So by  
19 definition, the mLs are the color.

20 CDR. HOLQUIST: So this would take the  
21 whole undertaking of kind of making every manufacturer  
22 label their product exactly the same way? Because  
23 some label with cc's, some label with mLs. And  
24 there's even confusion among, you know, what that  
25 means versus --

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1 DR. BROSELOW: Well, any time there is  
2 confusion, then there is a possibility --

3 CDR. HOLQUIST: Right.

4 DR. BROSELOW: -- of a standard system to  
5 reduce that, you know. So we would hope that people  
6 going -- and, of course, to go to a more standard  
7 system would help with that.

8 I would like to say, you know, as a  
9 doctor, when I got into medicine -- are you parents --  
10 a lot of you parents -- didn't you always wonder why -  
11 - how come ten pounds isn't always a teaspoon? Right?  
12 How come?

13 Well, I was very naive. I started  
14 learning about some of this other stuff. I thought  
15 well, you know why not. Because if you made the so-  
16 and-so more concentrated, it wouldn't taste as good,  
17 you know? And I've got my whole company set up to do  
18 this. And I'm not going to change my concentration.

19 I think Tony Temple years ago wanted to  
20 have a standardization whereby the dose was similar.  
21 And the problem was all the drug companies would have  
22 to reformulate. I mean it's a ridiculous idea.

23 But the color takes care of that. You  
24 don't reformulate anything. From the point of view of  
25 the person using it, it's always a blue dose, see? We

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1 put the color on the bottle. We do with paper what  
2 you would have to do by redoing your whole  
3 manufacturing process. We save you money. We allow  
4 you to communicate.

5 We don't have your drug representatives  
6 going into -- with a wonderful new drug that's  
7 wonderful and spending a half an hour trying to figure  
8 out how to get the doc to use it because doc is older  
9 like me and he can only remember the doses he already  
10 knows.

11 So you give him pinwheels. And you give  
12 him this which all makes sense when you get one or two  
13 or three or five. But when you have 10 or 20 or 30,  
14 it stops making sense.

15 So from the pharmaceutical industry point  
16 of view, having a standard way to communicate -- it  
17 doesn't have to be the only way. There can be other  
18 ways. We're not trying to give anything less than you  
19 already have. This is an additional system. But you  
20 can buy into it whenever you come in and say this is  
21 the drug, the dose. And by the way, it's standard  
22 color coding. The dose is standardized.

23 DR. SELIGMAN: So at present in emergency  
24 rooms, are these user applied? In other words, in the  
25 emergency rooms, do they have to organize themselves

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1 along this line if they use the tape? I saw drawers  
2 in a crash cart that looked like they were  
3 corresponding to those colors as well.

4 DR. BROSELOW: Right.

5 DR. SELIGMAN: And again, they emergency  
6 room would have to organize itself in a way that puts  
7 the right endotracheal tubes and all the various  
8 devices as well as drugs in the appropriate bins, is  
9 that right?

10 DR. BROSELOW: Right. They don't have to.  
11 But that's been what has happened. Because, you  
12 know, we started out with the community hospitals,  
13 which do not have a lot of resources. And for them it  
14 was a no-brainer. You know they're not a children's  
15 hospital but it makes it easier for them.

16 The thing about a system is not just that  
17 things fit. It's that they're there. I found one of  
18 the biggest problems was that you had four No. 2 tubes  
19 and one No. 7, and no No. 6. So our system makes you  
20 go through everything. That's the advantage of a  
21 system. It makes you think of every little portal and  
22 to try to fill that portal.

23 So yes, the tape is used probably in 80 to  
24 90 percent of at least the community hospitals in  
25 America. And it is used some abroad. The equipment

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1 storage system, I mean when I went to Duke years ago,  
2 they just took the tape and put color bins. I just  
3 saw an article in Australia where they just took bins  
4 and put it in. But a lot of them use that at least to  
5 store equipment.

6 DR. SELIGMAN: Given its claimed  
7 widespread use, has there been an expression of  
8 interest on the behalf of device manufacturers for  
9 labeling their products in a way that would correspond  
10 to the color schema that you have?

11 DR. BROSELOW: Yes, GE actually -- you  
12 know a number of years ago, there was an issue. I  
13 don't know if you followed it about radiation,  
14 excessive radiation in children.

15 DR. SELIGMAN: Yes.

16 DR. BROSELOW: That they were setting  
17 their CT scanners for adults. Why? Because you never  
18 want to miss anything, you know, so you turn it up.  
19 And there was an epidemiological study that there  
20 could be as many as 10,000 cases of cancer when those  
21 children grew up.

22 So the people at Duke got interested in  
23 working with GE to make settings for children and also  
24 using our color code to make it easier. What they  
25 found was one -- and so they used the color code and

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1 they found two things in their study. One is it was  
2 more accurate. I don't know why. You'd think they'd  
3 be able to make a chart but for some reason it was.  
4 But two was like there were 17 techs and like 16 of  
5 them preferred color coding.

6 So what does that mean? It means you can  
7 do it. In other words, if it is easy to do, people do  
8 it. And so we want to make it easy for people to make  
9 this step.

10 So as the result of that, GE actually  
11 licensed the color code. And now all their new CT  
12 scanners have the software in it that if the child  
13 comes in with an armband or sticker and they want to  
14 use the color, they can set it.

15 Jerome Medical makes cervical devices.  
16 And they color code those because they have Miami J as  
17 their collars but they have sizing.

18 So our hope is we're looking at how it  
19 could work with infusion devices and different kinds  
20 of manufacturers we've talked to.

21 Had an FDA presentation with Meridian with  
22 the idea of color coding the autoinjectors for  
23 children because they have a size problem. One of the  
24 ironic things is the bigger autoinjector is for the  
25 smaller kids. So they want to have a simple way of

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1 recognizing size.

2 We met with a manufacturer of bone marrow  
3 needles who is talking about color coding that.

4 So we're just getting started with that.  
5 But our hope is that we would set a platform. And  
6 once the platform were in place, other people could  
7 tie into it and simplify things.

8 DR. SELIGMAN: Yes, Wiley?

9 DR. CHAMBERS: Do you envision this color  
10 wheel for to be on the box of a medication? On the  
11 label of the bottle? As a pull-out? Where did you --

12 DR. BROSELOW: This is information. In  
13 other words, we want to show that you can use color to  
14 get information. As far as the exact tool that people  
15 would use, I would say that we would need to  
16 communicate with the people and what the issues are.  
17 Whether sizing is in issue in general, I don't know  
18 the answer.

19 DR. CHAMBERS: Right. But you've  
20 obviously thought about this for a while. Where do  
21 you think it is most useful? To be on the carton?

22 DR. BROSELOW: On an over-the-counter  
23 medicine, I would like to see a little universal  
24 label, mLs label, on any bottle that can be given to  
25 children. That's what I would like to see.

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1 DR. CHAMBERS: On the bottle? Or on the  
2 carton? Or both?

3 DR. BROSELOW: I would actually see it  
4 right on the bottle.

5 DR. CHAMBERS: Okay.

6 DR. BROSELOW: Because you take it out of  
7 the carton and so that's where I would like to see it.  
8 I mean I would see the little rainbow there. I would  
9 like to think of a little symbol that showed  
10 frequency. Because if we had some way of showing the  
11 frequency or the number of times a day to give it plus  
12 the dose in mLs, that would be truly international.

13 And so I think -- I've given some thought  
14 to that but I don't have a good solution for that.

15 DR. CHAMBERS: Having spent time trying to  
16 fit everything that is required to be on the label of  
17 a bottle --

18 DR. BROSELOW: Yes.

19 DR. CHAMBERS: -- I'm just trying to  
20 envision where there is extra room to go and put  
21 something else. Or what you can take off if you put  
22 this on instead.

23 DR. BROSELOW: You'd have to ask them what  
24 we'd take off. But, yes, I don't know the answer to  
25 that. And you'd like it to be big. You'd like it to

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1 be so older people can read it. You know one of the  
2 things we looked, as an error prevention system, was  
3 the size of decimal points. And all those issues.

4 And I'd like it to be so that somebody can  
5 wake up in the middle of the night and look at a label  
6 and see a number and know the dose. So it would be  
7 nice if there was room to make it larger. It  
8 certainly could be in a little thing that came out  
9 that was a pediatric thing.

10 DR. SELIGMAN: How accepting has the sort  
11 of organized pediatric community been in terms of the  
12 American Academy of Pediatrics and others in adopting  
13 such a system? Are pediatricians at the point now of  
14 calling and telling parents at well-child visits or on  
15 other visits that you are a yellow or a white or a  
16 green?

17 DR. BROSELOW: In some ways, this has been  
18 very difficult for us to decide how to do. The  
19 standard system has been present for a number of  
20 years.

21 My biggest criticism of color coding would  
22 be how about if I train all my residents and it isn't  
23 there? How about if it isn't there three years from  
24 now? How broad is this going to be?

25 So it was our feeling that we had to fully

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1 develop the system and know how everything worked.  
2 And then come out with it at the same time so people  
3 would see the inevitability of it.

4 So we have taken a long time. Now we're  
5 kind of coming out of the closet so to speak on this  
6 and that we have a number of centers, Christian in  
7 Delaware, NYU in New York, Mayo Clinic ER, and a  
8 number of other hospitals that have looked at this.

9 I can tell you there is a very strong  
10 interest in error reduction. I can tell you that  
11 there is a huge anxiety about children from the lay  
12 public to adults.

13 So we think the timing is correct for  
14 this. In some ways, I didn't know whether to go over  
15 the counter, you know I have an agenda. I want to get  
16 this going. In some ways, you could go to over the  
17 counter like at Tylenol and they could push this  
18 agenda almost on to physicians coming out of over the  
19 counter.

20 My feelings were I'd like it to come out  
21 of medicine. I don't want something to be foist on  
22 doctors. So what we're doing is kind of -- my goal  
23 was to communicate it through the medical community as  
24 a paradigm shift when people start going to color-  
25 coded tools.

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1           But then this came up and I was quite  
2 concerned, especially about my friends with ISMP about  
3 the negativity of colors, you know. And I very much  
4 wanted to answer that we see our system as an error  
5 prevention system more like the red light and the  
6 green light.

7           In other words, one of the most successful  
8 error reduction systems in the world is color coded.  
9 So we don't want to throw it all away. But it has to  
10 be pretty darn universal.

11           And the other thing is there cannot be two  
12 color-coded systems. By definition, you would have  
13 none. So one of the reasons explaining to everybody  
14 say if you go in on the same one, then we have  
15 something that can travel. It can travel to other  
16 countries.

17           And, you know, we have other goals for  
18 this. I'm rambling. But car restraints is another  
19 area where there is a lot of awkwardness about  
20 information.

21           I presented this to their group about  
22 using length and color for car restraints because it  
23 doesn't -- it's a single measurement. It's a  
24 surrogate for size, for weight, and for length. And  
25 you don't have to speak English.

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1                   So we're interested in tying it into lots  
2 of things. But I think the timing is right now so  
3 we're trying to get interest in it really. That's why  
4 I'm here.

5                   DR. SELIGMAN: Any questions? Comments  
6 from the audience?

7                   (No response.)

8                   DR. SELIGMAN: Well, thank you very much.

9                   DR. BROSELOW: Thank you.

10                  DR. SELIGMAN: We appreciate your  
11 traveling today. You gave an excellent presentation.

12                  And I want to thank you all for attending  
13 today's meeting. Appreciate all the speakers and  
14 their input and all the comments they've made as well.

15                  And again, we want to remind everyone that  
16 you do have the opportunity to submit written comments  
17 to the docket to our Dockets Management Administrator  
18 by April the 7th. And these will all be taken into  
19 consideration as the FDA considers any future plans  
20 regarding the use of color in both drugs as well as  
21 devices.

22                  Thank you very much.

23                  (Whereupon, the above-entitled hearing was  
24 concluded at 12:43 p.m.)

25

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