

FOOD AND DRUG ADMINISTRATION
+ + + + +
STANDARDIZING AND EVALUATING RISK EVALUATION
AND MITIGATION STRATEGIES (REMS)

+ + + + +
PUBLIC MEETING
+ + + + +

THURSDAY
JULY 25, 2013
+ + + + +

The Public Meeting convened in the
FDA White Oak Great Room, Building 31, Room
1503, 10903 New Hampshire Avenue, Silver
Spring, Maryland 20993, at 8:30 a.m., Theresa
Toigo, Panel Chair, presiding.

FDA PANEL

THERESA TOIGO, R.Ph., M.B.A., Associate
Director for Drug Safety Operations,
Panel Chair

CDR CHARDAE ARAOJO, Pharm.D., M.S., Deputy
Director, Office of Medical Policy
Initiatives

MICHIE HUNT, Ph.D., M.B.A., Program Analyst,

Office of Executive Programs

MWANGO KASHOKI, M.D., M.P.H., Associate
Director for Safety, Office of New
Drugs

ADAM KROETSCH, M.S., Operations Research
Analyst, Office of Program and
Strategic Analysis

ELAINE LIPPMANN, J.D., Regulatory Counsel,
Division of Regulatory Policy II

CLAUDIA MANZO, Pharm.D., Director, Division
of Risk Management
MEGAN MONCUR, M.S., Regulatory Health Policy
Analyst, Division of Risk Management
KATE OSWELL, M.A., Health Communications
Analyst, Division of Risk Management
CAPT KEVIN PROHASKA, D.O., M.P.H.,
Director/Medical Officer, Division of
Safety Compliance
GARY SLATKO, M.D., Director, Office of
Medication Error Prevention and Risk
Management
ANAHITA TAVAKOLI, M.A., Health
Communications Analyst, Division of
Risk Management

SPEAKERS

GENERAL STANDARDIZATION SPEAKER SECTION 1
SARAH A. SPURGEON, Pharmaceutical Research
and Manufacturers of America (PhRMA)
ANDREW EMMETT, Biotechnology Industry
Organization (BIO)
PAUL SHEEHAN, Celgene Corporation
JEFF FETTERMAN, ParagonRx
JOANN STUBBINGS, B.S.Pharm., M.H.C.A.,
University of Illinois at Chicago

PAUL BROWN, National Research Center for
Women and Families

PHYLLIS GREENBERGER, MSW, Society for
Women's Health Research

GENERAL STANDARDIZATION SPEAKER SECTION 2
GARY APPIO, Pharm.D., M.B.A., Novartis

Pharmaceuticals Corporation

JIM DEVITA, CVS Caremark

STEPHEN A. GOLDMAN, M.D., F.A.P.M., Stephen
A. Goldman Consulting Services, L.L.C.

PAUL SELIGMAN, Amgen

BRIAN J. MALKIN, Partner, Frommer Lawrence &
Haug, L.L.P.

BILL MARTIN, Express Scripts

PRESCRIBER & PATIENT DIRECTED TOOLS SPEAKER
SECTION

ANN KARTY, M.D., F.A.A.F.P., American

Academy of Family Physicians

MURRAY KOPELOW, M.D., Accreditation Council

for Continuing Medical Education

ANDREW KOLODNY, M.D., Physicians for

Responsible Opioid Prescribing

NATALIE O'DONNELL, B.S.N., R.N., United

BioSource Corporation

REMS TOOLS IN DISPENSING SETTINGS SPEAKER
SECTION

KEVIN NICHOLSON, R.Ph., J.D., National

Association of Chain Drug Stores

STACIE MAASS, B.S.Pharm., J.D., American

Pharmacists Association

CAROLYN HA, Pharm.D., National Community

Pharmacists Association

DAVID CHEN, R.Ph., M.B.A., American Society

of Health-System Pharmacists

MARY JO CARDEN, R.Ph., J.D., Academy of

Managed Care Pharmacy

LINDSEY R. KELLEY, Pharm.D., M.S.,

University of Michigan Health System

KATIE STABI, Pharm.D., B.C.P.S., Cleveland

Clinic

TABLE OF CONTENTS

Opening Remarks/Overview of REMS	
Theresa Toigo, R.Ph., M.B.A.	6
Standardizing REMS	
Adam Kroetsch, M.S.	29
Prescriber-Directed Tools in REMS	
Kate Oswell, M.A.	57
Patient-Directed Tools in REMS	
Anahita Tavakoli, M.A.	63
Dispensers and Dispensing Settings in REMS	
Megan Moncur, M.S.	70
General Standardization Speaker	
Section 1	
Sara A. Surgeon.....	83
Andrew Emmett.....	91
Paul Sheehan.....	102
Jeff Fetterman.....	109
JoAnn Stubbings, B.S.Pharm.,	
M.H.C.A.	119
Paul Brown.....	129
Phyllis Greenberger, M.S.W.	131
FDA Questions	139
General Standardization Speaker	
Section 2	
Gary Appio, Pharm.D., M.B.A.	164
Jim Devita.....	169
Stephen A. Goldman, M.D.,	
F.A.P.M.	178
Paul Seligman.....	188
Brian J. Malkin.....	199
Bill Martin.....	211
FDA Questions	215

TABLE OF CONTENTS (Con't.)

Prescriber and Patient Directed

Tools Speaker Section

Ann Karty, M.D., F.A.A.F.P.	235
Murray Kopelow, M.D.	245
Andrew Kolodny, M.D.	254
Natalie O'Donnell, B.S.N., R.N. .	266
FDA Questions	272

REMS Tools in Dispensing Settings

Speaker Section

Kevin Nicholson, R.Ph., J.D.	287
Stacie Maass, B.S. Pharm., J.D. .	297
Carolyn Ha, Pharm.D.	305
David Chen, R.Ph., M.B.A.	318
Mary Jo Carden, R.Ph., J.D.	328
Lindsey R. Kelly, Pharm.D., M.S.	333
Katie Stabi, Pharm.D., B.C.P.S. .	345
FDA Questions	358

Concluding Remarks

Theresa Toigo, R.Ph., M.B.A.	376
-----------------------------------	-----

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

(8:33 a.m.)

MS. TOIGO: Okay, so I have got 8:33. So we are starting a little bit late. But good morning and welcome to our public meeting on REMS standardization and evaluation. Good morning to both the people in the room and those of our participants who are joining us through the live webcast.

I am Terry Toigo and I am the Associate Director for Drug Safety Operations in the Center for Drug Evaluation and Research and I am going to serve as your moderator today and as the Chair of the FDA panel.

So before we start the meeting, I get to do the housekeeping. First, if you can turn off your cell phones or silence them so that we are not interrupted.

We ask that everybody sign in for the meeting on both days. We are trying to really understand who is interested in this topic and who joined us for the meeting. The

1 doors were open at 7:30 today and they should
2 open at the same time tomorrow.

3 We are scheduled to go to 4:30
4 today and we probably will go to 4:30
5 tomorrow. It depends on the open public
6 speakers as to how long the meeting is going
7 to go. And we have had a few cancellations,
8 so we have juggled the agenda but I think
9 time-wise, that is what your expectations
10 should be.

11 The restrooms, if you have never
12 been here before, are in the halls outside.

13 We are planning for a 15-minute
14 break in the morning and then another one in
15 the afternoon. The lunch break is scheduled
16 from 11:50 to 12:45. We are going to try and
17 stick to that. If you haven't been here
18 before, you know that you can get sandwiches,
19 salads, and beverages in the lobby. And they
20 do a pretty good job of moving people through
21 in a timely manner.

22 We do have two open public hearing

1 sessions and they are both tomorrow because we
2 wanted the standardization presentations to be
3 finished and that won't happen until tomorrow
4 morning. And so we wanted the open public
5 comment after that.

6 So if throughout the meeting there
7 are comments that you want to make that
8 haven't been heard, please sign up at the desk
9 and you can speak during the open public
10 section.

11 And then importantly, the docket
12 for written comments on this is going to
13 remain open indefinitely. But if you want the
14 comments considered either for the projects,
15 the priority projects that we have to identify
16 or for the report that we have to write, we
17 need your comments to the docket by September
18 16th. And then the transcripts will be
19 available in I will say plus or minus 60 days
20 and you can check the meeting website and that
21 is where you will find the transcript, when it
22 is available.

1 So the rest of my presentation, of
2 my moderator presentation is divided into two
3 parts. Well my presentation is divided into
4 two parts. The moderator part I will tell you
5 what to expect for the day, the purpose of the
6 format, and the meeting agenda. And then I
7 will switch and put on my panel chair hat and
8 I will give you an FDA update on REMS.

9 So the purpose of the meeting is
10 to create a forum for interested stakeholders
11 to provide input on REMS. Specifically, as
12 the Federal Register Notice stated, we are
13 looking for your feedback on standardizing and
14 assessing REMS. And we are also looking for
15 your suggestions for some potential projects
16 that will help standardize REMS and integrate
17 them into the healthcare system.

18 And then importantly, this meeting
19 also serves to meet some PDUFA commitments
20 that we made. Despite the fact that the
21 resources haven't come yet, we have been able
22 to accomplish this particular commitment under

1 our PDUFA agreement.

2 So the format for the meeting will
3 include FDA presenters, stakeholder panels,
4 the FDA panel, and then an open public
5 session.

6 The purpose of the FDA presenters
7 is to introduce the topics for the panel
8 sessions and then highlight the information
9 that was included in the background document
10 that you will find on the meeting website. If
11 you haven't read the background document, I
12 encourage you to do so. We created this
13 document to familiarize stakeholders with our
14 experience with REMS since they were first
15 introduced in 2007. So that is available on
16 the meeting web page.

17 And then each of our stakeholder
18 panels will provide input on the questions
19 that were listed in the Federal Register
20 Notice. So that is the intent of these
21 panels.

22 We organized the panels based on

1 the outlines that were submitted by the
2 presenters prior to the meeting and we
3 acknowledge that some of the stakeholders
4 intended in their comments to cover multiple
5 topics but we tried to put them on the panels
6 that we thought were most appropriate for what
7 they told us they were going to cover.

8 And then our FDA panel and many
9 other FDA staff in the room will be listening
10 to the presentations and our FDA panel members
11 will have an opportunity to ask the speakers
12 questions at the end of their panel, as time
13 permits.

14 So we only have about ten minutes
15 for FDA questions on most of these panels but
16 we are going to do our best to get some
17 questions in.

18 And then as I mentioned, we have
19 the two open public sessions tomorrow and we
20 welcome you to sign up and speak during those
21 sessions.

22 So as you can see from the agenda,

1 we have seven FDA presentations. And then you
2 will hear from about 40 stakeholders spread
3 throughout six panels over the course of the
4 two days. Each of the registered speakers has
5 been given a ten-minute slot on the agenda,
6 with an opportunity, as I said, for FDA to ask
7 questions after the panel members have spoken.

8 And I will be using a timer. The
9 light will be green for the speakers when you
10 start. It will turn yellow when you have two
11 minutes left and then red when your time is
12 up.

13 The microphone will not turn off
14 at the end of ten minutes but if you go over,
15 I will kind of encourage you to wrap up and
16 then, at some point, if you continue to go
17 over, you will be finished but we will not cut
18 you off with the microphone.

19 So then before I put my panel
20 chair hat on, I would like the FDA panel
21 members to introduce themselves. They and
22 many of our other FDA staff have been very,

1 very involved in planning and preparing for
2 this meeting over the past few months. And
3 thinking about standardization and the
4 challenges really takes a lot of people to
5 look at what we have done, look at where we
6 are now, and think about possibilities for the
7 future. So I would like them to introduce
8 themselves just so you know who the FDA panel
9 members are.

10 DR. SLATKO: Good morning. I'm
11 Gary Slatko. I direct the Office of
12 Medication Error Prevention and Risk
13 Management in CDER.

14 MR. KROETSCH: Hi. I'm Adam
15 Kroetsch and I am here in the Office of
16 Program and Strategic Analysis.

17 MS. OSWELL: Good morning. Kate
18 Oswell. I am a health communications analyst
19 in the Division of Risk Management.

20 MS. TAVAKOLI: Good morning. Ana
21 Tavakoli. I am also Health Communications
22 Analyst in the Division of Risk Management.

1 MS. MONCUR: Good morning. I'm
2 Megan Moncur and I am a Regulatory Health
3 Policy Analyst also in the Division of Risk
4 Management.

5 DR. HUNT: Hello. I'm Michie
6 Hunt. I'm in the Office of Executive
7 Programs.

8 DR. KASHOKI: Good morning. My
9 name is Mwango Kashoki and I am the Associate
10 Director for Safety in the Office of New Drugs
11 in CDER.

12 DR. MANZO: Good morning. My name
13 is Claudia Manzo. I am the Director of
14 Division of Risk Management.

15 DR. ARAOJO: Good morning. I am
16 Chardae Araujo. I am the Deputy Director of
17 the Office of Medical Policy Initiatives.

18 MS. LIPPMANN: Good morning. I'm
19 Elaine Lippmann in the Office of Regulatory
20 Policy.

21 DR. PROHASKA: Good morning. My
22 name is Kevin Prohaska. I am the Director of

1 the Division of Safety Compliance, which
2 includes REMS compliance oversight.

3 MS. TOIGO: Okay, thank you.

4 So now I am putting on my panel
5 chair hat and I will give you the FDA update
6 on REMS.

7 I serve as the chair of several
8 REMS-related steering committees and working
9 groups. So my intent is to just spend about
10 20 minutes on giving you an update on REMS.

11 Some brief background, a little
12 bit about stakeholder feedback to date, some
13 of the challenges that we face in our working
14 groups, and then a little bit about how we are
15 dealing with those challenges.

16 So every drug has risks. And it
17 is important to point out that REMS are not
18 intended to eliminate all risks from drugs.
19 Instead, they are really targeted to
20 circumstances in which FDA believes that
21 additional safety measures beyond those that
22 are mentioned in the product's label are

1 needed to ensure that a drug's benefit
2 outweighs its risks.

3 REMS authority was granted to FDA
4 in 2007 by the Food and Drug Administration
5 Amendments Act and this authority enables FDA
6 to approve and patients to have access to
7 certain drugs whose risks would otherwise
8 exceed their benefits and may not be
9 approvable.

10 All REMS impose some burden and
11 multiple REMS increase the burden on the
12 healthcare system. So I think we would all
13 agree that some changes are needed to improve
14 REMS efficiency and reduce burdens on the
15 healthcare system but we really haven't
16 defined what those changes are yet.

17 And then finally on the
18 background, PDUFA fees provide for some
19 support for changes that will better integrate
20 REMS into the existing and evolving healthcare
21 system.

22 So where are we in 2013? If you

1 go to the FDA website and you type REMS in the
2 FDA search engine, here is where it takes you,
3 to a REMS website.

4 If you count, you will find that
5 there are, depending on how you count, but
6 there are about 200 REMS that have been
7 approved since 2008. Many were MedGuide only
8 REMS, which have been released. As of this
9 month, there are 72 REMS; 66 are for
10 individual drugs; and six are share system
11 REMS that actually include 88 applications,
12 both NDAs and ANDAs.

13 And over the period of -- since we
14 have been working with REMS, we have regularly
15 sought and received stakeholder feedback in a
16 variety of forms. Public meetings like this,
17 advisory committees, and listening sessions.
18 And PDUFA V further highlighted the importance
19 of gathering stakeholder input to better
20 integrate REMS into our healthcare system.

21 My FDA colleagues will focus on
22 some of the things we have heard from

1 stakeholders that are specific to their
2 presentations related to standardization,
3 evaluations, and REMS tools.

4 But my next three slides are going
5 to present stakeholder feedback just a little
6 bit differently. I have got some quotes that
7 we have heard over the years.

8 So we have talked to healthcare
9 providers and we talked to patients.

10 Healthcare providers acknowledge that time-
11 consuming REMS tools can be helpful but they
12 are less helpful when they interrupt the
13 workflow of the healthcare provider. We all
14 need to do a better job about REMS, if there
15 are healthcare providers who see REMS only as
16 filling out paperwork. Some patients have
17 told us that they liked the reinforcement and
18 repetition of safety messages beyond just the
19 first time they receive a drug.

20 And then we know from discussions
21 that some prescribers avoid REMS drugs. But
22 as one of the prescriber's said, we are always

1 afraid of things but when you try it, it is
2 like eating your vegetables. You know when
3 you try it, it is just a whole lot easier.
4 And we have had discussions with stakeholders
5 who initially were reluctant and when they
6 actually got some experience with the program,
7 found out that it wasn't just as bad as they
8 thought.

9 So we have listened to the
10 pharmaceutical industries. Industry
11 stakeholders highlighted the need for
12 flexibility within any standardization that we
13 come up with. We also heard about the need to
14 consider how REMS tools may impact patient
15 access issues and industry reminded us that
16 one size does not fit all.

17 And we also held the listening
18 session with our FDA reviewers and the
19 Division of Risk Management. And this slide
20 lists some of the comments that we heard from
21 reviewers. They are examples of things that
22 sponsors can do to help facilitate the review

1 of REMS submissions. Our reviewers talked
2 about the challenges we face in reviewing
3 submissions when we really don't know company
4 business processes, such as the relationship
5 between the company and vendors. And this
6 impacts developing and finalizing REMS
7 materials and timeframes. And so us not
8 having a complete understanding of that
9 process sometimes we might be able to do
10 things a little bit differently.

11 And then finally reviewers
12 consider it a gift when companies do
13 pretesting of materials and then actually
14 react based on the pretesting that they hear.
15 So that is sort of some selected, acknowledged
16 selected feedback but it was interesting to
17 talk to people or read about things that
18 different people have said.

19 So you will hear a little bit more
20 about stakeholder feedback from our other
21 panel members. And we really are looking
22 forward to this session to get additional

1 stakeholder feedback.

2 So as you can imagine, we have run
3 into challenges based on our experience
4 implementing REMS over the past five years.
5 Pharmaceutical risk management science is
6 relatively new and it is evolving and so is
7 our statutory framework. We still have a lot
8 to learn about REMS programs that can easily
9 be implemented and integrated into the
10 existing healthcare system as well as doing a
11 better job of measuring effectiveness and
12 burden.

13 At the same time, the lessons
14 learned have highlighted challenges and
15 opportunities associated with REMS policy,
16 standardization, integration and evaluation.
17 These are listed on the next three slides and
18 you will hear more about these from my FDA
19 colleagues during their presentations.

20 So what are some of the policy
21 challenges. Well we have questions like when
22 may an alternative to REMS be appropriate to

1 address a serious risk. What do you suggest
2 as alternative to REMS in terms of things that
3 can be done to minimize risks? What
4 characteristics or processes or features
5 within the healthcare system can help manage
6 risks? What are the indicators that product
7 labeling is insufficient to communicate the
8 drug's risk and conditions of safe use? And
9 what are indicators that REMS is no longer
10 necessary to ensure that the benefits of the
11 drug outweigh the risks?

12 So what about design and
13 standardization? What are some of the
14 challenges we face there? And none of these
15 slides are comprehensive or exhaustive. They
16 are really just some of the things that the
17 working groups are grappling with.

18 So how do we best customize
19 standardization? How do we balance
20 customization and standardization? How much
21 variation is necessary and unavoidable? How
22 do you best target interventions to prevent or

1 mitigate failures? And what is the
2 appropriate tradeoff between enhanced safety
3 and the additional burden to the healthcare
4 system?

5 So those are some of the questions
6 that the Standardization Work Group is talking
7 about.

8 What about assessment? Well
9 these, listed on this slide, are some of the
10 challenges that we face related to the
11 assessment of REMS. So what are valid proxy
12 measures of patient and provider behavior to
13 determine if REMS goals have actually been
14 met? How do you associate particular REMS
15 interventions with particular outcomes? How
16 do you use limited data to determine whether
17 or not the REMS is actually effective?

18 Well, the challenges we faced
19 implementing REMS over the past five years
20 together with our anticipation of PDUFA
21 reauthorization presented us with an
22 opportunity to better organize ourselves

1 around some of the specific goals that are
2 listed on this slide: policy for requiring a
3 REMS, designing REMS that can be better
4 integrated into the healthcare system, and
5 improving REMS assessment.

6 So how did we do that? Well, we
7 established what we called the REMS
8 Integration Steering Committee or the RISC to
9 oversee the activity of the work groups and
10 then to ensure stakeholder participation. The
11 Policy Work Group is clarifying and issuing
12 guidance on the criteria for requiring a REMS.
13 The Design and Standardization Work Group is
14 focused on the standardization of REMS tools.
15 And the Evaluation Work Group is looking to
16 better understand alternative methodologies
17 for evaluation -- for REMS assessment,
18 including developing a REMS assessment
19 framework.

20 So the next three slides will
21 elaborate on the activities of the three
22 working groups. Again, as I mentioned the

1 REMS Policy Work Group is developing a draft
2 guidance to provide information about how FDA
3 applies statutory criteria factors, as well as
4 other factors, to determine whether REMS is
5 necessary to ensure that the benefits of the
6 drug outweigh the risks.

7 The guidance will incorporate
8 considerations FDA take into account in the
9 current risk-benefit assessment of drugs to
10 maximize the agency's consistency and
11 decisionmaking about the need for a REMS and
12 it will also provide information about when it
13 may be appropriate to employ measures other
14 than REMS to address particular risk.

15 I am not going to spend time on
16 the next two slides because my FDA colleagues
17 will discuss these in their later
18 presentations. Adam Kroetsch will talk about
19 the Standardization Work Group on this slide
20 and then Gary Slatko will talk about the
21 Evaluation Work Group. But I just wanted you
22 to have it in the overview.

1 So this slide, Slide 24,
2 highlights our efforts over the past few
3 months to engage with stakeholders on
4 challenges and opportunities with REMS. We
5 think that input from multiple stakeholders is
6 critical in helping us meet our goals.

7 Today's meeting is an important
8 stakeholder engagement activity for our REMS
9 Integration Work Groups. We look forward to
10 hearing from the panels on the specifics of
11 the questions that we posed in the federal
12 register notice.

13 And then today's meeting is not
14 your last chance to comment. As I mentioned,
15 the docket for written comments will remain
16 open indefinitely but we need your comments by
17 September 16th to be considered for the report
18 of our findings on standardization and
19 evaluation and for the identification of
20 priority projects.

21 The background document and/or
22 today's discussion may stimulate some thinking

1 or may encourage. It may prompt you to want
2 to speak in the open public session because
3 none of the panels have covered issues that
4 you wanted to make sure that we heard
5 publicly. So again, I encourage you to sign
6 up to speak in the open public session because
7 we welcome your input.

8 So then to summarize, stakeholder
9 feedback is really important to us. And my
10 previous job was I worked a lot with
11 stakeholders. And so I am committed as the
12 leader of the -- chair of the REMS Integration
13 Steering Committee to ensuring that
14 stakeholder input is involved through all
15 stages of this project. We need to know where
16 are things working. And I think the listening
17 sessions that we have had over the past few
18 months, we learned from stakeholders there are
19 things that are working. So we really are
20 interested in learning what does work.

21 At the same time, we need to know
22 what we need to fix. And we can develop

1 something and it can be approved and we can
2 think it is perfect. And once it gets out
3 there and stakeholders are having to implement
4 it, questions come up. And we have learned
5 that as we have put REMS in place. But if we
6 don't hear the feedback, we can't learn from
7 it and we can't make the changes. So
8 stakeholder feedback is critical.

9 We need to know where we can
10 standardize. I think you heard from -- you
11 saw from the quotes on all the stakeholder
12 slides that one size really doesn't fit all.
13 And so this standardization, we have to really
14 think about where are the opportunities for
15 standardization and where do we not
16 standardize. We need your help on that.

17 And then what projects can help us
18 better understand where those opportunities
19 for standardization are. We really do need to
20 hear your input on that as well.

21 And then that looks like I am
22 finished for my overview. So I hope that sort

1 of sets the stage for today's meeting and how
2 the groups have been trying to tackle this
3 problem. And this meeting is at a critical
4 point for us to kind of take a step back, what
5 have we learned, and where do we need to spend
6 more time on more focused meetings. And that
7 is kind of the overall purpose of this meeting
8 because we will do some expert panel meetings
9 but we want to do those thoughtfully because
10 that is going to take another investment of
11 time and effort. So we hopefully will get
12 some feel for that today, where we need to put
13 some more resources.

14 So Adam Kroetsch who works closely
15 with Gary Slatko, who leads our Design and
16 Standardization Group is going to talk to us
17 about standardizing REMS.

18 MR. KROETSCH: Okay, thank you,
19 Terry.

20 So I am Adam Kroetsch and I am
21 going to be spending some time today talking
22 about some of the work we have been doing to

1 standardize REMS. And as Terry mentioned, the
2 REMS integration initiative is composed of a
3 few different work groups and one of them is
4 the REMS Design and Standardization Work
5 Group. So what I will be talking about
6 relates to the work of the REMS Integration
7 Steering Committee or the REMS Integration
8 initiative as a whole, as well as our
9 individual REMS design and standardization
10 Work Group. And we will be talking a little
11 bit about what we have been doing to
12 standardize REMS.

13 And specifically, I am going to
14 start by introducing what we mean when we talk
15 about standardization, what exactly it is that
16 we are standardizing and why we are
17 standardizing. And then after I provide that
18 introduction, I will be spending some time
19 talking about the steps that we are actually
20 taking towards standardizing REMS.

21 So I would like to start off by
22 talking a little bit about our commitments

1 under PDUFA V because these are some of the
2 major drivers of the work that we have been
3 doing of this meeting today.

4 Under the PDUFA V commitments, we
5 have a couple of things that we have committed
6 to do related to standardizing REMS and
7 integrating into the existing and evolving
8 healthcare system and that includes holding a
9 public meeting on REMS standardization with
10 the goal of reducing REMS burden and issuing
11 a report of our findings, where we identify
12 some priority projects in several areas to
13 help us move towards standardization.

14 And I should also mention that
15 although these are the things that we have
16 committed to related to standardization, we
17 know that there is much more to standardizing
18 REMS than just these two commitments. And so
19 we are doing a lot of work that I will be
20 talking about today to actually move us
21 towards standardization of REMS.

22 Now when we talk about

1 standardization, it is really important to
2 think about what exactly do we mean by
3 standardization? What are standardizing? And
4 we often find it is useful to kind of divide
5 what we are doing into two pieces.

6 First, we talk about REMS design
7 and standardizing REMS design. And by that,
8 we mean the method by which REMS tools are
9 selected. And this starts for drugs where we
10 know we are going to have a REMS. We think
11 about what the risk is and what is required to
12 mitigate it. And once we know that, we are
13 thinking about standardized methods that we
14 may be able to develop to really help identify
15 which tools are necessary. So we need to
16 think about how we characterize how the drug
17 is actually likely to be used in the real
18 world and where it is going to get used.

19 And then we need to think about
20 the gaps in the healthcare system that might
21 lead to a greater risk because ultimately we
22 often find that REMS are targeting some of

1 these gaps. And then we need to think about
2 the safe use conditions. I mean what
3 stakeholders need to know and do in order to
4 address those gaps and then select appropriate
5 REMS tools to help us address those gaps.

6 So these are all standard steps in
7 kind of building the logic of a REMS to help
8 us decide what tools are needed.

9 The other thing that we think
10 about a lot when we talk about standardization
11 is REMS tools. And these are the systems and
12 processes and materials that we use to
13 actually carry out what we refer to in a
14 previous slide as these safe use conditions
15 and what stakeholders need to know and do.
16 And this includes -- standardizing REMS tools
17 includes standardizing what REMS are used so
18 the things like maybe having a standardized
19 REMS toolkit, how exactly those tools are
20 implemented and integrated into the healthcare
21 system and then how we assess those tools.
22 And this is one of the key links between

1 standardization of REMS and assessment of REMS
2 and is part of the reason that we are talking
3 about both of these issues today. And REMS
4 tools happen to be a major focus of today's
5 meeting. And a lot of the questions that we
6 asked in the federal register notice in
7 advance of the meeting are centered around
8 ways that we might be able to standardize REMS
9 tools.

10 So now I am going to talk a little
11 bit -- shift gears and talk a little bit about
12 why it is that we are standardizing and again
13 what standardization means. And a good thing
14 to think about when you are trying to figure
15 out why we are standardizing is why REMS have
16 varied in the first place. And one of the
17 major reasons is simply that risks vary. So
18 REMS are designed to address specific serious
19 risks. So the steps that are needed to
20 actually mitigate those risks is going to
21 vary. And another important thing is that the
22 context of care varies. And when I talked

1 about understanding the setting in which a
2 drug is likely to be used, that can have a
3 really huge impact on what kinds of REMS are
4 put into place because different REMS drugs
5 may be used by different providers in
6 different healthcare settings and for
7 different patient populations.

8 Another thing about things that is
9 varied is the developers of those REMS. So
10 there isn't a single body that is developing
11 the entire REMS program or implementing it.
12 Instead, there are actually REMS that are
13 proposed by a diverse set of sponsors and
14 negotiated with FDA review teams.

15 And finally, we are still learning
16 about best practices in REMS. Those are still
17 evolving. The science of pharmaceutical risk
18 mitigation is relatively new and our REMS
19 authority is relatively new. And so we have
20 continued to develop best practices. And I
21 think what all of these variations point out
22 is that there are variations perhaps that are

1 necessary and inherent in how REMS are put
2 together and that we might even want to
3 preserve. But then there is also some forms
4 of variation that might be unnecessary and
5 those are some of the areas where there might
6 be opportunities for standardization.

7 One other thing we have done, and
8 Terry mentioned this before, is we have
9 reached out a lot to stakeholders to get their
10 sense of how they are affected by variation in
11 REMS and what their thoughts are in
12 standardization and how it affects them.

13 And variation, they have told us,
14 makes it really difficult to adapt to new
15 REMS. So there is a saying I have heard
16 stakeholders tell us, which is if you have
17 seen one REMS, you have seen one REMS. So
18 even stakeholders with a lot of REMS
19 experience can take a lot of time to integrate
20 new REMS into their workflow and to actually
21 understand those REMS and what they need to do
22 to implement them.

1 Another thing we have heard is
2 that REMS successes aren't actually always
3 copied. So sometimes a stakeholder would tell
4 us about their favorite REMS or a best
5 practice that they noticed in a REMS but we
6 didn't necessarily see those successes and
7 those best practices repeated across REMS. A
8 lot of them were more one off successes.

9 And another thing we have heard
10 from stakeholders is that their perceptions of
11 REMS and whether they were working and how
12 they should work varied a lot depending on the
13 setting that they were in. And this gets to
14 this fundamental issue of standardization
15 versus customization. A one size fits all
16 approach isn't necessarily going to work
17 because REMS really need to be tailored to the
18 different stakeholders and settings in which
19 they are implemented.

20 So when we think about addressing
21 those concerns, we really are trying to set
22 out two goals for standardization. And one is

1 to minimize that unnecessary variation, make
2 REMS more predictable, more consistent, easier
3 to understand but also have them customized to
4 specific settings. And we think those two
5 things are mutually compatible but they will
6 require some careful thought and they will
7 require their input to learn exactly how to do
8 that.

9 And another thing we need to do is
10 actually improve the quality. We heard about
11 these best practices. We heard that they were
12 not necessarily replicated across different
13 REMS and we need to make sure that as we
14 standardize we are establishing those best
15 practices that could make REMS more effective,
16 less burdensome and all the while maintaining
17 patient access.

18 And I think if you put all of
19 those things together you get a good picture
20 of what exactly standardization looks like.
21 It includes, in the world of REMS design, you
22 could imagine a standardized REMS design would

1 mean that REMS with similar risks in similar
2 settings are using similar tools and that the
3 approach that we use to choose which tools the
4 REMS are using are really rigorous and
5 evidence-based.

6 And then in the area of the REMS
7 tools themselves, you could imagine
8 standardized REMS using similar tools that are
9 perhaps drawn from a standardized REMS
10 toolkit. And then those tools in the toolkit
11 would be informed by the latest science, by
12 stakeholder feedback, and by established best
13 practices and the lessons that we have learned
14 from previous REMS.

15 And so that kind of is a quick
16 overview of what exactly what we mean by
17 standardization. So now I will talk a little
18 bit about what our Work Group has been doing
19 to actually move towards standardizing REMS.
20 And we really have mapped this out into three
21 phases here, although the process is actually
22 somewhat more iterative than that and not

1 quite as sequential.

2 But the first thing that we really
3 needed to do in order to standardize REMS is
4 to characterize the existing REMS and actually
5 have an understanding of where it is that REMS
6 vary and why. And that includes kind of
7 having a catalogue of what REMS exist and what
8 kind of tools they are using and what
9 approaches they are taking and then think
10 about ways to put some clear definitions
11 around that and help us actually share
12 information about REMS.

13 And then we get to the next step,
14 identifying best practices. And this is
15 really where we are right now. And this means
16 getting feedback from external and internal
17 even stakeholders and experts. And that was
18 one of the major focuses of the PDUFA
19 commitments and one of the major focuses of
20 our meeting today.

21 And then we also want to be able
22 to identify some really important priority

1 projects that will help us move toward
2 standardizing REMS.

3 And then finally once we have
4 characterized the REMS and we have identified
5 those best practices, we can really start
6 standardizing the REMS and that means actually
7 completing those projects potentially, sharing
8 findings about best practices, finding a way
9 to actually get those out there and get those
10 lessons learned incorporated into new REMS and
11 perhaps develop or update some guidance around
12 what REMS, what a standardized REMS should
13 look like.

14 So I am going to -- since
15 characterizing existing REMS is the first step
16 and something that we have been working a lot
17 on, I am going to go into a little more detail
18 on what exactly we have been doing in that
19 area. And really a lot of the need to
20 characterize REMS is driven by the fact that
21 REMS lack common definitions and clear
22 requirements in many cases. So we know that

1 the format of the REMS documents and materials
2 varies. And if you look at the background
3 materials, you will see some links and
4 attachments to REMS materials and it will give
5 you a bit of a sense of exactly how much they
6 vary and how they vary.

7 REMS also lack consistent
8 terminology. And as a simple example, we will
9 often see similar tools in REMS having
10 different names. And we will even sometimes
11 see different tools using the exact same name.

12 We have found that when we talk
13 about REMS, these regulatory terms like
14 elements to assure safe use for ETASU or
15 communication plans, they don't necessarily
16 actually provide really useful information
17 about how REMS programs work and sometimes you
18 can get caught up in regulatory questions that
19 distract you from what the REMS is actually
20 doing. So in fact when we talk about
21 standardizing REMS and the standardized tools,
22 we are going to some degree steer clear of

1 that terminology.

2 And another thing that kind of
3 drove up to try and catalogue and characterize
4 what we have in REMS is that it is not always
5 easy right now with the REMS documents that
6 are out there to find information on what is
7 expected of healthcare providers and patients.
8 You may, for example, want to know how many
9 REMS have laboratory tests, let's say. And
10 you can look in the documents and the
11 information is there and it may even be in a
12 logical place. But if you look across the
13 entire span of REMS, it can be really tricky
14 to find exactly what it is you are looking for
15 in a systematic way. And when you have those
16 sorts of unclear definitions, it can make
17 standardization really difficult.

18 And this list is an example of
19 what happens when those definitions are
20 unclear and inconsistent. And this is just a
21 small list of some of the different forms that
22 prescribers and patients are asked to fill out

1 when they actually start using a drug in a
2 REMS. And a large number of REMS have forms
3 like these. I am not meaning to pick on the
4 drugs on this list. This is just a small
5 subset but there are a lot of forms like this
6 and they all, you will probably notice right
7 away, have very different names. And they all
8 serve somewhat different functions but you
9 will also sometimes see cases where two forms
10 are serving very similar functions, for
11 example, that rosiglitazone patient enrollment
12 form includes patient agreements, prescriber
13 agreements and patient enrollments. But then
14 in the Thalomid REMS there is a patient
15 physician agreement form which contains some
16 of the very same things. So again there is
17 some logic to the name and there is some logic
18 to the REMS individually but in aggregate it
19 can become very confusing and it can become
20 difficult for stakeholders who are approaching
21 us or even us trying to think about how to
22 standardize REMS to really wrap our heads

1 around all the different variations.

2 And so what we have been doing has
3 been to try to come up with a way to better
4 describe how REMS vary. Because really before
5 we can standardize REMS, we need to have that
6 common language to describe what is in the
7 REMS and how they vary. And we have
8 catalogued and characterized a lot of the
9 documents and materials, including the text of
10 the REMS document itself, some of the
11 information about the REMS materials, for
12 instance training materials and tools, and
13 then information about specific REMS
14 requirements like the need to become
15 certified. And a lot of the results of our
16 characterization and cataloguing have been
17 included in the background materials. And
18 again, since we want to have a common language
19 to be able to talk about this, I would really
20 encourage you to take a look at those
21 background materials, if you haven't done so
22 already because it really tries to capture the

1 landscape of a REMS in a way that can help us
2 kind of have a conversation about them.

3 One of the other things that we
4 are going to be doing to try and improve how
5 we characterize and capture information about
6 REMS is we are interested in incorporating
7 REMS information into SPL or Structured
8 Product Labeling. And I should mention right
9 from the start that the term Structured
10 Product Labeling is a little bit of a misnomer
11 because the actual SPL information captures a
12 lot more than just labeling. But SPL, in a
13 general sense, is a broadly used standard to
14 capture structured information about drugs and
15 their labels. And it is developed with the
16 health of stakeholders. It is an HL7 standard
17 so there is opportunity for public input into
18 what goes into it and it is included in the
19 materials that REMS sponsors send to FDA.

20 And one of the nice things about
21 using SPL to help catalogue information about
22 REMS is that it can include marked up

1 documents themselves similar to the drug label
2 or the REMS document and then some structured
3 machine-readable information to support
4 electronic health records.

5 So if you were to kind of think
6 about what exactly does SPL mean, you could
7 almost think of it as a way of building a
8 database of what is in REMS with standardized
9 format and content and information.

10 One of the other benefits of SPL
11 is that there is already an infrastructure in
12 place to share that kind of information across
13 the healthcare systems. So when an SPL
14 document or information is submitted to FDA
15 for a drug, once that drug is approved, it is
16 actually entered into a repository that is
17 kept by the national library of medicine and
18 made available through their DailyMed website.
19 And that allows patients and the healthcare
20 providers and the public in general to be able
21 to access any information that is included in
22 SPL. And it is also able -- that information,

1 that repository provides information to the
2 healthcare information suppliers who then give
3 it to health information technology vendors.
4 And that is a way of taking REMS information
5 and incorporating it into electronic health
6 records, ePrescribing, pharmacy systems. Once
7 the information is included in SPL, it is
8 possible for it to propagate through the
9 healthcare system all the way to some of these
10 point of care tools that prescribers and other
11 healthcare providers are using.

12 And as I mentioned before, when
13 you have a standardized way of talking about
14 REMS, it really helps you develop standardized
15 REMS. And one of the things that SPL can do
16 is to help develop consistent REMS documents.
17 Through SPL you can define the exact format
18 that you would want in a REMS document and
19 make sure that that format is actually
20 followed. So it actually can facilitate
21 efficient review of these documents and that
22 allows us to have a standardized document in

1 a single point of reference for people who are
2 interested in learning more about the REMS
3 that are out there. And it also supports some
4 of our future standardization efforts because
5 it makes it a lot simpler to track how
6 different REMS tools are being used and where
7 we might actually need greater
8 standardization.

9 And SPL actually goes beyond that
10 because it really makes it easier for
11 stakeholders to implement REMS. So it is
12 actually helping us take a step towards
13 standardizing the REMs themselves by
14 clarifying what exactly it is that the REMS
15 requires of patients and healthcare providers.
16 We could use SPL to consistently describe what
17 the REMS requirements are. And is putting
18 relevant REMS information into one place. So
19 when you have the information structured in a
20 standardized format in a single place online,
21 it makes it a lot easier for stakeholders to
22 understand what REMS are and to even build

1 REMS portals with information about a wide
2 range of REMS. And then it allows that
3 information, as I mentioned before,
4 incorporated into a lot of these electronic
5 health records and health information systems.

6 So now I am going to talk a little
7 bit -- we have talked about how we are going
8 to capture and describe and define the
9 information in REMS. We talk a little bit
10 about how we can take that information and us
11 it to help us identify best practices.

12 And as I mentioned before, a lot
13 of the things that we are doing in this area
14 are related to the PDUFA commitments that we
15 made to have a public meeting and then to
16 report on our findings and develop some
17 priority projects.

18 So in the coming months and today
19 of course, we are going to be seeking
20 stakeholder and expert feedback on ways to
21 build more effective and better integrated
22 REMS tools. And we are also going to be

1 looking for more information on methods to
2 assess and characterize the risks and select
3 appropriate REMS tools or interventions. And
4 this gets back to that REMS design piece I was
5 talking about before. We want to be able to
6 look at tools like for instance perhaps
7 failure modes and effects analysis or other
8 standardized methodologies that could allow us
9 to design REMS in a more analytically rigorous
10 way and in a more standardized way. And to
11 explore this further, we are going to be
12 holding an expert workshop in the fall.

13 On the area of specific REMS
14 tools, which as I mentioned is one of the
15 major focuses of this meeting, we put out that
16 Federal Register Notice where we actually
17 asked about tools and a few areas related to
18 what stakeholders are actually dealing with.
19 So we talked about -- we had questions about
20 prescriber-directed tools, for example, what
21 are the best ways to educate and train
22 prescribers and other healthcare providers.

1 We asked about certification. How can we
2 streamline certification and enrollment into
3 REMS. And then on the area of patient-
4 directed tools, we asked what are the most
5 effective and efficient ways to educate
6 patients, especially given the wide variety of
7 information needs and learning styles that
8 patients have. And how can we improve patient
9 counseling in REMS. It is a really common
10 feature in a lot of REMS.

11 And then finally, we also asked
12 about tools and dispensing settings. How can
13 we manage certification dispensers given that,
14 again, wide variety of dispensing settings
15 that we see in REMS. And how can we make sure
16 that REMS, which have distribution controls,
17 that those are compatible with some of the
18 established systems for procurement and
19 distribution and dispensing of drugs. That is
20 something that we have heard a lot of concerns
21 about from stakeholders.

22 And then next three presentations

1 after mine will focus largely on these sorts
2 of questions and provide you with some
3 background information to help think about how
4 to approach answering those questions.

5 Another major goal for today, and
6 this gets back to some of the PDUFA
7 commitments that we made, we are looking for
8 help in identifying priority projects. And
9 these are projects that could help us identify
10 or test new ways to standardize and integrate
11 REMS.

12 And the PDUFA V commitment
13 identified four project areas. And I am going
14 to just state them exactly as they are stated
15 in PDUFA V. They have asked us to look into
16 projects in educating prescribers, providing
17 benefit-risk information to patients, pharmacy
18 systems, and then practice settings.

19 And then under PDUFA V, we have
20 committed to developing a work plan for
21 completing each project and that work plan
22 will be included in the report that follows up

1 this meeting.

2 And then finally, once we have
3 identified those best practices we have looked
4 at those priority projects, we have gotten
5 that feedback, we have characterized the REMS.
6 At that point, we are going to be able to
7 standardize the REMS. And that includes
8 completing those priority projects and sharing
9 our findings. And then perhaps developing and
10 updating guidance, as I mentioned before.

11 And as we do this, it is really
12 important for us to follow certain principles.
13 And a lot of these come from the feedback that
14 we have gotten to this point. And one of
15 those principles is to listen to stakeholders.
16 We need to work collaboratively with patients
17 and practitioners and industry and outside
18 experts to really identify the best practices.

19 We know that there are often
20 concerns about the lack of input that
21 stakeholders, healthcare providers and
22 patients have into the development REMS and we

1 see standardization as a real opportunity to
2 get their input included into REMS.

3 We also would like to build
4 evaluation into standards, make sure that we
5 are developing REMS that are measurable. As
6 we standardize the tools that we are using and
7 the approaches that we are using, we need to
8 make sure that these pieces are aligned so
9 that we actually start building an evidence-
10 base of what works and what doesn't.

11 We also need to work iteratively.
12 So we know that the healthcare system changes.
13 We know that new risks will need to get
14 addressed and we need to make sure that these
15 standards are evolving over time, as we learn
16 more about these best practices and as things
17 change.

18 And then that also relates to this
19 final point, which is we really need to be
20 flexible. As we standardize, we don't want to
21 -- we know that one size fits all is not going
22 to work. We also know that we can't make our

1 standards too rigid. We really need to be
2 able to encourage new and innovative
3 approaches.

4 And when you actually do all of
5 those things, what you can do is you get a
6 positive feedback loop in which you are really
7 continuously continuing all of the REMS. And
8 the ability to do this comes down to the kind
9 of standards that we set. When we incorporate
10 what we know about know about best practices,
11 what we have heard from stakeholders, when we
12 use common metrics, when we build lessons
13 learned into the REMS standards, we can then
14 use those standards to improve all of the
15 REMS. And then by building the evaluation
16 into the REMS standards, circle back and
17 continuously improve.

18 And with that, I am going to turn
19 it over to my colleagues who are going to go
20 into some more detail about the different
21 tools that are used in REMS and help set the
22 stage for answering some of the questions that

1 we asked in the Federal Register Notice.

2 Thank you.

3 MS. OSWELL: Thank you, Adam.

4 Good morning. My name is Kate
5 Oswell and I am a health communications
6 analyst in the Division of Risk Management.
7 And I am going to be speaking about prescriber
8 directed tools in REMS this morning.

9 My objectives today are to provide
10 an overview of prescriber-directed tools used
11 in REMS, share some of the feedback from
12 stakeholders about these tools, and finally to
13 share some promising practices.

14 REMS programs use a number of
15 tools to educate healthcare providers and
16 ensure that healthcare providers carry out
17 REMS requirements, including screening,
18 monitoring, and counseling patients.

19 Please note that the title of my
20 talk is called Prescriber-Directed Tools in
21 REMS, however, the educational tools I discuss
22 really apply to a broader category of

1 healthcare providers. These tools apply to
2 professionals that may not have actually
3 prescribed the drug, such as other physicians
4 caring for the patient, nurses, physicians
5 assistants, as well as pharmacists or any
6 other dispensers of the drug.

7 A number of different tools have
8 been used to educate healthcare providers.

9 Although produce labeling is considered a
10 tool, it is usually not a part of the REMS
11 materials and is not reviewed as part of the
12 REMS as the only educational component.

13 Therefore, my presentation today will touch on
14 the last four tools seen here that may be part
15 of a REMS program. And these consist of REMS
16 program communications, REMS training
17 materials, additional REMS materials, and
18 enrollment forms to support certification.

19 REMS program communications are a
20 tool that have been used to deliver messages
21 to healthcare providers about serious safety
22 issues, including drug risks and REMS program

1 requirements. They also include resources of
2 where to find further information.

3 The target audience of these
4 communications may be healthcare providers,
5 pharmacy representative, infusion center
6 directors, and professional societies. A
7 variety of REMS program communications have
8 included Dear Healthcare Provider letters and
9 emails, letters to professional societies,
10 fact sheets, REMS dedicated websites and
11 journal information pieces.

12 And note that journal information
13 pieces were used in previous REMS programs but
14 we have seen what the move towards electronic
15 journals with minimal advertising, these have
16 not been used in more recent REMS programs.

17 Training materials are another
18 tool used in REMS programs. They provide
19 comprehensive training on the risks addressed
20 in REMS and how to mitigate these risk. And
21 they explain how the REMS program operates and
22 describe the prescriber roles and

1 responsibilities.

2 Healthcare providers are usually
3 expected to review the training materials
4 prior to prescribing and dispensing the drug.
5 Some examples include program overviews,
6 prescriber guides, and training modules such
7 as slide decks.

8 REMS programs have used a variety
9 of delivery methods to disseminate training
10 components. This may be in person or over the
11 phone, print or electronic form, such as
12 online or DVD versions and may be with or
13 without an audio component.

14 REMS programs offer different
15 training options, as providers have different
16 learning styles, as well as various
17 limitations with access to these materials.
18 For example, rural areas may not have access
19 to in-person training or online training at
20 the office.

21 REMS have also included additional
22 materials to address specific issues related

1 to the safe use of the drug, as well as
2 enabling tools to support ongoing patient
3 care. For example, a checklist may be used to
4 solicit information about a patient's risk
5 factors for an adverse event, or their
6 likelihood of benefitting from the drug to
7 inform prescribing decisions.

8 A counseling tool may be used to
9 guide a conversation with the patient about
10 the benefits and risks of different therapies
11 to determine if a REMS drug is appropriate or
12 inform the patient about the safe use of the
13 drug and any actions to take. And dosing and
14 administration guides have been used to
15 support ongoing care.

16 Enrollment forms are used to
17 enroll the prescriber into the REMS program.
18 These forms collect prescriber demographic
19 information and include acknowledgments and
20 agreements that the provider has met the
21 requirements for certification and will adhere
22 to the REMS requirements. Enrollment forms

1 allow sponsors to track certification of
2 healthcare providers and communicate with them
3 about the REMS program. They allow the
4 sponsor to monitor or audit compliance with
5 REMS program requirements and agreements on
6 these forms reinforce key messages from the
7 training through the certification process.

8 Some of the feedback that we have
9 heard from stakeholders are to offer different
10 options for training. And we have heard that
11 including an option for in-person training
12 initially and then online for certification
13 may be helpful. Others have desired both
14 online and print options for different
15 preferences and learning styles.

16 We have also heard from
17 stakeholders to standardize enrollment forms,
18 including limiting the length of the forms.
19 And then of course we have heard that
20 streamlining the processes will reduce burden.
21 And some stakeholders have stated that having
22 a one-stop website for all REMS programs in

1 one place to find further information is
2 helpful, as well as having an option for
3 patient enrollment through the REMS website at
4 the physician office which could reduce burden
5 on both the patient and the prescriber.

6 Here are what was see as some
7 promising practices with REMS programs.
8 Offering CE credit for REMS training.
9 Currently we are exploring this option as part
10 of REMS programs; including checklists in REMS
11 programs are helpful to healthcare providers,
12 as well as quick summaries that describe the
13 REMS programs and the role of the healthcare
14 provider; and lastly, having a single web
15 portal for similar programs can reduce the
16 burden in regards to prescriber certification.

17 We look forward to hearing from
18 you today. Thank you.

19 MS. TAVAKOLI: Good morning. My
20 name is Ana Tavakoli and I am a health
21 communications analyst in the Division of Risk
22 Management within the Office of Surveillance

1 and Epidemiology. I am going to be speaking
2 about patient-directed tools in REMS today.

3 The objectives of my talk are to
4 provide an overview of patient-directed tools
5 in REMS, to share feedback from stakeholders
6 about patient-directed tools, and to show the
7 importance of consumer testing materials prior
8 to dissemination.

9 REMS programs use a number of
10 tools to educate and counsel patients, provide
11 patients with information about the risks of
12 the drug, and to help ensure that patients use
13 the drug safely.

14 At the present time, patient-
15 directed REMS tools include the following:
16 Medication Guides; patient print materials,
17 which include patient guides, booklets,
18 overviews in brochures; counseling tools,
19 which may be part of prescriber or healthcare
20 provider training materials; Patient-
21 Prescriber Agreement Forms, also referred to
22 as PPAFs or PAFs, short for patient agreement

1 forms; patient enrollment forms; and REMS-
2 dedicated websites.

3 I will now discuss each tool
4 further. Medication Guides are the most
5 frequently used patient educational medication
6 materials in REMS. Their purpose is to
7 provide information when the FDA determines in
8 writing that it is necessary to patient's safe
9 and effective use of a drug product. They are
10 usually about one to eight pages long, with a
11 format consisting of text and bulleted
12 statements for ease of readability. MedGuides
13 are provided to patients by the pharmacist or
14 healthcare provider or can also be accessed by
15 the patient on the FDA and REMS-dedicated
16 website. It should also be noted that in REMS
17 elements to assure safe use or ETASUs,
18 prescribers or healthcare providers may be
19 asked to review the Medication Guide with
20 patients and use them in patient counseling.

21 REMS print materials include
22 patients guides, booklets, overviews, and

1 brochures. Their purpose is to focus on REMS
2 risk and REMS program information.

3 Prescribers may use these tools to counsel
4 patients on risk and facilitate discussions.
5 Their length has varied anywhere from two to
6 eighteen pages, depending on the risk and
7 requirements of the REMS program. Their
8 format consists of text, bulleted statements,
9 tables, and graphics. They are provided to
10 patients by the healthcare provider and can
11 also be downloaded from a REMS-dedicated
12 website.

13 Counseling tools and printed
14 material is used by healthcare providers to
15 counsel patients about the safe use of a drug.
16 They include the risk of a drug, patient
17 responsibility, and encourage patient-
18 prescriber discussions. They are usually
19 about one to two pages long, with a format
20 consisting of text, bulleted statements, and
21 tables. These tools are provided to patients
22 by healthcare providers.

1 Patient-Prescriber Agreement Forms
2 or PPAFs also referred to as PAFs, short for
3 Patient Agreement Forms, are used to document
4 that an informed discussion of the drug's
5 benefits and risks took place and that the
6 patient understands the risk and REMS program
7 requirements. Patient-Prescriber Agreement
8 Forms support patient counseling by providing
9 information for prescribers to review with
10 patients. They are usually about one to two
11 pages long with a format consisting of text
12 and bulleted statements for ease of
13 readability. PPAFs are given to the patient
14 by the healthcare provider or prescriber and
15 signed by both patient and prescriber to
16 reinforce understanding of the risk message.

17 Patient enrollment forms contain
18 agreements and acknowledgments of safe use
19 conditions. They are used to enroll patients
20 into REMS programs in order to receive the
21 drug. Patient enrollment forms also allow
22 sponsors to track patients and ensure that

1 only those who have completed the form and are
2 enrolled in the REMS program can obtain the
3 drug. Patient enrollment forms are the same
4 length and follow the same format as the
5 Patient-Prescriber Agreement Form and are
6 given to the patient by the healthcare
7 provider.

8 As you heard earlier from my
9 colleagues, in the past few months the FDA has
10 received feedback from patients. And these
11 are some examples of what patients say about
12 REMS programs. Patients state that repeated
13 counseling by a healthcare provider can be
14 beneficial in helping them retain information.
15 They would like to see more straightforward
16 patient documents, such as a checklist.
17 Patients also want to be offered a variety of
18 tools, including both print materials and
19 digital media, such as apps for phones and
20 tablets and websites with essential portal
21 directed only to patients.

22 In addition and naturally, they

1 perform materials that are patient-friendly,
2 and written at an appropriate reading level.

3 The Agency has seen modifications
4 submitted by sponsors based on consumer
5 testing of REMS materials that have shown
6 improvements in them. Some REMS materials
7 that have been previously tested by sponsors
8 include the Patient Provider Agreement Form
9 and a REMS dedicated website.

10 Results of consumer testing
11 materials indicate that patients prefer forms
12 that are formatted for easier readability and
13 understandability. For example, including
14 more shading and boxes to define sections of
15 the form. Materials in which both risks and
16 benefits of drugs are clearly defined and
17 materials in which the content is written
18 using plain language principles.

19 Since improvements can often be
20 made when materials are pre-tested with
21 patients prior to dissemination, we encourage
22 sponsors to test their materials prior to

1 submitting them for review.

2 This concludes my presentation.
3 We are looking forward to our stakeholders for
4 help in ways to improve REMS materials and
5 information dissemination. Thank you.

6 MS. MONCUR: Good morning. I am
7 Megan Moncur from the Division of Risk
8 Management and I am going to be talking about
9 dispensers and dispensing settings in REMS.

10 So I am going to spend the
11 majority of my presentation providing an
12 overview of dispensers and dispensing settings
13 in REMS. And I am going to talk a little bit
14 about the variability across these different
15 settings. And because of that variability, my
16 presentation is going to have a little bit
17 different focus than those that came before
18 for prescribers and patients. And I am going
19 to be focusing on the role of these different
20 dispensers and dispensing settings in REMS and
21 the requirements for dispensers.

22 Then, as with my previous

1 colleagues, I am going to share some example
2 feedback that we have received and also share
3 some promising practices.

4 So drugs are dispensed in a wide
5 range of settings. They are dispensed in
6 pharmacies, hospitals, and outpatient clinics.
7 And as you can see even just from the limited
8 examples I have included here on this list,
9 there are different types pharmacies. There
10 are different types of outpatient clinical
11 settings. And each has their own set of needs
12 and faces unique challenges.

13 However despite this diversity,
14 there is one feature that they all have in
15 common as dispensers. And that is, they are
16 often the final checkpoint before a drug is
17 administered to a patient.

18 So how is this critical role that
19 dispensers and dispensing settings play in the
20 patient care process. How is that
21 incorporated in REMS?

22 So I am first just going to

1 provide some general requirements and then in
2 subsequent slides, I will provide some
3 specific requirements. So REMS may require
4 all or any of the following: practitioners or
5 dispensing settings that dispense a drug are
6 specially certified. And by specially
7 certified, that means that the dispenser is
8 going to have meet certain requirements, such
9 as being trained or enrolling in the REMS.
10 Additionally, REMS may require that the drug
11 is dispensed only in certain healthcare
12 settings, such as in a hospital. Or the REMS
13 may require that the drug is only dispensed
14 after the dispenser has verified documentation
15 or evidence of safe use conditions. So that
16 may be lab test results or that may be
17 verifying that the prescriber is certified or
18 that the patient is enrolled.

19 Okay, so moving into the specific
20 requirements. Just for the purposes of this
21 presentation, we have organized these
22 requirements by what a dispenser needs to do

1 to be certified to be able to dispense a drug.
2 Sometimes we refer to these as startup
3 requirements. Then next what dispensers might
4 have to do on a day to day basis. So what
5 might dispensers be required to do at the time
6 of dispensing. And then finally, what are
7 some things that dispensers may need to
8 periodically do to maintain compliance with
9 the REMS.

10 Okay, so to be certified to
11 dispense, dispensers may be required to
12 designate an authorized party who would enroll
13 the facility. They may be required to train
14 or ensure that their staff are trained. They
15 may be required to enroll. And they may be
16 required to establish systems or modify
17 existing systems and processes to comply with
18 REMS requirements.

19 So for example, they may have to
20 modify existing system for tracking and
21 training of their staff or they may have to
22 create a new system. And they might have to

1 modify their process for procuring some
2 medications because some REMS do include
3 distribution controls.

4 So once a dispenser is certified,
5 there are some things that they may need to do
6 at the time of dispensing before the drug is
7 dispensed. And one of those is verify
8 documentation of safe use conditions. And so
9 as we have mentioned before, that could
10 include verifying lab results or verifying
11 that the prescriber is certified. Now what
12 that also involves is they may be asked to
13 record or document that they have verified
14 that the safe use conditions are present and
15 that may be a manual process. And the other
16 component of this is that they may have to
17 resolve verification failures. So what we
18 mean by that is that if they are going to
19 dispense a drug and they find out that a
20 prescriber isn't certified or the lab tests
21 aren't available, then that is going to take
22 some time for them to potentially sort that

1 out. And additionally, they may be asked to
2 provide a Medication Guide or provide patient
3 counseling.

4 And finally, there are some things
5 that dispensers may be required to do
6 periodically in order to maintain their
7 certification. So they may be required to re-
8 enroll. They may be required to train new
9 staff as they come onboard. They may be
10 required to participate in audits and also
11 they need to be aware of any new or modified
12 REMS requirements that may need to be
13 implemented.

14 So I have just covered some of the
15 common requirements that dispensers encounter
16 in REMS. However, there are some things that
17 we, in our experience with REMS, have
18 determined that impact our decisions in what
19 we require and how those requirements are
20 implemented. So different features or
21 dimensions that vary across these different
22 settings.

1 So for example, the role that the
2 dispensing setting plays in the care process.
3 And some dispensing settings dispense directly
4 to a patient and other will dispense to a
5 healthcare provider who will administer to a
6 patient.

7 Existing safe use controls. So
8 what we mean here is what is already present
9 in that context of care to assure safe use of
10 the drug. So if you compare the outpatient
11 setting to an inpatient setting, you can
12 imagine that in the inpatient setting there
13 might be controls to both monitor a patient
14 for adverse events or treat a patient if an
15 adverse event should occur.

16 And in terms of existing
17 electronic health systems, this is things like
18 pharmacy management systems or electronic
19 health records. And in some REMS, these
20 systems can be leveraged to automatically
21 either document or verify safe use conditions.

22 Corporate or organizational

1 structure. So is the dispensing setting
2 independent or is it part of a larger system?
3 And so for example, is it a chain pharmacy or
4 is it an independent pharmacy? Is it an
5 independent hospital or is it part of a larger
6 hospital health system?

7 And understanding that has
8 implications for choices about what we refer
9 to as level of certification. So who needs to
10 be certified? Is it the pharmacist or is it
11 the pharmacy? Is it the hospital or is it the
12 hospital system?

13 And related to organizational
14 structure is whether the dispensing setting is
15 part of an integrated or closed healthcare
16 system because that has implications for how
17 the healthcare system might communicate with
18 the REMS system.

19 And the procurement process. So
20 as Adam has already stated, we at FDA need to
21 make sure that REMS are compatible with
22 existing procurement and distribution systems.

1 So it becomes especially important to
2 understand this if a REMS includes
3 distribution controls.

4 And in terms of transitions of
5 care, so thinking of a transition between an
6 inpatient setting and an outpatient setting,
7 REMS can impact transitions of care and they
8 can do that -- they can either facilitate that
9 or it might interrupt that. So you need to be
10 very aware of that.

11 So although there is this
12 diversity across these different settings and
13 across dispensers, we have heard some common
14 themes in our feedback. And further, these
15 themes highlight this principle of balancing
16 standardization of REMS, implementation in a
17 unique dispensing setting.

18 So first of all, we have heard
19 that REMS need to clearly and concisely convey
20 what dispensers are required to do. And the
21 information that is conveyed needs to be
22 relevant to that dispenser.

1 Additionally, REMS processes
2 should be automated and integrated into the
3 workflow. We have heard a lot from
4 stakeholders that manual processes lead to a
5 lot of interruptions in their workflow. REMS
6 requirements should be customized to the
7 different dispensing settings. And further,
8 dispensers want flexibility in how REMS
9 requirements are implemented.

10 So we have seen some promising
11 practices or some promising approaches to how
12 -- that have actually addressed some of the
13 feedback that we have received from
14 stakeholders.

15 So for example, some examples
16 where REMS have been integrated into the
17 existing systems and workflow, some REMS have
18 used inpatient order sets to either document
19 or verify safe use conditions. Additionally,
20 we have a REMS that uses the outpatient
21 pharmacy management system and the claims
22 process to automatically verify that

1 documentation of safe use conditions has
2 occurred.

3 And finally, we have REMS that
4 provide instructions on how to adapt a
5 particular REMS form to be compatible with an
6 existing healthcare system. So again, that
7 speaks to flexibility and implementation.

8 And then some examples of setting
9 specific customization. So we have several
10 REMS that have different requirements for
11 outpatient and inpatient pharmacies, which
12 again sort of speaks to that existing safe use
13 controls that may be available.

14 And also we have customized
15 processes for clothes or integrated systems,
16 so that their systems -- so that they can
17 participate in a REMS, even if their system
18 does not communicate with it.

19 And finally we have taken standard
20 forms, like an enrollment form and customized
21 it for independent pharmacies, chain
22 pharmacies or closed system pharmacies.

1 So these are what we consider some
2 promising practices that both speak to
3 standardizing REMS and also customizing them
4 for different dispensing settings but we look
5 forward to hearing from you to hear some other
6 ideas. And with that, I will turn it over to
7 Terry.

8 MS. TOIGO: Okay, so we set this
9 panel up again to walk people through the
10 background document and also to highlight some
11 of the challenges that we are going to face
12 with standardization.

13 So if you have had experience with
14 REMS, you may have had experience with a
15 particular REMS but hopefully these
16 presentations have highlighted the variability
17 in patient tools, in prescriber tools, and the
18 diverse dispensing settings that we need to
19 consider as we think about standardization.

20 So my FDA colleagues have been
21 disciplined in keeping to their time
22 constraints and that leaves us in the unusual

1 position of being finished early with this
2 session and giving you a half hour break. So
3 as opposed to 15 minutes, you get a half hour.
4 Hopefully, the coffee is available. Extra
5 time for networking, since we only have -- we
6 may have a shortened lunch. And the reason we
7 are not going to speed up is because the next
8 panel is our public panel and we don't want --
9 our public panel had expectations as to what
10 time they had needed to be here and we don't
11 want to start a panel without them here.

12 So you will start back at 10:30
13 and we will get organized before but we will
14 start right at 10:30.

15 So thank you and I hope this has
16 walked you through the background document and
17 stimulated some thinking and will encourage
18 you to give us additional feedback.

19 (Whereupon, the foregoing
20 proceeding went off the record at 9:48 a.m.
21 and went back on the record at 10:30 a.m.)

22 MS. TOIGO: This is our first

1 panel and they are going to be addressing
2 general standardization issues. And we have
3 seven speakers. Each of them are going to
4 spend -- or they have been allotted ten
5 minutes. And then we have time for FDA
6 questions at the end of the presentations.

7 So I think our speakers know the
8 drill. You have got ten minutes. At eight
9 minutes, the yellow light will come on. So
10 that is two minutes left. And red will come
11 on when your ten minutes are done. And at
12 that point, it is time to think about wrapping
13 up and turning it over to the next speaker.

14 So I think Sarah Spurgeon from
15 PhRMA is our first presenter. And I don't
16 think you have any slides, Sarah, right?

17 MS. SPURGEON: Right.

18 MS. TOIGO: Okay.

19 MS. SPURGEON: Hi, good morning.
20 I am Sarah Spurgeon, Assistant General Counsel
21 of PhRMA.

22 PhRMA is a voluntary, non-profit

1 association that represents the country's
2 leading pharmaceutical, research, and
3 biotechnology companies. We are dedicated to
4 developing medicines that allow patients to
5 live longer, healthier, and more productive
6 lives.

7 In 2012 alone, PhRMA members
8 invested approximately \$50 billion in
9 discovering and developing new medicines. We
10 represent the vast majority of private
11 investment in biopharmaceuticals in the United
12 States.

13 For PhRMA and its member
14 companies, protecting patient safety and
15 enhancing the implementation of REMS are of
16 utmost importance. PhRMA appreciates the hard
17 work of FDA and its recent efforts to fulfill
18 its commitments under PDUFA V. PhRMA,
19 however, remains concerned that REMS programs
20 can create an undue burden on the healthcare
21 system, limiting appropriate use of and access
22 to much needed medical treatment. We

1 appreciate this opportunity to convene with
2 stakeholders to discuss ways to improve the
3 implementation of REMS. In doing so, we hope
4 to promote patient safety and public health.

5 During this morning's panel, PhRMA
6 will comment on FDA's efforts to develop
7 analytically rigorous approaches to
8 standardizing REMS programs. Tomorrow
9 afternoon, we will comment on the Agency's
10 efforts to develop a consistent evidence-based
11 approach for evaluating the effectiveness of
12 REMS programs.

13 PhRMA and our member companies
14 share FDA's views that standardization can
15 make REMS more predictable, easier to measure,
16 and may improve stakeholder compliance.
17 However, PhRMA believes that some variation
18 and flexibility in REMS is necessary and
19 appropriate to address specific risks posed
20 by particular drugs and a wide range of
21 patient populations in healthcare settings.
22 And it is recognized that standardization

1 alone cannot mitigate the need for strong
2 sponsor stewardship over a product's REMS.

3 For REMS elements that are
4 amenable to standardization, PhRMA would like
5 to share the following specific comments:

6 1) PhRMA believes that similar
7 risks can and should be regulated in a
8 comparable manner. For example, FDA should
9 use the same REM elements across products that
10 share similar risks. Such elements should be
11 the least burdensome possible to achieve risk
12 minimization. PhRMA recommends that FDA work
13 to design general REMS templates and tools for
14 elements that address similar risk, as well as
15 a mechanism to share such standardized
16 materials with stakeholders.

17 In developing these templates and
18 tools, PhRMA supports collaboration with
19 stakeholders who have experience in developing
20 and disseminating standardized information.
21 Possible stakeholders included standard
22 development organizations, third-party drug

1 information providers, professional societies,
2 accreditation organizations and continuing
3 medical education programs. Once finalized,
4 FDA should articulate in guidance the
5 circumstances under which such standardized
6 REMS, tools and templates are required.

7 2) Importantly, before any
8 standardized tools are deployed, FDA should
9 conduct user testing and make the results
10 available publicly for comment. Furthermore,
11 the standardization process should remain
12 sufficiently flexible to allow for the
13 innovation of new tools and methods, which can
14 help to further improve REMS programs.

15 3) PhRMA members support the
16 exploration of greater technology utilization
17 to better integrate REMS into the existing
18 healthcare setting. Any technology promoted
19 must not disrupt the normal practice and
20 workflow of the healthcare professional. For
21 example, PhRMA encourages FDA to consider
22 innovative technology platforms, such as

1 mobile applications. PhRMA also suggests that
2 FDA explore the integration of REMS into
3 existing healthcare information systems, such
4 as EMRs and also to partner with companies
5 that provide timely medical information to
6 practitioners.

7 To gain insights on feasibility,
8 PhRMA supports FDA's efforts to identify high
9 quality projects that could offer stakeholders
10 the opportunity to develop, test, and
11 implement new approaches to standardizing REMS
12 utilizing healthcare IT.

13 4) While PhRMA believes that
14 standardization as a whole can reduce the
15 burdens of REMS, FDA should still allow
16 sponsors, without the need for prior approval,
17 to make minor administrative and editorial
18 adjustments. For example, moving from a paper
19 form to a web-based system can improve the
20 enrollment process. Another example is a
21 sponsor adding a phone number to a phone to
22 improve data collection. Such minor changes

1 create a more efficient REMS without altering
2 the underlying risk-benefit balance.

3 As PhRMA is not presenting during
4 the prescriber standardization session, we
5 would like to share a few general comments on
6 that topic now. With the caveat that
7 different clinical specialties or disease
8 areas may warrant flexible approaches to
9 prescriber interaction, PhRMA believes that
10 there can be certain common elements to REMS
11 communications to assist with prescriber
12 comprehension. Such common elements could
13 include:

14 1) An FDA design REMS brand or
15 logotype that sponsors would include on all
16 REMS communications to prescribers. This
17 easily identifiable brand or logo would alert
18 prescribers that the communication relates to
19 a REMS program.

20 2) A standardization for
21 frequently used REMS communications, such as
22 Dear Healthcare Provider letters should be

1 used. This template could incorporate
2 elements such as standardized font and page
3 design.

4 3) There should be a common one-
5 stop shop internet location where prescribers
6 could access REMS information online. For
7 example, the current FDA portal listing
8 approved REMS could be amended to include
9 links to each product's REMS website, if
10 available.

11 4) Streamlined prescriber
12 enrollment forms that eliminate duplicative
13 information contained in the prescriber
14 training material would be appropriate. While
15 streamlining the form, flexibility should be
16 retained for the prescriber to complete and
17 submit such form by fax, email, mobile app, et
18 cetera.

19 In conclusion, PhRMA appreciates
20 the efforts of FDA in organizing today's
21 meeting. We hope to continue to serve as a
22 constructive partner, together with other

1 stakeholders, as the Agency continues to
2 implement its REMS authorities.

3 Thank you.

4 MS. TOIGO: Thank you, Sarah.

5 Next we will hear from Andrew
6 Emmett from BIO.

7 MR. EMMETT: Good morning and on
8 behalf of the Biotechnology Industry
9 Organization, thank you for the opportunity to
10 provide comments on the issues and challenges
11 associated with the standardization and
12 assessment of Risk Evaluation and Mitigation
13 Strategies for drug and biological products.

14 BIO supports FDA's ongoing PDUFA V
15 initiatives to identify potential projects
16 that may help to standardize REMS and
17 integrate them into the healthcare delivery
18 system.

19 BIO represents more than 1,100
20 biotechnology companies, academic
21 institutions, state biotechnology centers, and
22 related organizations across the U.S. and in

1 30 other nations.

2 BIO has long advocated for a
3 holistic approach to drug safety. And the
4 PDUFA V framework demonstrates industry's
5 commitment to a lifecycle approach to product
6 evaluation by strengthening FDA's post-market
7 surveillance and benefit-risk management
8 capacity.

9 Drug safety is not absolute but
10 rather a matter of balancing a drug or
11 biologics predicted benefits against known
12 risks. A product is considered safe if it has
13 an appropriate benefit-risk balance for the
14 intended population and use. And REMS
15 programs can play an important role in
16 minimizing risk to maximize the drug's
17 potential benefit-risk profile.

18 Effective risk management
19 approaches including REMS can help facilitate
20 appropriate patient access to efficacious
21 therapies with known safety issue that may not
22 otherwise receive FDA approval.

1 As the Agency continues its
2 efforts to make REMS less burdensome to all
3 stakeholders and more predictable and simpler
4 to understand, implement, and measure, BIO
5 asked the agency to keep in mind the following
6 principles.

7 First, FDA sponsors should
8 communicate about REMS and risk management
9 strategies as early as possible in the review
10 cycle. Second, comprehensive REMS
11 implementation efforts should be reserved for
12 REMS with elements to assure safe use
13 programs. Third, standardization should
14 include establishing a standard set of best
15 practice principles, regarding the design,
16 development, testing, implementation,
17 evaluation, and modification and termination
18 of REMS tools. And finally, REMS program
19 effectiveness assessments should evaluate the
20 totality of the REMS programs.

21 I am going to speak to each of
22 these in a bit more depth. First, to better

1 standardize a REMS program, it is critical
2 that FDA and sponsors initiate risk management
3 planning and dialogue early and often during
4 product development and the FDA review phase.
5 FDA and sponsor require an understanding of
6 when and how to communicate regarding the
7 potential REMS. For this reason, the PDUFA V
8 NME Review Program provides structured
9 opportunities for FDA-sponsored communication
10 at key points in the review, including the
11 pre-NDA/BLA meeting, the mid-cycle
12 communication and the late cycle meeting.

13 The program also promotes early
14 cross-disciplinary engagement by staff of
15 FDA's Office of New Drugs and Office of
16 Surveillance and Epidemiology to assess if a
17 REMS is needed to mitigate a potential safety
18 issue.

19 By proactively discussing risk
20 management strategies and potential REMS
21 earlier, FDA sponsors can reserve adequate
22 time in the review process to develop an

1 optimized and standardized REMS program that
2 could minimize the burden on the healthcare
3 delivery system. BIO is looking forward to
4 the release of the independent contractor
5 evaluation of the NME Review program in 2015.
6 So it would have been better assessed if risk
7 management discussions are in fact taking
8 place earlier than previous experience.

9 We also look forward to evaluating
10 how early communication of draft REMS
11 proposals can align with application
12 requirements for assuring that commitments for
13 a complete application are made at the pre-
14 submission and have been addressed.

15 Second, to ensure that an approved
16 REMS can be efficiently and effectively
17 implemented, BIO believes that REMS efforts
18 should be reserved primarily for REMS programs
19 that include elements to assure a safe use or
20 ETSU. Many approved REMS consist only of
21 communication-based risk management
22 strategies, rather than more restrictive ETASU

1 tools. For example, as of July 2013 only 36
2 of 72 approved REMS included ETASU while the
3 remaining 50 percent of REMS focused solely on
4 patient and provider communication elements
5 through MedGuides and communication plans
6 only.

7 BIO believes that patients and
8 physicians need timely accurate and relevant
9 information about the benefits and the risks
10 of the drug, so that they can make well
11 informed choices about therapies. But we
12 think that more meaningful progress and
13 effectively communicating benefit-risk can be
14 achieved through complementary mechanisms
15 outside of REMS programs. For example, BIO
16 supports FDA's ongoing initiative to develop
17 patient medication information or PMI, a
18 single unified patient benefit-risk
19 communication tool that would minimize
20 redundancies and public confusion around the
21 distribution of MedGuides, patient package
22 inserts and consumer medication information.

1 Additionally, FDA's November 2011
2 guidance clarifying that MedGuides can be
3 administered outside of the context of a REMS
4 program was an important step in improving the
5 efficiency of the REMS framework. We
6 encourage FDA and stakeholders to also
7 evaluate whether effective and efficient
8 benefit-risk communication is better achieved
9 by limiting communication plans to ETASU REMS
10 to explain restricted distribution plans to
11 patients and provides and by implementing
12 routine benefit-risk communication to all non-
13 ETASU drugs outside of the context of REMS
14 programs.

15 These various approaches have the
16 dual benefit of enhancing benefit-risk
17 communication towards patients and provides
18 while reserving comprehensive REMS
19 implementation efforts for ETASU programs, so
20 that all stakeholders in the healthcare system
21 can focus limited attention and resources on
22 the most critical risk minimization

1 activities.

2 With this in mind, we suggest that
3 priority projects for standardizing risk
4 management tools under the REMS and
5 integration initiative should focus primarily
6 on ETASU REMS elements.

7 Third, BIO supports FDA's efforts
8 to standardize REMS where appropriate with the
9 goal of reducing burden on implementing REMS
10 on practitioners, patients, and other various
11 healthcare settings.

12 While REMS standardization can
13 help eliminate unnecessary variation between
14 REMS programs, it should be noted that
15 standardization for the sake of
16 standardization alone is not always consistent
17 with best practices for managing the diverse
18 risks associated with different types of drugs
19 and biologic products.

20 BIO recommends a standard set of
21 best practice principles regarding the design,
22 development, testing, and implementation,

1 evaluation, modification, and termination of
2 REMS tools, which will promote program
3 stability, while at the same time preserving
4 the necessary flexibility to address and
5 mitigate product-specific risks and associated
6 REMS goals. These principles should include
7 a shared understanding between FDA and
8 sponsors of the standard principles and
9 methods used by FDA to assess and characterize
10 risk and related appropriated REMS tools or
11 interventions.

12 BIO looks forward to working with
13 FDA to develop these best practices and to
14 ensure they are based on practical evidence of
15 the latest advancements of the science of
16 pharmaceutical risk management.

17 And finally, BIO supports
18 development of an evidence-based approach to
19 the measuring the effectiveness of REMS. BIO
20 believes that any successful program
21 assessment requires FDA and sponsor
22 understanding and prior agreement on outcomes

1 goals. Without such shared understanding and
2 agreement, assessment tools may not properly
3 measure and capture whether any given program
4 is appropriately mitigating the identified
5 risk necessarily to ensure that a drug
6 product's benefits outweigh those particular
7 risks. BIO also believes that it is important
8 for any assessment to evaluate the totality of
9 the REMS program. For example, while the
10 availability of information about a drug can
11 empower a patient to make sound decisions
12 about his or her health, it should be
13 understood that patient knowledge of a
14 specific risk does not always translate into
15 actual behavioral change that can in fact
16 minimize the risk involved. This fundamental
17 limitation should be acknowledged when
18 assessing REMS tools and medical outcomes,
19 especially in light of reliance on assessment
20 surveys that measure understanding, as opposed
21 to behavior.

22 A holistic approach to assessment

1 should, therefore, also include measures of
2 implementation fidelity such as engagement
3 with and adherence to program-specific
4 processes and procedures put in place to
5 control exposure to risks and ensure proper
6 use.

7 It is also important to recognize
8 that program assessment tools can then
9 themselves place a burden on the healthcare
10 delivery system, including patient prescriber
11 and dispenser time and resources. As FDA
12 reliance on REMS grows, the effectiveness of
13 REMS programs and the burden on the overall
14 healthcare delivery system must be carefully
15 measured. The effect of system burden
16 measurements requires the collection and
17 review of standard data that also look across
18 programs, products and tools.

19 As sponsors are but one part of
20 the healthcare delivery system and have
21 limited access to such data, FDA and other
22 REMS stakeholders should collaborate in

1 collecting and evaluating system-related
2 burden data to judge whether a particular REMS
3 program or tools overburdens the healthcare
4 system and modify the REMS requirements
5 accordingly.

6 In conclusion, BIO appreciates
7 this opportunity to comment on REM
8 standardization and we look forward to
9 continuing to work with FDA and other engaged
10 stakeholders to further streamline REMS
11 programs and minimize the burden on the
12 healthcare delivery system. And we plan on
13 submitting written comments to the docket.

14 Thank you very much.

15 MS. TOIGO: Thank you, Andrew.

16 Next we will hear from Paul
17 Sheehan of Celgene Corporation.

18 MR. SHEEHAN: Good morning. May
19 name is Paul Sheehan and I am the head of the
20 U.S. REMS Department of the Biopharmaceutical
21 Company Celgene Corporation. I would like to
22 thank the FDA for providing the opportunity to

1 share some of our perspectives regarding REMS
2 standardization and assessment.

3 At Celgene, Safety is a hallmark
4 of our commitment and our responsibility to
5 improve the lives of patients worldwide.
6 Beginning in 1998 in the absence of an
7 existing model to reference, Celgene created,
8 developed, and introduced the Thalomid Steps
9 Risk Management Plan, followed by a RiskMAP
10 for Revlimid called RevAssist in 2005. In
11 2008, both programs became the deemed REMS
12 that include elements to assure safe use and
13 implementation systems. Earlier this year, we
14 developed and introduced the third REMS
15 program, the Pomalyst.

16 REMS programs are introduced for a
17 particular drug to ensure its benefits
18 outweigh its risks. The goals addressed by
19 the program components are unique to each
20 REMS. Therefore, to increase efficacy and
21 reduce patient and physician burden,
22 standardization should be a desired policy

1 goal only in situations where the risk of the
2 drug, the target populations, and the REMS
3 designs are similar.

4 Celgene supports the
5 recommendations that PhRMA and BIO presented
6 at the December 2012 FDA public hearing about
7 teratogenic drugs and risk management, which
8 supported that REMS programs can be
9 standardized and at the same time retain
10 flexibility in approaches given drug benefits,
11 risks, characteristics, disease, et cetera.

12 While we recognize that certain
13 components of a comprehensive REMS program may
14 benefit from standardization, we support the
15 FDA's approach in designing specific solutions
16 to each specific REMS situation.

17 REMS programs are typically
18 designed after extensive industry
19 collaborations. The success of a REMS program
20 is not measured in the first few months after
21 their initial release but is continuously
22 assessed throughout the lifespan of the

1 program. Ensuring the REMS program is focused
2 on achieving the stated objectives, analyzing
3 results for continuous improvement, and
4 evaluating proposed future enhancements is of
5 vital importance. To ensure an effective
6 execution of these concerns, they are most
7 appropriately managed by a single accountable
8 party.

9 In February of this year, Celgene
10 introduced standardized and harmonized REMS
11 programs for Revlimid, Pomalyst and Thalomid.
12 Patient and prescriber enrollment forms were
13 standardized, simplified, and technology was
14 introduced to help increase completion
15 accuracy and reduce the necessary burden.
16 Redesigning the patient enrollment forms to
17 ensure they are easily understood by providing
18 content at the eighth grade level has reduced
19 processing times by about 25 percent per form.

20 Celgene introduced the FDA's
21 recommendations for standard terminology. We
22 changed the titles of our patient risk

1 categories and REMS program names across our
2 educational materials, forms, and computer
3 systems. We expect that the transition period
4 for these changes may take up to 12 months.

5 As the FDA considers further
6 changes to the REMS environment, due
7 consideration must be given to the
8 implementation challenges of educating,
9 distributing, and implementing changes to
10 established REMS practices.

11 As part of our harmonization
12 initiative, Celgene introduced an option or
13 comprehensive online solution for prescribers
14 to manage their REMS activities for our
15 products. Celgeneriskmanagement.com provides
16 a single site to obtain educational material,
17 enrollment to any of our REMS programs,
18 complete necessary REMS transactions and view
19 an activity dashboard that highlights next
20 steps.

21 This integrated environment offers
22 tremendous advantages to the prescribers who

1 choose or are able to use it, as it delivers
2 timely reminders and alerts and reduces the
3 overall REMS administration processing time.

4 Although technology may offer
5 advantages to some of the challenges facing
6 REMS programs, it is vital to remember that
7 the lowest common denominator for any REMS
8 implementation system must continue to be a
9 fax machine.

10 To facilitate future innovation
11 within the implementation of existing REMS
12 programs, we ask that FDA provide guidance on
13 how companies with approved REMS can
14 initiative pilot projects without requiring
15 these ideas to be formally included in the
16 REMS before they have proven to be successful.

17 Celgene is interested in pursuing
18 discussions with representatives of the
19 pharmacy industry to see how the REMS
20 information is required to be sent to Celgene
21 during a dispense, can be entered into and
22 delivered from their pharmacy management

1 system. Such an approach will integrate REMS
2 transactions into existing workplace systems.

3 Similarly, analysis should be
4 conducted into how data elements from
5 prescribing systems could be utilized for REMS
6 purposes, how alerts could be provided to
7 practitioners when they are prescribing a REMS
8 drug and how ePrescriptions could be delivered
9 to a certified REMS pharmacy for fulfillment.

10 The experience going from
11 implementing REMS programs over several years
12 provide Celgene with unique insights that we
13 look forward to sharing further.
14 Standardization of key definitions would be
15 helpful but we recognize that there are limits
16 to the extent of possible standardization if
17 programs are to maintain effectiveness.

18 Thank you for your time today.

19 MS. TOIGO: Thank you, Paul.

20 Next we will hear from Jeff
21 Fetterman at ParagonRx.

22 MR. FETTERMAN: Good morning. I

1 am Jeff Fetterman. I am President of
2 ParagonRx and Adjunct Professor of Healthcare
3 Systems Engineering at Lehigh University. And
4 I appreciate the invitation to speak on the
5 topic of REMS standardization methods.

6 I will start by sharing an
7 observation that many have had in that it is
8 somewhat paradoxical that during the time of
9 greatest control of clinical trials that we
10 use the greatest extent of standardization.
11 But at the time that when the medication is
12 introduced into the wild state of the real
13 world, we use intuitive and ad hoc approaches
14 to design risk management programs. And while
15 this may not be logical, perhaps it is not
16 surprising because most people consider
17 themselves actually to be risk managers.

18 We are all risk managers and some
19 of us have formal training but others have
20 learned through life experiences how to manage
21 risks. And we manage those risks constantly
22 related to a variety of topics, health,

1 safety, financial, security. And this
2 informal risk management is a way we cope with
3 daily experiences and as such, it is something
4 that we do subconsciously.

5 So think about the various
6 activities that all of us do as part of our
7 daily lives that we introduce some sort of
8 standardization to minimize uncertainty, our
9 morning routine, the way we drive to work in
10 the morning, the way we go about our work
11 habits during the day, and even what we do at
12 the end of the day. And so this intuitive
13 approach is good for everyday life but not for
14 drug safety risk management.

15 So stakeholders who work in other
16 risk-intensive industries do more. They have
17 ingrained standardized methods and tools into
18 their practices after years of using them.
19 And I would suggest that that is where we need
20 to be as an industry.

21 So standardized risk-intensive
22 industries used standardized risk evaluation

1 methods. Let's think about some of these.

2 The aviation, military, nuclear, aerospace,
3 healthcare, are all risk-intensive industries
4 that have adapted an advanced risk management
5 method to evaluate and anticipate and prevent
6 failures. All of us are familiar with
7 aviation as an example, so let's look at that.
8 Redundancy: there are multiple pilots,
9 multiple engines on every aircraft. Training:
10 not only is training provided in the form of
11 educational content but also in simulations
12 that enable learning. Passengers receive
13 drills.

14 So if we think about all of these
15 other industries, we can learn much from
16 aviation and from others. As pharmaceutical
17 professionals, we were not trained to think
18 this way and we need to adopt some more
19 effective methods.

20 Standardized risk evaluation
21 methods that have been used in other
22 industries are well-documented. The use of

1 probabilistic risk assessment and FMEA by the
2 nuclear industry and regulated by the NRC is
3 well-documented. HACCP by the food side of
4 FDA and FMEA by other divisions like CDRH
5 within FDA as well. I would like to look at
6 FMEA as one of the most widely adopted
7 practices.

8 So Failure Mode and Effects
9 Analysis is a systematic approach to
10 proactively analyzing and improving a product
11 or process in order to achieve a better
12 outcome. Some of the key attributes: it is
13 preemptive; it looks ahead and anticipates to
14 avoid risks; it is systematic and, therefore,
15 it is comprehensive in its view; it
16 prioritizes by means of degree of hazard; and
17 it is flexible and feasible and as such, it
18 has been demonstrated to be effective across
19 a broad range of industries.

20 So I would like to look at some
21 healthcare applications of this. The VA
22 National Center for Patient Safety looked at

1 various risk evaluation methods. They looked
2 at HACCP and they liked the idea of the
3 decision tree. They looked at root cause
4 analysis. It is retroactive but the scoring
5 matrix was really appropriate. And they
6 melded those with the fundamentals of FMEA and
7 preserved the basic principles. And in 2002,
8 published a tutorial about HFMEA methodology
9 and the Joint Commission Journal on quality
10 improvement.

11 Likewise, the Institute for Safe
12 Medical Practice has been advocating FMEA
13 since 1994. In this case, ISMP analyzed the
14 IV patient-controlled analgesia process. They
15 used the methodology to map the process,
16 evaluate what could go wrong in that process,
17 identify why those things went wrong, and then
18 pinpoint specific interventions that measure
19 follow-up. So it is this type of detailed
20 process analysis that I believe we now have
21 the opportunity to embrace as a new standard
22 in pharmaceutical risk management.

1 FDA has also been advocating use
2 of standardized evaluation methods for some
3 time. There are multiple guidances that have
4 cited FMEA in the past and I suggest there is
5 an opportunity to use methods such as failure
6 modes and effects analysis as a standardized
7 part, a standardized methodology for
8 pharmaceutical risk management.

9 I would like to walk through a
10 pharmaceutical adaptation of HFMEA and some of
11 the modifications that were made are
12 attributable to some important disciplines.
13 One is human factor failures and the
14 recognition that we can never eliminate human
15 failure. So the best thing to do is to put in
16 place redundancies of tools and of
17 stakeholders to make sure that you minimize
18 the frequency of the failure and mitigate the
19 risk when it occurs.

20 Second is adult learning and
21 recognizing that individuals do not learn
22 strictly by the communication of content but

1 they also need to have enabling tools that
2 allow them to apply to their everyday lives.

3 And so with these modifications,
4 here is a brief overview of what the process
5 looks like. The analysis breaks down
6 medication use into process and sub-process
7 steps. It then looks at what why and how.
8 What could go wrong? We call that the failure
9 mode. And in this case, the healthcare
10 professional did not counsel a patient. They
11 didn't act.

12 The why, why did it occur? What
13 was the underlying reason? In this case, the
14 healthcare professional forgot. There could
15 be other reasons as well. They could have
16 ignored.

17 And then finally, how to go about fixing
18 this particular problem. And in this
19 particular case, there is both reminders for
20 the healthcare professional as well as some
21 enabling tools and then back up information
22 for other healthcare providers, in this case

1 a nurse and a patient.

2 So here is the elegance of this
3 approach. It defines what everyone needs to
4 do to back one another up, when to do it, and
5 it is linked back to the failure that can be
6 avoided.

7 So there is many demonstrated
8 applications of FMEA in pharmaceuticals that
9 has been used to design a de novo REMS. It
10 has been used to redesign existing REMS.
11 There has been other applications as well.
12 But I really want to focus in on its use to
13 validate risk management planning. You will
14 not that this says validate a RiskMAP because
15 that is what this case study I'm about to
16 share is from and it shows the duration of
17 time, frankly, that methods like this have
18 been applied.

19 So in this particular case study,
20 an organization brain stormed a set of 30
21 possible risk management tools based on
22 intuition. And while that is not particularly

1 unusual again, given my opening comments, many
2 people are doing this via an ad hoc or
3 intuitive approach, they wanted to validate
4 their selections. And so they used FMEA to
5 validate and identified all the high-priority
6 hazards that could occur. And then they
7 compared those to the tools and they found
8 that of the 30 tools they identified, only 16
9 addressed high hazard failures; 14 were
10 unusable because they didn't address any of
11 those high hazard failures; and 12 new tools
12 were required to mitigate risks of high
13 hazards that were not mitigated by the
14 original 30. Then all of those were combined
15 into 18 enabling and educational tools, again,
16 thinking about adult principles, and then
17 implemented across a redundant group of
18 audiences.

19 So here is the lessons learned out
20 of this. Intuitive brainstorming, while it is
21 common and while it is relatively
22 straightforward is inaccurate and it creates

1 waste in gaps. FMEA validation generated a
2 more focused program with fewer tools that
3 were more targeted and redundancy has the
4 promise of alleviating burden on any given
5 stakeholder.

6 Some key takeaway points. Number
7 one, risk minimization of medications, and
8 devices for that matter, requires more than
9 intuitive design. I hope that is clear
10 through the discussion today.

11 Secondly, FMEA has a proven
12 history of systematically guiding design of
13 risk minimization and other risk-intensive
14 industries, and likewise in healthcare.

15 And finally, our assertion that
16 systematic use of FMEA or other standardized
17 methods in the design of risk minimization
18 tools for medications and devices enables
19 standardization and transparency.

20 Thanks very much.

21 MS. TOIGO: Thank you, Jeff.

22 Next we will hear from JoAnn

1 Stubbings from the University of Illinois at
2 Chicago.

3 MS. STUBBINGS: Thank you. My
4 name is JoAnn Stubbings and I am Assistant
5 Director of Specialty Pharmacy Services at the
6 University of Illinois Health Sciences System.
7 We call it UI Health. UI Health is a closed
8 healthcare system and it is comprised of a
9 495-bed hospital and 11 federally qualified
10 community health centers. There are seven
11 health services colleges and an outpatient
12 care center that has a 600-physician group
13 practice.

14 We have pharmacies. We have seven
15 outpatient pharmacies that service UI Health
16 and we fill over 1,000 prescriptions per day.
17 And most of our business is in the specialty
18 pharmacy area, due to the nature of the
19 practice in the outpatient clinic. We could
20 be referred to as a controlled dispensing
21 setting.

22 The population we serve is about

1 two million people, primarily an under-served
2 community. Thirty-five percent of our
3 population is Hispanic and another 35 percent
4 is African American.

5 Just as a little bit of
6 background, we believe that the conditions are
7 becoming more favorable for integration of
8 REMS into the healthcare system. So what I
9 would like to talk about today is the proposal
10 that we have developed for integrating REMS
11 into the healthcare system. And the two main,
12 most important points are that the lines
13 between inpatient transitions in care and
14 outpatient are beginning to disappear. And
15 also healthcare systems have access to records
16 that are required for implementation and
17 evaluation for REMS. REMS can impact the
18 system, such as inpatient and transitions in
19 care, both in a positive and negative way.

20 There are four goals that are
21 involved in integrating a REMS system into a
22 healthcare system and I would like to go

1 through each of these goals individually.

2 First is to improve REMS standardization and
3 integration; secondly, to increase access to
4 high-risk medications for patients; third,
5 improve the potential for assessment and
6 evaluation; and fourth, to reduce the burden
7 on healthcare providers.

8 So the first goal is to improve
9 REMS standardization and integration. And we
10 heard discussion this morning about having
11 web-based portals. And I believe that is a
12 great start. And the web-based portal in a
13 healthcare system can be used on its own or it
14 can be integrated into the electronic health
15 record or the pharmacy system.

16 Recognizing that hospitals use
17 different EHRs or different pharmacy systems,
18 then this integration could be designed or
19 done at the individual systems or done through
20 a series of links into the EHR. And we heard
21 the discussion from Adam Kroetsch this morning
22 about SPL structured product labeling and this

1 is something that would have great potential
2 for integration into either the pharmacy or
3 the electronic medical record.

4 I would like to show some quick
5 examples of attempts that we have made for
6 this integration. And one would be with ESAs,
7 the second is with clozapine, and the third is
8 with lenalidomide. And the starting point
9 that we use for any of the integration or any
10 of the REMS proposals is to develop a set of
11 policies and procedures. And this is a policy
12 and procedure for ESAs. And I will point out
13 that we will be submitting these policies in
14 their entirety to the committee in our written
15 comments because this is not readable in this
16 slide.

17 But this is a policy and procedure
18 for ESAs and it basically states -- it defines
19 the REMS when the indication is for cancer-
20 induced anemia. So we have incorporated the
21 indication into the electronic order entry and
22 this is kind of a marked up prescription that

1 was entered for one of the ESAs. And
2 basically, the prescriber has to provide the
3 indication into the order for the medication.
4 And here, this prescription is for anemia,
5 which is non-chemotherapy related. So as a
6 result, the remainder of the REMS is not
7 required. But at the point of dispensing the
8 pharmacist sees that indication on the
9 prescription and the pharmacist verifies that
10 by going back to the electronic medical record
11 and doing a check.

12 So the advantage of having this
13 integration into the healthcare system is that
14 we have the access to the EMR and we can go
15 back and do those checks.

16 The next one is the policy and
17 procedure for clozapine. Clozapine policy and
18 procedure focuses on inpatient and discharge
19 care. And it basically incorporates the REMS
20 and then goes above and beyond by
21 incorporating other policies and procedures
22 within the health system. For example, one

1 procedure that we have is that if the
2 discharged patient is going to continue their
3 treatment at UI Health, they are referred to
4 a medication management clinic within the
5 psychiatry clinic. So in addition to the REMS
6 requirements that we are meeting, we have
7 other procedures that we follow.

8 So the discharge policy for
9 clozapine has emphasis on establishing access
10 to the medication prior to discharge.

11 The next one is the lenalidomide
12 procedure and we have access to all of the
13 manufacturer information and checklists. And
14 what you see on the upper left-hand corner of
15 the slide is the checklist for pharmacist.
16 And we developed a workflow document that
17 helps in training and helps in implementation
18 of the REMS at the point of dispensing in the
19 oncology clinic. And this workflow is a
20 series of links. So each of these boxes
21 represent links to additional workflow
22 information.

1 So for example, if you click on
2 "New Rx-Male," you go to a series of decision
3 points and a decision tree. And there are
4 links on each of these -- at each of these
5 points that take the prescriber or the
6 pharmacist to some individual documents from
7 the company REMS. So this is our way of
8 attempting to provide integration. So you see
9 how that goes further.

10 And then this is the same sort of
11 thing for the new Rx-Female and there are
12 links to the MedGuide and the other patient
13 information.

14 So just to back up, to summarize,
15 there is potential for integrating -- the
16 integration of REMS into the standard of care
17 in the healthcare system and we have attempted
18 to do that for several medications and to
19 improve patient care and to facilitate
20 transitions in care.

21 The second goal of the integration
22 of the REMS system is to increase access to

1 high-risk medications. And we would like to
2 propose that the link between REMS and limited
3 distribution be broken. We believe that
4 sometimes there is a perception that if a drug
5 has an ETASU REMS in particular, that the
6 distribution must be limited and controlled.
7 And we believe that there could be access to
8 medications through health systems, through
9 various controlled measures. And what we are
10 starting to see, for example, is specialty
11 wholesalers, where distribution can be only to
12 health systems that can meet the requirements
13 and provide access to medications and improve
14 patient care.

15 We believe also that allowing
16 access for health systems would improve
17 transitions in care, would avoid delays at the
18 point of discharge, and also shorten the time
19 to start of therapy for patients.

20 The third goal is to improve the
21 potential for assessment and evaluation. And
22 the second point here is to utilize the

1 richness of electronic health record to assess
2 and evaluate outcomes. And health systems
3 have access to data that could potentially
4 improve the assessment and evaluation and,
5 therefore, make REMS more robust.

6 And then to the fourth goal is to
7 reduce the perceived burden on healthcare
8 providers. And health system pharmacists,
9 especially those who practice in the clinical
10 setting are many times an untapped resource
11 for REMS implementation and management. And
12 we believe that a new thing that is being
13 talked about a lot is pay for performance and
14 many models are being tested. And we believe
15 that pay for performance, a mechanism for
16 implementation and assessment, could be linked
17 to improved outcomes and cost savings for
18 REMS.

19 And many models are being tested.
20 And these can be as simple as just allowing
21 access for the health system or having
22 discounts or incentive payments. And various

1 payers are experimenting with models such as
2 Medicare, Medicaid, insurers, health plans,
3 and pharmaceutical companies.

4 So in conclusion, the healthcare
5 system is evolving into an integrated model.
6 So I believe that REMS could be part of this
7 integrated model. And I talked about four
8 goals for an integrated REMS system, which
9 would be a standardized REM integrated into
10 EHRs and pharmacy systems; secondly to break
11 the link between REMS and limited
12 distribution; thirdly, to integrate into
13 health systems, allowing for more robust
14 evaluation and assessment; and fourth to
15 include pay for performance in order to reduce
16 the perceived burden on providers.

17 And finally, REMS should be a
18 standard of care in all health systems. Thank
19 you very much.

20 MS. TOIGO: Thank you, JoAnn.

21 Our next speaker is Paul Brown
22 from the National Research Center for Women

1 and Families.

2 MR. BROWN: Good morning. Thank
3 you for the opportunity to speak. I am Paul
4 Brown with the National Research Center for
5 Women and Families. I am also with the
6 Patient Consumer and Public Health Coalition.
7 My brief comments are from a consumer-patient
8 point of view.

9 The REMS program made it possible
10 for the FDA to approve drugs with known or
11 potential risks that may outweigh the
12 benefits. The plan was to develop strategies
13 to reduce those risks. That is essential
14 because if a known risk or potential risk
15 cannot be minimized, these drugs should not
16 have been approved.

17 The HHS Inspector General has done
18 an excellent job in reviewing the REMS
19 program. The HHS report FDA lacks
20 comprehensive data to determine whether Risk
21 Evaluation and Mitigation Strategies improve
22 drug safety. That report found that nearly

1 half, nearly half of the sponsors did not
2 include all the information requested for
3 their REM assessments. That is a failing
4 grade by any standard. Only seven of 49 met
5 all of the FDA's goals. To industry
6 representatives here today, your companies
7 can, your companies must do a better job of
8 providing this information.

9 The FDA should not be so focused
10 on the burdens of REMS, given that the entire
11 goal of REMS was to put riskier products on
12 the market. For that reason, the focus should
13 be on protecting patients from medications
14 that are known to have risk or where the
15 potential for harm is great.

16 There are some flaws in the
17 current REMS program which affects the ability
18 to assess the programs. Sponsors are not
19 providing information needed to assess the
20 success of their REMS strategies. FDA
21 assessment plans are not enforceable. And
22 nobody knows if the strategies are working.

1 The National Research Center for
2 Women and Families has great concerns about
3 the REMS program and many members of the
4 patient, consumer, and public health coalition
5 share those concerns.

6 We believe that drugs with higher
7 risk are being approved under the assumption
8 that REMS strategies will protect patients but
9 there is little evidence that REMS are
10 effective in providing that protection. And
11 if it is, to what percentage of the patients.

12 Thank you for the opportunity to
13 speak.

14 MS. TOIGO: Thank you, Paul.

15 Our last speaker on this panel is
16 Phyllis Greenberger from the Society for
17 Women's Health Research.

18 MS. GREENBERGER: Well, good
19 morning and thank you for the opportunity. My
20 name is Phyllis Greenberger, President and CEO
21 of the Society for Women's Health Research and
22 we are a nonprofit advocacy organization in

1 Washington.

2 I commend the FDA on convening
3 this public meeting to evaluate Risk
4 Evaluation and Mitigation Strategies and
5 appreciate having the opportunity to speak
6 this morning regarding REMS standardization.
7 I hope that you will take our comments into
8 consideration in your final meeting
9 recommendations.

10 The Society has long advocated
11 that FDA's approval decision should be based
12 on evidence that is data-driven and science-
13 based. Further, we believe in particular that
14 these decisions should evaluate and consider
15 the impact on women and sub-populations.

16 Society believes the reporting and
17 analysis of demographic data, in particular
18 that of sex, should be a part of any
19 standardization at FDA in addition to the
20 standardization of REMS. However, in the
21 interest of safety, today I ask for some
22 caution in the application of standardization.

1 We believe that in some cases such
2 standardization can and will particularly and
3 adversely impact women.

4 Many of you know, I hope, that the
5 society is the thought leader in sex
6 difference research and has been the driving
7 force behind research into women's health
8 since 1990. It has only been in the last
9 decade that scientists have truly begun to
10 uncover significant biological and
11 physiological differences between men and
12 women from the composition of bone matter and
13 the experience of pain to the metabolism of
14 certain drugs and the rate of
15 neurotransmitters synthesis in the brain.

16 This is important to realize
17 because in the context of establishing REMS
18 years ago, it was the fact that there were
19 clear sex differences between men and women,
20 especially adverse reaction to prescription
21 drugs and severe side effects that
22 particularly spurred the need for REMS. We

1 know that of the ten prescription drugs
2 withdrawn from the United States market
3 between January 1997 and December 2000, eight
4 caused statistically greater health risks for
5 women than men. Thankfully over the last
6 decade since that report, there has been a
7 greater emphasis on risk management.

8 While we know that sex differences
9 exist in drug metabolism and drug's effects on
10 people, not enough has been done to date to
11 provide this information to patients. We
12 applaud the FDA's decision earlier this spring
13 to change the dosing for prescription sleep
14 medications and to particularly emphasize the
15 impact on women and the need for women to take
16 a lower dose. This is a step in the right
17 direction but all patients should have access
18 information regarding benefits and risks
19 broken down by sex differences that is easily
20 accessible on the FDA website.

21 It is our belief that to the
22 extent existing REMS are collecting data

1 ensuring, we hope, that risk
2 disproportionately suffered by women are
3 mitigated, standardization should be
4 approached with careful evaluation,
5 consideration, and transparency.

6 Whatever standardization across
7 different REMS the FDA might consider, such
8 standardization should only modify existing
9 REMS to the extent it will not compromise the
10 safe use that the current REMS currently
11 provides. To do otherwise would compromise
12 patient safety in the name of standardization
13 and this would not be an acceptable outcome
14 for patients, providers or the FDA.

15 For example, certain existing
16 REMS, including REMS that predate the Food and
17 Drugs Administration Amendment Act of 2007,
18 FDAAA, manage unique risks that may not lend
19 themselves to standardization and, in some
20 cases, have a particular disproportionate
21 impact on women. A one size fits all approach
22 can cause more harm and disrupt the drug

1 supply system and is not the direction medical
2 practice is taking.

3 The Society believes that these
4 REMS must ensure that harm is not done and
5 extreme care is taken, as there are public
6 health and safety concerns relating to those
7 REMS which may not lend themselves to being
8 standardized. Our focus on some of the older
9 drugs and its concern over the risk mitigation
10 systems is directly proportional to the
11 particular impact many of these drugs have on
12 women and the lack of study and analysis of
13 sex in the approval of these drugs which is
14 clearly not the same issue for new drugs that
15 the FDA has yet to approve.

16 During the debate over the passage
17 of the Food and Drug Administration Safety and
18 Innovation Act of 2012, FDASIA, last summer,
19 the Society wrote to Congress with respect to
20 its concerns over REMS, specifically those
21 imposed on high-risk drugs where expanded
22 access to REMS restricted innovative drugs is

1 being granted to generic manufacturers to
2 conduct bioequivalence or clinical testing.
3 These drugs have frequently had a
4 disproportionate effect impact on women and
5 the Society believes that the safety standards
6 for the generic drug should be as rigorous as
7 those in place for the innovator drugs.

8 We recognize the importance of
9 generic drugs to the medical community and to
10 patients. We also recognize, however, that
11 all drugs and biological products can
12 potentially pose serious safety risks and that
13 costs should never trump safety. FDAAA gives
14 the FDA authority to require REMS from
15 manufacturers to ensure that the benefits of
16 a drug or biological product outweigh the
17 risks.

18 In 2009, the Society convened a
19 stakeholder meeting on REMS, resulting in the
20 publication of a detailed report in March 2010
21 titled optimal futures for risk evaluation and
22 mitigation strategies, where issues related to

1 generic drug manufacturers addressed, as
2 several cases have caused concern within the
3 advocacy community.

4 One specific instance involved the
5 acne treatment isotretinoin where a less-
6 rigorous risk management system for
7 teratogenic drugs had caused unplanned
8 pregnancies among patients. The society's
9 report recommended that policies be in place
10 that will assure all drug manufacturers are
11 held to the same standards when implementing
12 tightly controlled restricted distribution
13 programs.

14 The society also recommended that
15 the FDA develop quantitative methods to
16 evaluate a generics risk management program
17 and to develop a contemporaneous monitoring
18 and enforcement policy.

19 In closing, I want to reiterate
20 that the society believes risk mitigation
21 remains an evolving effort and were of great
22 importance in the weighing of benefit versus

1 risks to patients. Further, we believe that
2 the focus of standardization should be on new
3 chemical entities only. A one size fits all
4 standardization approach could have unintended
5 consequences of minimizing well-established
6 safety protections, as well as potentially
7 compromising access to treatments that but for
8 the REMS programs would not otherwise be
9 available to patients.

10 Patients and their advocacy
11 organizations have fought hard for the access
12 to and benefits of these drugs. And we thank
13 you for the opportunity to provide these
14 comments. Thank you very much.

15 MS. TOIGO: Thank you, Phyllis.
16 And thank you to our panel for some
17 informative comments.

18 Next we now have time for FDA
19 questions to our panel members, either to
20 clarify some of the points that they made or
21 if their comments spurred some new questions
22 in your mind that you might want to probe a

1 little bit more for our panel members.

2 So I will look to my left and see
3 who might want to start questions. Okay,
4 Claudia, and then Gary, and then Mwango.

5 DR. MANZO: My question is for
6 JoAnn Stubbings. You made a comment about
7 breaking the link between REMS and limited
8 distribution. I wonder if you would elaborate
9 a little bit more on that point.

10 MS. STUBBINGS: There is a
11 perception that REMS is a requirement for
12 limited distribution or that limited
13 distribution happens or is necessary because
14 of REMS. And that is something that in the
15 health system that it would be better for
16 transitions in care and overall patient care
17 to be able to have access to the medication in
18 addition to being able to administer the REMS.

19 DR. SLATKO: So my question is to
20 Paul. Could you tell us a little bit more
21 about the electronic system the
22 celgeneriskmanagement.com? I think you said

1 that the system cues the person who is using
2 it to complete that they walk them through the
3 remaining steps of the process to get to
4 completion. So it kind of gives a feedback
5 mechanism about what they still need to do in
6 order to achieve that. Can you describe how
7 that works a little more?

8 MR. SHEEHAN: Sure. So one of the
9 features of celgeneriskmanagement.com is a
10 prescriber dashboard. And for the patients
11 that prescriber has enrolled into any of the
12 three REMS programs that we have, the
13 dashboard will advise the prescriber either
14 that the prescription has been dispensed, the
15 patient needs to take a particular action, or
16 that there was a problem with the prescription
17 and the prescriber needs to contact Celgene.
18 So it acts as a kind of workflow management
19 system.

20 DR. SLATKO: And do you have any
21 information on how that has been -- I don't
22 know how long this has been in place but any

1 comparative information since you implemented
2 that to prescribers and patients their ability
3 to implement the program to be facilitated?

4 MR. SHEEHAN: Sure. So for those
5 prescribers who choose and are able to use it,
6 it is an optional element. But for those that
7 are using it, we have had some tremendously
8 positive feedback that it is helping them
9 implement the REMS into their processes far
10 more efficiently and effectively than before.

11 DR. SLATKO: Thank you.

12 DR. KASHOKI: Hi. My question is,
13 and I have, I think, three, for Andrew Emmett
14 with regard to the information that you had on
15 your principles for REMS integration slide.
16 You had two bullets that are of interest to
17 me. The first one was about that said
18 comprehensive REMS implementation efforts
19 should be reserved with REMS with ETASU. And
20 then your last bullet there that said REMS
21 program effectiveness assessments should
22 evaluate the totality of the REMS program.

1 So with regard to your first --
2 that first one. I was wondering if you could
3 say a little bit more. I believe I heard you
4 say that we should try and limit or consider
5 limiting our communication efforts that are
6 done under REMS to specifically those programs
7 that have elements to assure safe use or ETASU
8 and have those communication efforts be
9 targeted around what are the requirements for
10 providers and patients as to what they should
11 do.

12 And I believe you prefaced that by
13 saying that in other areas of communication,
14 for example, about what the risks are, we have
15 other tools or other mechanisms that can be
16 used. You highlighted the PMI and MedGuide as
17 potential tools.

18 So here is my question. What
19 information are you using or what is your
20 belief about the effectiveness of these non-
21 REMS communication efforts that you said we
22 could do outside of the REMS program that

1 would adequately convey information about a
2 drug's risks and how to appropriately use
3 them. So what is the basis of that kind of
4 belief or assertion?

5 MR. EMMETT: Sure. Thank you for
6 the question. And as I noted, half of the
7 proof REMS have elements to assure safety use
8 and the other half are a combination of
9 MedGuides or communications plans or
10 communication plan or normally MedGuide only.

11 And I really have to commend FDA
12 for the progress that you have made in driving
13 the patient medication information initiative
14 forward. And I think it is quite exciting
15 about how we can improve benefit-risk
16 communication not just for REMS products but
17 routine benefit-risk communication for all
18 products.

19 And I understand the Agency is
20 going through the process of validating the
21 PMI tool to really ensure that it is a more
22 effective way of communicating benefit and

1 risks in a balanced manner.

2 And as that tool and others come
3 onboard, I think it may be an opportunity for
4 us to think about how we utilize benefit-risk
5 through REMS. And as we look at communication
6 plan-only REMS, does that make sense? Or
7 should we really be looking at the
8 communications plan as an opportunity to
9 describe the ETASU elements to REMS, to
10 describe the limited distribution or other
11 risk mitigation steps to patients and
12 providers and then utilize PMI and other
13 routine risk management tools to complement
14 that REMS.

15 And I believe that the
16 communication plans would be much more
17 effective in that manner describing the ETASU
18 elements. And I think that that would really
19 free up much of the time and resources of
20 stakeholders to really focus on the risk
21 mitigation elements related to the ETASU REMS
22 themselves.

1 DR. KASHOKI: My second question
2 has to do with your suggestion that we have
3 the assessments evaluate the totality of the
4 program. And unfortunately I don't have the
5 statute in front of me but it does talk about
6 the REMS - that sponsors are required to
7 assess the effectiveness of their programs.
8 And it seems that in part of our assessments
9 as we recommend for sponsors to do are often
10 targeted toward the goal.

11 So if there is a goal to inform
12 patients, inform providers, we will focus the
13 assessments to ensure that the REMS is meeting
14 the goals. So I wasn't sure what you meant by
15 evaluating the totality of the effectiveness
16 of the program. It seemed to be saying look
17 at what the program is doing overall in terms
18 of our global outcomes where there is
19 decreased adverse events in terms of
20 percentages or whatever or whether you were
21 indeed echoing some of what we were already
22 doing and saying yes we can look at various

1 aspects of the REMS, how it is working in
2 those specific aspects but consider the
3 information together.

4 So could you clarify that?

5 MR. EMMETT: Yes, I think to a
6 certain extent we were making both points,
7 that it is important to look at the REMS in
8 its totality and is it successfully mitigating
9 the risks that it purports to risk. But we
10 also need to evaluate whether each individual
11 tool is being effective and if it is not, how
12 it can be improved or further amended or
13 released.

14 To the other point, it is
15 important that as FDA and sponsors design REMS
16 and discuss REMS during the review stage, that
17 they have a clear understanding around what
18 outcomes the REMS are intended to rest and
19 that the assessments fully address those
20 outcomes. And I think that there has been
21 some tension about whether the assessment is
22 intended to understand things such as patient

1 comprehension of risk management
2 communications and tools or actual behavior
3 change is the risk actually being mitigated.

4 And I think that there needs to be
5 a greater understanding between FDA and
6 sponsors about which goal we are working
7 towards. And that needs to be part of the up-
8 front discussion of the REMS and the REMS
9 outcome. And to my earlier point, making sure
10 that there is adequate time during the review
11 process to have that robust discussion is
12 absolutely critical.

13 MS. TOIGO: Thank you, Andrew.
14 Megan and then Adam.

15 MS. MONCUR: Thank you, Terry. My
16 question is also for JoAnn Stubbings and it is
17 also related to the discussion about breaking
18 the link between ETASU REMS and limited
19 distribution.

20 You mentioned an entity and I
21 wrote it down as specialty wholesaler. Can
22 you clarify what that is and sort of what that

1 entity makes possible?

2 MS. STUBBINGS: A specialty
3 wholesaler could be a division of a major
4 wholesaler and they are kind of a form of
5 restricted distributions. So they, instead of
6 providing medication to anybody who orders it,
7 they restrict distribution.

8 So we are able to orders some
9 medications only from specialty wholesalers.
10 So rather than getting the medication from the
11 general larger wholesaler, for example like
12 McKesson. There is McKesson and then there is
13 McKesson Specialty. So some specialty
14 medications are only available from McKesson
15 Specialty or a specialty wholesaler. And then
16 those can be designated only for certain
17 customers such as health systems.

18 And I would propose that as a way
19 for allowing access not to the entire market
20 or if there is a need to have some sort of
21 control, then that control can be established
22 by having the product distributed only through

1 the specialty wholesaler.

2 MS. TOIGO: Adam?

3 MR. KROETSCH: My question was
4 directed towards the comment that Phyllis
5 Greenberger made but actually probably
6 something that all of you have been talking
7 about. And that is to say that we should be
8 focusing our standardization efforts on new
9 drugs, NMEs I think was what I heard, and that
10 we should not do too much to disrupt some of
11 the REMS tools that are being used in some of
12 the existing programs.

13 So my question is how do we
14 balance this idea that we need to standardize,
15 make REMS more consistent and incorporate best
16 practices with the desire to make sure that
17 the individual REMS don't undergo changes that
18 could be confusing. And I am curious how we
19 might reconcile those two things.

20 MS. GREENBERGER: Are you asking
21 me how to do that?

22 MR. KROETSCH: So this question is

1 directed towards everybody. But I mean if you
2 have thoughts, I know since you brought it up,
3 I am curious how would we reconcile those two
4 things?

5 MS. GREENBERGER: I'm not sure how
6 you would reconcile it. Our concern is that
7 there are a number of drugs out there that are
8 specifically related to women who have risks
9 that are specifically for women and that those
10 particular drugs we would not like to see
11 changed for the reasons that it seems to be
12 working.

13 In other instances, there may be
14 other opportunities to standardize, which we
15 understand obviously is preferable in the
16 long-run and just in terms of ease for all the
17 different entities involved. But the ones
18 that have been working and that have had these
19 -- could have detrimental effects on women, we
20 don't want to see those changes. And we don't
21 want to see sort of derivatives of those
22 drugs.

1 The REMS standardized to reduce
2 any of the risks that -- the potential
3 benefits that we have now. So we are sort of
4 happy with ones that we know. We don't want
5 those changed.

6 MR. EMMETT: Now I would add that
7 it is important to look at REMS
8 standardization for new drugs as well as
9 existing drugs. I think that a lot of lessons
10 learned from existing REMS programs can be
11 applied to new REMS programs as new drugs are
12 approved. And to the extent that stakeholders
13 and the provider and pharmacy in patient
14 communities are suggesting that certain REMS
15 elements may be a burden on the healthcare
16 delivery system. I think it is important that
17 we do assess that for existing drugs.

18 MR. FETTERMAN: I would just add
19 three quick points. First of all, it is a
20 foundation of every quality process that there
21 needs to be continuous quality improvement,
22 that the lessons of the past are incorporated

1 into the revisions of the future.

2 And so that clearly needs to be
3 applied to existing REMS programs, as well as
4 REMS for new molecular entities.

5 Secondly, another principle that
6 is applied across quality programs is
7 prioritization. So that doesn't mean that
8 every program has to be updated immediately.
9 There can be a prioritization of which ones
10 should receive immediate attention and which
11 ones can be staged at a later time.

12 And thirdly then, that could
13 itself be informed by reassessment of the
14 benefit-risk profile because benefit and risk
15 is a characterization at a point in time and
16 that evolves over time. And so that it is
17 possible that updated benefit risk assessment
18 may be one of the prioritization methods by
19 which you would determine which ones that
20 exist come to the top of the queue.

21 MS. TOIGO: So I have a couple of
22 questions but I will just ask one. I think

1 JoAnn you laid out some SOPs that UIC has in
2 place. And so when we think about looking at
3 burden and making decisions about REMS, what
4 kind of things are either features or
5 processes are in place within your healthcare
6 system that would enable you to safely
7 administer drugs without a REMS?

8 When we think about formulary
9 systems or the guidelines and training within
10 your institution, you have pointed out where
11 you have worked REMS into your SOPs. So, have
12 they added to your SOPs? I'm trying to --
13 when we think about burden and where the
14 healthcare system takes care of the risks
15 versus where it doesn't. And those factor
16 into our decisions about whether or not a REMS
17 is necessary.

18 So do you have those kind of
19 discussions I mean when you are writing those
20 SOPs?

21 MS. STUBBINGS: Well, we are
22 actually having a lot of discussions on

1 managing safety, especially in the outpatient
2 side because safety is an important part of
3 inpatient care with safety committees and the
4 safety officers and the inpatient. And we are
5 starting to have a lot of discussions. And we
6 have a presentation tomorrow that is going to
7 elaborate on your question actually and how to
8 incorporate safety management into the
9 outpatient setting because high-risk drugs are
10 being increasingly used in the outpatient
11 setting.

12 And I am not sure -- I know there
13 is a lot of discussion about burden. But I
14 don't really perceive it as a burden because
15 I think you start with a high-risk medication
16 and the first step is either a guideline or a
17 policy and procedure. And then that helps to
18 inform exactly what needs to be done in terms
19 of either a rule built into the electronic
20 medical record or into the order entry or
21 something that has to happen at the point of
22 dispensing, some kind of check. And because

1 we have so much integration between inpatient
2 and transitions and discharge and outpatient
3 and we have the ability to go for anyone at
4 any point to check the medical record and to
5 verify things without it being an undue
6 burden, they don't have to call anybody. They
7 just check, the medical record to verify a lab
8 or verify a diagnosis.

9 So I think that it starts with the
10 policy and procedure, to answer your question.
11 And then the steps that are required after
12 that are defined based on the circumstance.
13 I don't think it could be standardized. I
14 don't think it is going to be like every REMS
15 is going to have the same kinds of things that
16 need to happen.

17 MS. TOIGO: Okay, thank you for
18 that. So if you could consider maybe in
19 looking at the different processes that you
20 have put in place and if you would be willing
21 to comment to the docket.

22 Because the question is if you put

1 those processes in place, just by looking at
2 a prescription drug label versus a REMS, so
3 trying to help us think about decision-making
4 of when a REMS is necessary and when labeling
5 is sufficient. So if the processes that you
6 have described, if the REMS helped you put
7 those in place because they described what was
8 needed versus why did FDA do this, we can just
9 read the label and have done this all
10 ourselves because we are sophisticated and
11 could develop these SOPs.

12 So to the extent that you have had
13 those discussions or could think about that
14 and share some of that feedback to the docket,
15 that would be helpful. Because while not
16 particular to this meeting, but we are
17 thinking about those issues as well. And when
18 you see presentations when people have pretty
19 detailed SOPs, it stimulates that kind of
20 question.

21 So thank you, if you would willing
22 and anyone else who might be willing to think

1 about that question.

2 MS. STUBBINGS: Are you asking for
3 a comment now or comment later?

4 MS. TOIGO: You can comment now.

5 MS. STUBBINGS: I think the REMS
6 is definitely an important driver in
7 developing SOPs but it is not the only driver.

8 We have an example of another
9 category of medications that do not have REMS
10 that we have implemented guidelines and
11 similar processes where we do checks, we do
12 lab checks, we work with the prescribers and
13 the patients to make sure that labs are done.
14 And they are actually not -- they are not REMS
15 requirements.

16 So there is a lot of discussion
17 and it is not entirely driven by REMS.

18 MS. TOIGO: We used up an extra
19 time there for my questions. And we are
20 getting close for lunch. So go ahead with
21 your question.

22 MR. KROETSCH: Okay and I am

1 afraid that this is a two-parter also but I
2 will try to keep it quick.

3 Related to this idea of building
4 policies and procedures, I think one question
5 we might have is what can REMS do and I talked
6 about SPL as one avenue of helping clarify
7 what the requirements are, what are the things
8 that REMS programs can do to make it easier to
9 build these policies and procedures as a
10 health system? What are some best practices
11 when we are building REMS so that you don't
12 have to try to interpret what the REMS
13 documents are saying but to actually move
14 straight into integrating it into your system?

15 And the other question is, and
16 this would be for everyone, is there a forum
17 or a method by which you are able to -- we
18 could learn about what best practices are
19 being done? What kind of policies and
20 procedures are being created? Because it
21 sounds like these are ways of really taking
22 REMS to the next level and actually putting

1 them into practice. And we are very
2 interested in learning ways, effective ways to
3 do that and sharing those as widely as
4 possible.

5 MS. STUBBINGS: I think just
6 briefly the things that we have appreciated
7 the most that have offered the best
8 opportunity for integration have been REMS
9 tools that are online and that could be
10 available through links. And also REMS tools,
11 I think it is the TIRF REMS that are a part of
12 outpatient dispensing. So it integrated into
13 the outpatient dispensing system. And those
14 have been the most appreciated.

15 The second one, the question was
16 about a forum. That would be -- that is for
17 the whole group. Okay.

18 MR. KROETSCH: Yes, what might be
19 a good forum to help share these best
20 practices? And have you discovered similar
21 best practices in your involvement in REMS
22 that we could be learning from? I'm

1 acknowledging that we don't have a lot of
2 time.

3 MS. TOIGO: So Jeff and then
4 JoAnn.

5 MS. STUBBINGS: I'm not aware of a
6 forum, aside from our professional meetings
7 that we have. We have -- there is a
8 University Hospital Consortium that is made up
9 of academic medical centers and we do speak at
10 length about REMS and we are working on ways
11 of sharing practices. And actually there is
12 several people here from health systems. So
13 I am really looking to forward to hearing
14 their presentations on how they work with REMS
15 as well.

16 MR. FETTERMAN: There is a forum
17 of risk management professionals that has been
18 meeting for nine meetings now in regional
19 meetings and now one national summit. And the
20 group is called TERM. And there is
21 information at termcommunity.com that provides
22 additional information about ways that there

1 is some best practice sharing and new insights
2 from a variety of stakeholders that goes
3 beyond pharmaceutical-specific but academia
4 and other stakeholders as well. It is one
5 forum.

6 MR. KROETSCH: Thanks. And I
7 would encourage, since I know we are out of
8 time for this conversation, if you are aware
9 of those sorts of best practices to please
10 feel free to submit examples to the docket.

11 MS. TOIGO: Okay, well in the
12 interest of keeping us on schedule, thank you
13 very much to the panel for your thoughtful
14 presentations and for the dialogue and the
15 question and answer session. And I would
16 encourage you, if you could submit your slides
17 to the docket because we can't put those on
18 the FDA website but we can get access to them
19 if you put them in the docket.

20 And for those who have asked about
21 the FDA slides, yes, we can put those on the
22 FDA website and we will shortly after the

1 meeting.

2 So we will see everybody back here
3 at 12:55. Thank you.

4 (Whereupon, at 11:52 a.m., a lunch
5 recess was taken.)

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

1 A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

2 (12:53 p.m.)

3 MS. TOIGO: Okay, welcome back.

4 Hopefully you had a chance to enjoy the
5 glorious weather that we are having. This is
6 a gift. We don't get this kind of weather in
7 the end of July very often. So, hopefully you
8 got a chance to walk outside at lunchtime.

9 So we are back for round two of
10 the general standardization comments and we
11 have six speakers for this panel that are
12 going to share their perspectives on general
13 standardization issues and some other things,
14 based on the comments that we got. But we put
15 all of these gentlemen on the standardization
16 panel.

17 So we are going to start with Gary
18 Appio from Novartis Pharmaceuticals. And
19 Gary, you are up.

20 DR. APPIO: Good afternoon,
21 everyone.

22 I head the U.S. Safety Risk

1 Management area at Novartis and coordinate the
2 REMS processes. What I am looking at today is
3 REMS submissions to better standardize those,
4 especially with the a new indication, an
5 existing or released REMS and what is next.
6 So this is something I am going to go through.

7 I want to thank FDA for allowing
8 me to speak and share my views. And as my
9 disclaimer says, these are my views and not
10 necessarily those of Novartis. So make note
11 of that.

12 So question one. So if a product
13 has an improved REMS, an sNDA or another
14 indication is being submitted, is a REMS
15 submission necessary? So this one is pretty
16 straightforward, I think. You could maintain
17 the existing REMS, maybe modify it to
18 accommodate any new risks that may be in a
19 different patient population. And another
20 potential solution could be that when if you
21 are doing a REMS assessment and you saw that
22 the knowledge rate was only moderate in your

1 first assessment, then that may be a reason to
2 continue the REMS and, in this case, a new
3 like say prescriber population that may not be
4 as aware of the risk.

5 So this one is pretty
6 straightforward but I think we have a greater
7 opportunity with this next question. And in
8 it is, in evaluating a new indication for a
9 product that had a REMS and was released, say,
10 what does FDA consider in determining if a
11 REMS is necessary for the new indication?

12 So one example I cited here was a
13 product was approved for rheumatoid arthritis.
14 It had a REMS. The REMS was subsequently
15 released and after that point, the product did
16 gain an additional approval for moderate to
17 severe colitis. Now a REMS was not required
18 at that point.

19 So I guess the opportunity here
20 is, is there any way we can standardize as
21 again new indications are coming onboard and
22 not looking at it as again a unique risk-

1 benefit situation every time you have a new
2 indication. So there could be some factors
3 that the Agency could consider. And again,
4 looking at the prescriber population, is it
5 completely different or would they be aware of
6 the risks from earlier use?

7 Again, looking at the patient
8 population. So certainly if the risk in the
9 first patient population isn't as great as a
10 second one, that would be a consideration to
11 either reincorporate the REMS of some type.
12 Or the third potential could be that the
13 physicians and patients are well aware of the
14 risk and it could be considered that the
15 safety profile is well-established. That may
16 not require a REMS.

17 So these are some things to
18 consider. And we are thinking that some of
19 the potential solutions could be that if the
20 REMS was released, to have the sponsor
21 continue like posting the REMS say on a
22 website, like similar to the LABAS. We had a

1 LABA and the REMS was released but the Agency
2 asked us to continue to have the risk
3 messaging on our website. That is something
4 that could be a potential solution.

5 And then another could be is to do
6 another risk awareness testing, like in this
7 case if it is a new prescriber population.
8 And then really ascertain if they have enough
9 knowledge about the risk and that will dictate
10 if a REMS would be necessary or would need to
11 be restored.

12 So looking at recommendations and
13 benefits, we strongly recommend that FDA
14 develop guidance. And I believe that is why
15 we are all here today and really try and just
16 give some more input during the pre sNDA or
17 SBLA type meetings so we can get a better
18 understanding if a REMS will need to be
19 incorporated with a new indication.

20 And the benefits I have listed
21 here are pretty straightforward. We believe
22 it would be standardized and streamlined

1 submissions for drug sponsors and FDA review
2 to continue forward and that certainly would
3 help the process. It would really ensure
4 prescriber awareness of just the important
5 safety risks and really not having any REMS
6 programs diluted if either there is too many
7 of them or redundant programs out there.

8 Decrease the administrative burden
9 on the healthcare system with repetitive REMS
10 programs. We see that would be another
11 benefit and certainly would increase the
12 transparency between drug sponsors and FDA.

13 And I believe that is my
14 presentation. Thank you.

15 MS. TOIGO: Thank you, Gary. Our
16 next speaker is Jim Devita from CVS Caremark.

17 MR. DEVITA: Well, good afternoon.
18 On behalf of CVS Caremark I would first like
19 to thank the FDA for the opportunity to
20 provide further information on the development
21 and standardization of REMS programs.

22 My name is Jim Devita. I am the

1 Director of Quality Assurance in Patient
2 Safety for Retail Pharmacy Operations at CVS
3 Caremark Corporation. I am responsible for
4 the safe production and dispensing of
5 medications to our patients at retail.

6 My goal today is to provide the
7 committee with comments from the perspective
8 of a pharmacy services provider that manages
9 REMS programs with a broad and integrated
10 approach through retail specialty and mail
11 service pharmacies. CVS Caremark is the
12 largest provider of prescriptions, pharmacy
13 care and specialty pharmacy services in the
14 nation. We fill and/or manage over one
15 billion prescriptions annually. We employ
16 over 26,000 pharmacists. We have over 7,500
17 retail pharmacy stores, 43 retail specialty
18 pharmacy stores, and six mail order
19 pharmacies.

20 Since the implementation of the
21 Clozaril Patient Management System in 1990,
22 our pharmacies have gained over 20 years' of

1 experience developing, implementing, and
2 managing FDA-mandated drug safety management
3 programs both simple and complex. Today CVS
4 Caremark manages over 70 REMS programs.

5 So as we have submitted detailed
6 written testimony, I would like to use this
7 time today just to focus on three key points.
8 The first one is that REMS programs should not
9 only be standardized, they should be
10 integrated with workflow. Today many REMS
11 programs create unnecessary burdens,
12 impractical impediments to their
13 implementation, regardless of pharmacy
14 channel. Additional steps outside of workflow
15 processes can impede timely and effective
16 patient access to drugs and valuable focus on
17 patient care.

18 REMS programs should be user
19 friendly, standardized and system-based that
20 integrates into the workflows for not only
21 pharmacists but prescribers as well. These
22 are keys to delivering consistent results and

1 facilitating access to information.

2 So standardization and
3 efficiencies can be achieved in a number of
4 ways. First, creating consistency in
5 training, enrollment forms, and medication
6 information, establishing REMS level
7 identifiers, establishing a central database
8 for REMS information, and leveraging
9 prescribers' electronic prescribing system and
10 electronic medical records.

11 We recommend creating a focus
12 group of stakeholders that includes
13 prescribers, pharmacists, ePrescribing
14 software vendors and others to create
15 standardized REMS level identifiers within the
16 structured product labeling. Medications of
17 similar risks should be grouped together and
18 share the risk mitigation components that
19 trigger specific workflow processes.

20 So for example, a REMS level one
21 may be indicated for medications with
22 relatively lower risk and require a MedGuide,

1 whereas, a REMS level two could be for
2 medications with higher risks, such as
3 teratogenic risks and could require a
4 MedGuide, a negative pregnancy test, and a
5 completed patient prescriber agreement before
6 the drug distribution occurs.

7 The goal here is to minimize
8 unique drug-specific solutions and develop
9 uniform language that can be used by all
10 participants while standardizing and
11 automating manual administrative processes.

12 We also recommend creating a
13 central REMS database for all approved REMS.
14 This concept is currently being used and being
15 used successfully for the transmucosal
16 immediate release fentanyl medications or TIRF
17 medications. This limited central database is
18 a real-time REMS administrative solution that
19 nicely aligns with pharmacy workflow.

20 We should learn from this success
21 and create a database for all REMS drugs,
22 which could contain the REMS level identifier,

1 the REMS requirements including the elements
2 to assure safe use, and it could be a training
3 and enrollment portal as well that could check
4 for enrollment status for prescribers,
5 patients and pharmacies, and also facilitate
6 reenrollment.

7 This database could be accessed by
8 ePrescribing and claimed adjudication systems,
9 supporting both prescriber and pharmacy
10 workflow processes. This would streamline the
11 delivery of medication to the patient by
12 informing each provider of their REMS
13 responsibilities at the point of care.

14 This database could also be
15 leveraged in the future in conjunction with
16 NCPDP standards to share critical information
17 and allow for real-time communication between
18 the prescriber, pharmacy and others who
19 contribute to the patient's electronic medical
20 record, making medication history, lab values
21 and coverage information available to the
22 prescriber at the time of dispensing.

1 The second key point is that not
2 all REMS requirements integrate well with
3 existing retail pharmacy dispensing systems.
4 With over 65,000 pharmacies in the
5 distribution chain, standardization of REMS
6 will significantly enhance the effectiveness
7 of REMS programs for the many drugs where
8 there are similarities in risk profiles. But
9 experience tells us that there will be
10 product-specific situations where the
11 management of non-dispensing elements to
12 assure safe use might pose challenges for
13 providers, including community pharmacies.

14 REMS requirements that include
15 expanded or drug-specific counseling, drug
16 therapy management activities, and non-
17 dispensing interventions, such as lab testing
18 documentation, also often contain requirements
19 not supported by ePrescribing or claim
20 adjudication systems. By their nature, they
21 require partial if not total manual
22 intervention.

1 For example, some programs fit
2 better in the specialty environment due to the
3 burdensome time-consuming requirements such as
4 providing consultation on every fill, manually
5 obtaining and maintaining confirmation and
6 authorization numbers, tracking each
7 dispensing to adhere to quantity restrictions
8 and ensuring appropriate documentation is
9 received.

10 As specialty therapies become more
11 targeted and focus on modification of biologic
12 responses, we can only assume that the
13 prevalence of REMS will increase and include
14 more restrictive tiers, more REMS components,
15 education, and processes.

16 Drug products which meet these
17 safe use conditions should be labeled as such
18 through the REMS level identifier, allowing
19 pharmacy systems to determine if their
20 workflow provides appropriate levels of
21 support. At CVS Caremark, our specialty
22 pharmacies dedicate the necessary educational

1 and administrative time necessary to excel in
2 managing intricate and customized REMS
3 programs, filling the gaps beyond the scope of
4 retail pharmacy.

5 And the last key point is that the
6 FDA should require increased transparency in
7 REMS development, modification, and
8 surveillance. Prescribers and pharmacists
9 undertake a major responsibility in
10 implementing REMS and are on the front line of
11 facing the associated challenges. It is only
12 logical, therefore, that REMS applicants
13 should be required to consult early in the
14 design, development, and modification
15 processes with the pharmacies, pharmacists,
16 and prescribers who will be responsible for
17 implementing and complying with these new REMS
18 requirements.

19 Additionally, the FDA should
20 require that drug manufacturers set up a
21 mechanism to obtain ongoing feedback from
22 healthcare providers, practitioners, and

1 particularly pharmacists to ensure that REMS
2 programs are effective and adds no
3 unreasonable burden to the provider community,
4 nor does it impede patient access to these
5 medications. We consider transparency to be
6 a key success factor.

7 So in closing, CVS Caremark is
8 committed to the success of REMS programs,
9 including both existing and proposed REMS. We
10 look forward to being a partner in the REMS
11 program development, standardization,
12 implementation, and evaluation process in the
13 future. We thank you again for the
14 opportunity to comment.

15 MS. TOIGO: Thank you, Jim.

16 Next we will hear from Stephen
17 Goldman.

18 DR. GOLDMAN: Thank you, Terry.

19 I am going to provide a little
20 different perspective as an academic
21 physician, former regulator, former industry
22 physician, and for the past 12 years,

1 independent consultant internationally on drug
2 safety and pharmacovigilance.

3 I would point out that I was
4 honored to serve on the 1999 Task Force on
5 Risk Management, which established the concept
6 of a pre- and postmarketing continuum when it
7 came to risk management.

8 One thing that has been missing
9 from the discussion so far today is where REMS
10 fit. REMS are an end product of an entire
11 program of premarketing clinical safety and
12 postmarketing pharmacovigilance. They are not
13 an end unto themselves. They are part of that
14 continuum.

15 Secondly, the aspects of the
16 context for a REMS is case review, signal
17 detection, both national and international
18 compliance, and labeling which was mentioned
19 this morning, within an entire system of
20 assessment of product safety and risks
21 management. That is imperative for the
22 evaluation for the revision of REMS.

1 The system is designed within any
2 company to be designed to generate high-
3 quality safety data from all the varied source
4 of information we get, starting with the
5 animal data which leads to submission of the
6 IND; clinical trials, both pre- and
7 postmarketing; the underlying epidemiology of
8 disease states, which are becoming more and
9 more critical; spontaneous reports;
10 observational studies. REMS do not arise de
11 novo. They arise from the perceived need of
12 this type of data as to where the benefit and
13 risk are associated and the fact that benefit
14 must continue to outweigh risk.

15 To have optimal REMS evaluation,
16 you must have regulatory standards that are
17 reflective of the state of the art medical
18 product safety to enhance both the quality of
19 the data, compliance with requirements both
20 national and international, and the ongoing
21 evaluation of benefit-risk. Regrettably, in
22 the United States we do not have a state of

1 the art postmarketing standards. The proposed
2 rule remains a proposed rule since 2003,
3 unlike the IND reporting rule which was
4 recently revised. This is an ongoing problem,
5 particularly with Europe doing a complete
6 rewrite and change on the pharmacovigilance
7 regulations and modules.

8 Secondly, safety is global, just
9 like REMS are. Therefore, what happens in the
10 United States has an effect on what happens in
11 Europe, Japan, the product being used
12 anywhere. The drug is exactly the same
13 whether using it in Brooklyn or Australia.
14 Therefore, safety is global. REMS are no
15 different.

16 E2E is the true philosophical
17 viewpoint of how one does safety. It was
18 operationalized as a finalized guidance in the
19 United States but, unlike Europe, there is no
20 requirement for sponsors to submit either a
21 safety specification on pharmacovigilance plan
22 with new dossiers. That is the state of the

1 art but it is not required yet in the United
2 States. It is required in Europe and Japan in
3 relation to that.

4 It is interesting that it is not
5 required in the United States, considering the
6 FDA in the past two years has now begun to
7 utilize the philosophy of E2E and for example
8 the DSUR, the Developmental Safety Update
9 Report, which can now be submitted in place of
10 the IND annual report, which is based on the
11 E2D philosophy. And just this past year, the
12 FDA actually just in the past couple of
13 months, has stated that you can provide, you
14 can do the new Periodic Benefit-risk
15 Evaluation Report in place of the traditional
16 Periodic Safety Update Reports.

17 It is hoped that the FDA will see
18 the way to standardize E2E in relation to
19 submission of a pharmacovigilance plan and a
20 safety specification to show where REMS arise
21 from in the premarketing arena or in
22 postmarketing.

1 We were here three years ago
2 talking about where we are with REMS. And one
3 of the things that was mentioned was
4 consultation with prescribers, pharmacists,
5 patient groups, and others and to reduce the
6 burden to integrate REMS into the existing
7 healthcare systems. And again, this is one of
8 the stated objectives was to standardize REMS.
9 I am cautioning against standardization versus
10 a lock step because all REMS are not alike.

11 Why is that a concern? I spent
12 the year working with the American Society of
13 Health System Pharmacists with pharmacists.
14 I can tell you there was a lot of anger in the
15 first several months from pharmacists who were
16 working with some of the REMS and I was the
17 recipient of some of that anger. It was
18 understandable because one of the things that
19 happens is you are usually involved with one
20 REMS, not multiple ones, and that will often
21 be the reason why you feel the way you do
22 about REMS in general but all REMS differ. I

1 can tell you that one of the things that
2 became clear the longer I did this was if
3 people understood that the products they were
4 concerned about would not be on the mark
5 without a REMS, their view of that did change.
6 That was mentioned this morning in relation to
7 that. It can't be emphasized enough.

8 There are many reasons why REMS
9 are accepted or not accepted in relation to
10 their perceived necessity, the administrative
11 burden, the treatment setting, and of course
12 its clinical relevance.

13 This is from the FDA draft
14 guidance on REMS and it talked about using
15 relevant information. But again, a caution.
16 The relevance is dependent on the particular
17 disease state being treated, including its
18 potential lethality. The particular patient
19 population, the perceived benefit, the
20 perceived risks that need to be mitigated,
21 accumulating knowledge, and where the
22 healthcare delivery system is being delivered,

1 as we just heard concerning CVS.

2 The idea of consultation is
3 obviously a good one but with whom are you
4 consulting? And it really should be broadened
5 to include those who work in safety, quite
6 frankly, those who work with risk and disease-
7 specific experts. You cannot have a REMS that
8 focuses on a particular disease population if
9 you are not going to talk with the clinicians
10 who are going to see those patients or the
11 nurses or the pharmacists involved with that.
12 This is no different than what the FDA
13 requires for looking at packaging, naming, and
14 labeling in relation to looking at possible
15 risk factors. It should be exactly the same
16 with a REMS in relation to that.

17 I would advocate for clinically-
18 relevant patient-accepted evidence-based
19 variables. Think of it like a large simple
20 trial. No surrogate markers. The way that
21 you look for the effectiveness of a REMS was
22 to have direct clinical relevance, must be

1 directly relevant to patient care, and if
2 possible to the greatest extent, have those
3 tools be used at the point of care.

4 Other aspects I would point out,
5 there is clearly a need for greater
6 understanding of healthcare professionals
7 about the relationship between labeling and
8 REMS. In particular, box warnings and other
9 significant safety-related changes,
10 particularly with recent Supreme Court
11 decisions, particularly with the relatively
12 new package insert information, the terrific
13 new form that we have in the format and
14 information. People also need to understand
15 where REMS fit with the ongoing assessment of
16 pharmaceutical benefit risk and a greater
17 understanding of how a REMS is determined to
18 be necessary. I have to push this back to
19 again the E2E, the determination of whether
20 you are going to need ETASUs. When you are
21 going to need additional things than "routine
22 pharmacovigilance."

1 Let's be honest. No matter how
2 well a REMS is designed, it is going to add to
3 the workload of the healthcare professional.
4 But the benefits of that participation must go
5 beyond the simple need in relation to the
6 pharmaceutical simply being available.
7 MedSun, the program that is utilized in
8 medical devices, has a great two-way
9 communication. One of the complaints that I
10 heard from pharmacists and physicians is not
11 getting feedback, exactly the same complaints
12 that we heard about adverse event reporting in
13 relation to that. Timely feedback on an
14 ongoing basis, I believe again was mentioned
15 before.

16 Utilization of the data for
17 quality assurance, this is a P&T Committee,
18 peer review and accreditation, and treating
19 your participating healthcare professionals as
20 partners. If REMS are going to be accepted as
21 they need to be, there has to be made clear
22 what the benefits are not only to the patients

1 but the healthcare professionals and
2 administrators involved in their utilization.

3 Thank you.

4 MS. TOIGO: Thank you, Steve.

5 Next we will hear from Paul Seligman at Amgen.

6 MR. SELIGMAN: Good afternoon. My
7 name is Paul Seligman. I am the Executive
8 Director for U.S. Regulatory Policy at Amgen.
9 Thank you for the opportunity to address the
10 panel and for FDA's leadership in convening
11 this hearing to gather stakeholder input on
12 standardization and assessment of REMS.

13 Amgen looks forward to
14 participating with the FDA in risk management
15 efforts, with the goal of achieving safe and
16 effective use of medicines.

17 Prior to the FDA Amendments Act of
18 2007, which legislatively established REMS and
19 FDA's role in the process, how to effectively
20 manage the risk of medical products has been
21 an important and sometimes vexing issue for
22 the Agency and the U.S. healthcare system for

1 years. I had the privilege to work at the FDA
2 in postmarket safety for eight years during
3 this period and have the profoundest respect
4 for the challenges and struggles in crafting
5 programs to effectively mitigate or minimize
6 safety concerns.

7 Now in my current role, I have the
8 opportunity to draw upon an view Amgen's
9 significant experience with REMS since their
10 inception in 2008 and to share our views on
11 what we believe are the five key elements
12 required for a successful REMS program, as the
13 FDA and all stakeholders look to create more
14 effective and efficient ways to manage risk.

15 These five elements for success
16 include: 1) setting a clear measurable goal
17 as linked to achieving a desired behavior; 2)
18 embedding the risk management processes into
19 the healthcare system to attain these goals;
20 3) carefully and thoughtfully incorporating
21 the significant experience gained in the past
22 five years in the nearly 70 REMS programs,

1 particularly the 27 some-odd that have
2 specific elements to assure safe use or
3 ETASUs; 4) using the information technologies
4 now available to create an integrated and, if
5 possible or practicable, a universal platform
6 for managing and monitoring these REMS
7 activities; and finally 5) harnessing the
8 leadership role the FDA has so successfully
9 played in many critical drug development areas
10 in convening stakeholders to address and guide
11 implementation of the aforementioned element.

12 The first key to success requires
13 setting a well-defined public health goal.
14 Such a goal should be based on a risk that can
15 clearly be identified, a risk that is
16 preventable or can be mitigated or reduced in
17 frequency or severity. The risk management
18 goal should be explicitly stated in the REMS
19 document and the conditions for safe use
20 articulated on the label. It is a goal that
21 should be capable of being monitored by a
22 measurable metric, such as a laboratory value

1 or appropriate use of the product.

2 The goal must be tied to achieving
3 a desired prescribing, dispensing, monitoring,
4 or utilization behavior, rather than being
5 linked to knowledge acquisition. REMS should
6 not be used to address risks that cannot be
7 prevented, mitigated or reduced.

8 In general, while training and
9 education are important and vital parts of a
10 continuous running system, they are not
11 entirely reliable indicators of the ability or
12 willingness to incorporate learnings into
13 medical practice. Similarly, current paper-
14 based systems of certifications and
15 attestations, the use of stickers on
16 prescriptions all add burdens to the
17 healthcare delivery system without adding
18 clear, demonstrable benefits to patient
19 safety. Conducting surveys of and
20 demonstrating knowledge acquisition is not,
21 per se, an accurate indicator of REMS success.

22 A second element for success is to

1 embed REMS processes into and across the
2 healthcare system. To do so requires both a
3 clear articulation of the roles that key
4 stakeholders play and an understanding and
5 commitment by all to actively engage in the
6 management of pharmaceutical therapies.

7 The focal point of risk management
8 of marketed products needs to be shifted
9 permanently and decisively from the FDA and
10 sponsors to those who administer and deliver
11 healthcare, namely, dispensers, hospitals,
12 HMOs, ACOs, physicians, nurses, and
13 pharmacists.

14 One of the challenges is how to
15 move from the one off, product-specific or
16 product class-specific programs that involve
17 sponsors working directly with the FDA to
18 generalizable models for managing risk,
19 depending on the medical care setting patient
20 populations or the practitioners who prescribe
21 or administer the medication of concern.

22 The role of the regulator should

1 be to highlight the risk to mitigated and the
2 goal to be achieved. The sponsors and the
3 Agency can then work together with the medical
4 community to determine the best risk
5 management model to implement and the nature
6 of the regular assessments to be conducted.
7 Such an approach will allow each stakeholder
8 group to focus its efforts on those efforts
9 within its control and expertise.

10 A third element for success is
11 incorporating past experience. FDA has gained
12 significant experience across a variety of
13 REMS programs which should be integrated with
14 the experience of external stakeholders. This
15 combined experience should be a mine to
16 identify the situations, tools, and processes
17 that represents best practices, as well as to
18 characterize predictors of success.

19 It would be useful in identifying
20 what hasn't worked to date and in pinpointing
21 those areas that need further study or
22 piloting; for example, when a risk has not

1 been successfully mitigated.

2 The data from the assessments of
3 these programs need to be analyzed and the
4 result of these analyses made public. Without
5 the synthesis of experience from this public
6 health experiment that has been conducted over
7 the past five years, there is simply no way to
8 know what works, what doesn't, and how to
9 proceed to create a more efficient and
10 effective programs that are embedded inside
11 the healthcare delivery system. At present,
12 only the FDA has this information. Everyone
13 else, all the stakeholders represented here,
14 are looking at REMS based on their unique
15 experiences and vantage points, blind to the
16 experience of others.

17 A fourth element for success is to
18 adapt REMS to reflect a current and
19 anticipated realities of information
20 technology, increasingly centralized drug
21 dispensing, electronic prescribing, electronic
22 health records, and the push towards greater

1 accountability in healthcare organizations.

2 Currently, information systems and
3 tools are developed for each product and are
4 not aligned across REMS, resulting in an
5 increased implementation and operational
6 costs. As a result, clinics, hospitals, and
7 pharmacies in particular, find themselves
8 supporting multiple REMS programs. One remedy
9 to consider would be the development of a
10 single risk management system that would be
11 integrated, consolidated, and universal. It
12 would include a cloud-based platform with
13 dedicated portals for each stakeholder group.
14 For example, patients, healthcare providers,
15 hospitals, pharmacies, and distributors, with
16 all the tools essential to manage risk
17 tailored to each stakeholder group.

18 The distribution portal, for
19 example, could provide real-time approval to
20 distribute a medicine for the products that
21 require monitoring and/or limited
22 distribution. Such a system would be used for

1 all products determined to need risk
2 mitigation tools, regardless of the medical
3 product sponsor.

4 And finally, the fifth element for
5 success is to foster the engagements and
6 collaborations necessary to create such a
7 systems approach and withstand the test of
8 time. By exerting leadership as a catalyst
9 and a convenor of diverse stakeholder groups
10 in such areas as the Critical Path Initiative,
11 Quality by Design, and the Sentinel
12 Initiative, FDA has demonstrated its ability
13 to advance important public health issues that
14 go well beyond its circumscribed regulatory
15 function.

16 Risk management of products that
17 require specific elements to assure safe use
18 offers FDA just that opportunity to leverage
19 its knowledge and creativity across the entire
20 healthcare spectrum to improve patient safety.

21 The convening of key stakeholders,
22 of which this public meeting is certainly a

1 part, will help all stakeholders focus on
2 developing solutions that can be embedded into
3 and integrated across the healthcare system,
4 particularly in a world increasingly reliant
5 on web-based information systems and
6 electronic records.

7 Thank you for the opportunity for
8 allowing Amgen to share its views today. We
9 look forward to working with the FDA in making
10 the management and minimization of risks an
11 integral part of the way we collect and we
12 strive to improve healthcare and patient
13 safety.

14 MS. TOIGO: Thank you, Paul.

15 Our next speaker is Brian Malkin,
16 a partner at Frommer, Lawrence, and Haug.

17 MR. MALKIN: Hello. Good
18 afternoon. My name is Brian Malkin and I am
19 a partner at Frommer, Lawrence and Haug here
20 in D.C. I also edit a blog, FDA Lawyers Blog.
21 And just by way of quick background, I used to
22 work at FDA in the Office of the Commissioner

1 in the Center for Drugs from 1991 until 2000.

2 And I have been in private practice since
3 then, except for a stint for about two and a
4 half years when I went back to school to get
5 a biochemistry degree so that I could combine
6 my FDA law background with IP. So I am both
7 an FDA and IP attorney.

8 Now there are some disclaimers
9 which folks have been doing in this panel,
10 which is good. I definitely have to say here
11 I am speaking on my own behalf. I am not
12 speaking on behalf of the firm or any client
13 or potential client. And I also reserve the
14 right to take a contrary position, which is
15 what attorneys do from time to time.

16 What I am going to be taking a
17 position here on in terms of the overview is
18 that I want to talk about what are the
19 expectations of shared REMS operation. What
20 have I seen over the years? And I am talking
21 about years probably from 2000 to current time
22 when there were risk management programs and

1 then RiskMAPs and now REMS. So what has not
2 been working in terms of these programs being
3 effectively shared. And then some sort
4 suggestions to improve and things to think
5 about that maybe FDA could take up in a
6 subsequent meeting.

7 So what are the expectations for a
8 shared REMS operations? So just a little bit
9 of background. Just because haven't we really
10 talked about it earlier today, where the whole
11 concept of sharing a REMS sort of come from,
12 it came from FDAAA. And here it talks about
13 if they are ETASU, which we know what they
14 are, here in terms of Element to Assure Safe
15 Use, that it stipulates that the brand name
16 and the generic manufacturers should work
17 together on coordinating a single share of
18 REMS program, unless one of these two
19 situations occurs that FDA determines that the
20 burden of creating a single shared system
21 between competitors outweighs the benefits of
22 the shared system or an aspect of the elements

1 to assure safe use for the applicable listed
2 drug as claimed by a patent that has not
3 expired and the applicant for the ANDA
4 certifies that it has sought a license and
5 that is was unable to obtain a license.

6 And one of the programs described
7 earlier today from Celgene is protected by a
8 myriad of patents that is an example of a
9 program that would fall maybe into that
10 category.

11 Now for an ANDA REMS, what FDA has
12 sort of explained before, that they do not
13 necessarily need to have their own sort of
14 unique communication plan. FDA has described
15 before that they will undertake the
16 communication plan for both the NDA and the
17 ANDA and that means that the Medication Guide,
18 the patient package insert, the communications
19 and documents, they should all be aligned and
20 same.

21 The ANDA REMS are supposed to
22 share a single system and the way that my

1 understanding of how that program has worked
2 in the past, is when they are multiple ANDAs
3 that have applied for a drug that is now
4 covered by a REMS with ETASU. The ANDAs will
5 all receive a letter that tells them that they
6 now need to come up with a shared program,
7 talk to the innovator of the reference listed
8 drug and see if they can share into the
9 system. My understanding is that the
10 innovator does not always get that letter.
11 And it only goes to the ANDA applicants and
12 they are now supposed to go back and make that
13 communication and there also is an
14 understanding that I understand from FDA that
15 FDA then maybe will take a chance to try and
16 negotiate, if it doesn't work out by the ANDA
17 negotiators.

18 But the statute also notes that --
19 and if at that point if it fails then there is
20 the potential for a waiver, which we will get
21 to a little bit later.

22 The statute also notes that no

1 holder of an improved or a covered application
2 should use their -- this is sort of the ETASU
3 required for any REMS to block or delay
4 approval of an application under the 505(b)(2)
5 or the (j) the ANDA mechanism to prevent
6 application of such element for the purpose of
7 them getting approval when they are talking
8 about the ANDA.

9 So this is a list that is from
10 FDA's website of the products that right now
11 have shared REMS programs. As you will notice
12 by the asterisk, all of those are both the
13 brand and generic manufacturer programs. And
14 isotretinoin was one of the first ones that
15 started that was not protected by any patents.
16 And the subsequent programs that you look here
17 that they are all programs that don't really
18 fall into having a patent sort of issue. And
19 when it came to buprenorphine, there was not
20 a patent issue but as sort of described later,
21 there was an issue of the generic applicants
22 and the innovator coming to agreement for a

1 unified plan so, ultimately, FDA permitted a
2 waiver.

3 So what are some of the shares
4 REMS, the dysfunctions that have come up? And
5 so and this abbreviation is just meaning FDA
6 and FDAAA, sort of giving an example of what
7 goes on here, that it does not really define
8 what is meant by a single shared REMS. I mean
9 it talks about that the elements are supposed
10 to be shared but there are some significant
11 things that have come up at least in the past
12 as described in public documents about what
13 are the costs to develop and maintain, assess,
14 and amend the REMS and what might be some of
15 the liability costs for failures. So these
16 have not been described or explained, other
17 than that they are supposed to share the
18 elements.

19 The FDA and the FDAAA do not
20 provide any guidance about the negotiation
21 process between a generic and brand name and
22 how that is supposed to work. And how that is

1 supposed to work when there is concurrent
2 patent litigation and when some of the
3 litigation that could be going on could be
4 including some of the patented elements of the
5 REMS program.

6 And currently FDA and FDAAA do not
7 provide guidance about how the reference-
8 listed drug manufacturer and the ANDA are
9 expected to cooperate and share these elements
10 of the REMS and also another point of it is
11 that the samples for the reference-listed drug
12 which has been again, mentioned in some of the
13 citizen petitions which has been difficult for
14 the generic drug manufacturers to obtain at
15 times, because of the restricted distribution
16 by the nature of the ETASU. And they also do
17 not explain what the ramifications would be
18 for failing to cooperate on either side, once
19 FDA notifies the parties or maybe in the case
20 of just the ANDAs, that notifies the parties
21 of the need to come up with a shared program
22 with the innovator.

1 To date, FDA also has provided the
2 reference-listed drug manufacturer, the
3 innovator with really no incentive of why they
4 should be sharing their program. I mean it is
5 something that just says in the statute you
6 are supposed to share but it doesn't say what
7 you get sort for sharing. And is there
8 something like the royalties or exclusivity in
9 the past? I believe Celgene was provided
10 royalties for their patented elements in order
11 to design new iPLEDGE program. But similar
12 kinds of royalty agreements have not really
13 been crafted by FDA. And exclusivity, there
14 are no provisions for anything about that
15 right now.

16 FDA has provided the reference-
17 listed drug, according to the OIG's report
18 which has been alluded to earlier today, that
19 the reference-listed drug manufacturers have
20 been providing limited assessment information,
21 particularly the REMS programs that have
22 ETASU, which makes it difficult really for the

1 innovator and for the generic drug
2 manufacturers to understand what are the
3 essential risk control elements of those
4 ETASU, which just says you share all the
5 ETASU. But does everything have to be shared
6 or what does that really mean?

7 And again, I want to mention that
8 the public documents really provide little
9 guidance about how other parties are supposed
10 to negotiate a shared REMS and what elements
11 of the REMS are working. Because
12 theoretically some of the iffy elements are
13 not really working in the ETASU, that may be
14 a time when the generic is coming in to share
15 the elements that FDA may say okay this
16 element is discretionary. You don't have to
17 implement it anymore. Maybe that would be the
18 time to decide what the elements are.

19 Most shared REMS programs that I
20 showed in the prior program, as I mentioned
21 before in the prior slide is that there are
22 class-based REMS and they were all developed

1 after all the products were already approved.
2 So it was not done in the process where you
3 had the innovator's product approved and how
4 the generics are trying to get approval but
5 they need to have a REMS and it hasn't been
6 really conducted in that process, except for
7 the buprenorphine group which, at this point,
8 appears to be the first time that FDA granted
9 a waiver for the shared REMS, meaning that the
10 generics all have one program and then the
11 brand has another program, which are all for
12 the same products, in theory. But FDA
13 provided at this point not substantive
14 explanation for how the criteria were met,
15 other than there were a series of meetings,
16 the meetings didn't work out, and ultimately
17 they allowed a waiver.

18 And then that same decision letter
19 for the petition, FDA mentions that they
20 forwarded this over to the FTC for an
21 investigation because it appeared that there
22 were some -- that the innovator was not

1 sharing appropriately, was not working the
2 negotiations appropriately.

3 So I was thinking about what could
4 help in this situation where we are thinking
5 about shared REMS and trying to offer
6 something that might be considered in future
7 meetings just to sort of get that thought
8 process going.

9 And one thing that occurred to me
10 is that in terms of we are really talking
11 about sharing, there is a proprietary right
12 that the innovator has to the program that
13 they have developed. They put a lot of money
14 into it and a lot of time and effort. So
15 necessarily when it comes to the point where
16 the generics now come and knock on their door
17 and say we want to share into your program,
18 there is a understanding there would be some
19 hesitation, that there is not really anything
20 that has been provided to them to understand
21 what are they to gain from working in this
22 process and what are some of these costs and

1 other things that have been developed along
2 the way that would be shared.

3 So what I would suggest is that
4 there might -- I know there are some comment
5 rulemaking or procedure that goes on where all
6 parties can participate and where FDA could
7 then ultimately provide guidance to what the -
8 - the goal for this rulemaking procedure would
9 be to have expectations that would be spelled
10 out to the innovator and to the generics for
11 how you are supposed to negotiate and work for
12 a single shared REMS program.

13 Talk about what would be sort of
14 reasonable shared control or access to data;
15 how they would share the cost for the
16 development of a program or the maintenance of
17 the program; who is going to pay for the
18 assessments that go along the way and what
19 happens when there are amendments to the
20 process. And if there is some liability or
21 insurance costs that are involved with the
22 program, how those could be shared,

1 potentially.

2 And then if there is an
3 opportunity for royalties or exclusivity to
4 make the process work, that would be another
5 option for it, an example.

6 Okay, this is my last slide. And
7 the last slide is the second idea is we have
8 talked about this earlier today about having
9 a database. So when FDA is approving the
10 REMS, that FDA would create a public database
11 of the current elements for the innovators
12 REMS program and the assessments and also
13 provide some sort of public accounting of what
14 those assessments have been so there would be
15 an understanding of what the essential ETASU
16 elements are that must be shared, which would
17 be agreed to by the reference-listed drug at
18 approval. They would understand what those
19 are and how they could be modified over time,
20 based on the assessments provided and what the
21 ramifications would be for failure to provide
22 such assessments.

1 Thank you.

2 MS. TOIGO: Thank you, Brian. And
3 our last speaker on this panel is Bill Martin
4 from Express Scripts.

5 MR. MARTIN: All right, good
6 afternoon. I am Bill Martin. I am the Vice
7 President of Business Development with Express
8 Scripts. And Express Scripts is the nation's
9 largest pharmacy benefit manager. We manage
10 over a hundred million lives. Our specialty
11 pharmacy, Accredo Health is the largest and
12 most comprehensive specialty pharmacy in this
13 country, providing life-sustaining as well as
14 life-enabling medications to Americans with
15 chronic conditions. And as of our last count,
16 we directly dispense 81 of the roughly 88
17 drugs that are known to have REMS programs,
18 including all 27 with ETASU requirements.

19 Express Scripts currently fills
20 over 115 million prescriptions a year and we
21 have significant experience in assisting the
22 pharmaceutical companies, as well as the

1 patients adhere to these REMS programs. And
2 we believe that REMS programs have been a plus
3 for patient care, as well as safety.

4 The additional safeguards have
5 allowed for the approval of drugs that might
6 otherwise not have been approved and we
7 believe they have undoubtedly prevented many
8 adverse patient events.

9 A point that we would like to make
10 is simply this. The REMS system today works.
11 And we ask that you please view any changes
12 being made to this system through that lens.
13 REMS exist for the purpose of ensuring patient
14 safety, not provider or pharmacy convenience
15 or ease of administration. Certainly steps
16 can be taken to improve the ease and the
17 workability of these programs but we believe
18 that any changes made must not have a negative
19 impact on patient safety.

20 In our specialty pharmacy,
21 Accredo, we dispense literally hundreds of
22 thousands of prescriptions for drugs with REMS

1 protocols. And we have not found these
2 requirements to be unreasonable in practice.
3 We do believe, however, that some enhancements
4 can be made to this current process.

5 First, we believe that the patient
6 education portions of REMS would be well-
7 served by a greater involvement of allied
8 health professionals such as nurses and
9 pharmacists. At Express Scripts, we have
10 organized our health professionals into
11 disease specialties. For example, oncology.
12 This specialization coupled with our large
13 volume means that our specialized oncology
14 pharmacist likely counseled more oncology
15 patients per pharmacist than anyone in the
16 country.

17 The same statement applies to the
18 other disease specialties which we serve. FDA
19 should encourage pharmaceutical companies to
20 look to resources beyond the physician's
21 office when developing their patient
22 educational components.

1 Secondly, access. When access is
2 mentioned in the industry, it is often
3 referring to pharmacy access but we believe
4 that what is really important is patient
5 access. Patient access in today's era is much
6 more involved than simply expanding the number
7 of pharmacies that stock a drug. Patient
8 access in the United States is more often a
9 factor of insurance coverage, patient
10 authorizations, and completing the ETASU
11 protocols, for example.

12 Pharmaceutical companies should be
13 encouraged to do more to provide education to
14 physicians, as well as pharmacists in how to
15 best access their drugs and/or establish
16 patient hubs to help manage that process.

17 Third, we ask that the FDA require
18 early and better monitoring of REMS for
19 effectiveness. In recent years the level of
20 required monitoring appears to have declined
21 and we would like to see more vigorous early
22 monitoring done in a scientific manner and

1 then see those findings lead to improvements
2 in the existing REMS protocols.

3 Last, to address the question of
4 standardization, we would be in favor of more
5 standardization of the process and the general
6 structures of the required REMS. For example,
7 standardize the level of risk that would
8 require a patient registry versus physician
9 training. That would speed the approval
10 process and to provide a more similar REMS
11 protocol design for drugs for similar safety
12 profiles. We believe that the absolute or
13 total standardization of REMS protocols
14 themselves, however, would not be effective,
15 given the differences in drug profiles.

16 Thank you.

17 MS. TOIGO: Thank you, Bill, for
18 those comments. And thank you to our panel
19 members. And we are staying right on time.

20 So now it is time for questions
21 from the FDA panel. Who wants to get us
22 started? Mwango.

1 DR. KASHOKI: I'm still looking
2 through my notes so I am going to do my best
3 to be articulate here.

4 This question is for Dr. Seligman.
5 You raised several points in your presentation
6 and you suggested that we focus the REMS
7 efforts on risks that can actually, as you are
8 describing them, be mitigated and I believe
9 you said that those kinds of risk would be
10 those that could be reduced in frequency or
11 severity and could be measured in some shape
12 or form.

13 And you also went on to talk about
14 perhaps in terms of defining our goal,
15 removing some of the things that may not be
16 helpful in achieving REMS effectiveness, such
17 as some of the processes or tools that we use.
18 And later on you then said as we worked
19 towards standardization, we should try and
20 identify those processes or tools that do
21 work.

22 So starting with the last point,

1 in order for us to do that, we would have to
2 figure out what success means. Like when we
3 say a tool works or is effective, how were we
4 measuring that?

5 And so getting back to your
6 initial point about that we should be focusing
7 REMS efforts on risks that can be mitigated,
8 are you then saying that a successful tool or
9 process would be one that directly has such an
10 effect?

11 I am asking this because some of
12 the tools and processes that we use enrollment
13 forms, enrollment process for example, are
14 necessary steps in order for us to get to the
15 ultimate goal of reducing a particular risk.

16 So if you could just explain your
17 thought process as you went through those
18 concepts.

19 MR. SELIGMAN: So there are
20 certainly important and legitimate steps to
21 achieve the goal. I think that the ultimate
22 thing that we are trying to focus on is for

1 example in the area of fetotoxicity, where the
2
3 goal is to prevent exposure to the developing
4 fetus and where the risk mitigation and
5 management steps are ensuring that the patient
6 is not pregnant at the time the product is
7 either prescribed or doesn't become pregnant
8 during the course of therapy.

9 To me the performance of those
10 tests to ensure that there is a negative
11 pregnancy test, ensuring that there has been
12 adequate prescribing of either birth control
13 or some other means to ensure prevention of an
14 unwanted or unforeseen pregnancy, those to me
15 are the essential things that should be
16 focused on and the goal that should be -- the
17 metric that should be used to judge the
18 success of the program.

19 So I think that clearly there are
20 lots of other important elements or things
21 that go into ensuring that prescribers do the
22 right thing, that patients do the right thing.

1 But at the end of the day, I tend to look at
2 the bottom line and I think what I am
3 indicating in my presentation is that kind of
4 sort of bottom line approach to judging the
5 success of a REMS program is something that
6 should be focused on and that those programs
7 that can't be defined by essentially bottom
8 lines really we should take another sort of
9 hard look as to whether they are adding value.

10 DR. KASHOKI: Can I follow up?

11 So with regard to the programs
12 that we have where it is primarily an
13 information- or education-based focus for the
14 user risk that we may not be able to
15 intervene. We might need to have both
16 patients and prescribers aware of the
17 likelihood of exposure, likelihood of adverse
18 outcome by using the medication, are you
19 saying in those circumstances a REMS program
20 may not be appropriate indicated because there
21 is no measurable outcome. Are you saying
22 that?

1 MR. SELIGMAN: Yes.

2 MS. TOIGO: Sir.

3 DR. GOLDMAN: I published a paper
4 recently, I guess a few years ago, saying how
5 effective is effective enough. That is the
6 question you are asking.

7 Before there were REMS, there were
8 RiskMAPs. Before the RiskMAPs there were
9 programs like the clozapine program.

10 The point is that the data for
11 example on the original terfenadine
12 notification showed that co-prescription went
13 down significantly but it didn't go to zero.
14 We are going to have to determine what the
15 effectiveness is in relation to what we
16 determine to be effective. Otherwise, you
17 have to take something off the market without
18 even trying in relation to that.

19 There is significant data on
20 notifications. The question is why people
21 haven't looked at that information. Because
22 not only is there effectiveness data, there is

1 data on how the notifications are written,
2 including the very format they utilized. Qs
3 and As are month the most effective that we
4 can utilize in terms of that. There is
5 information out there and it certainly goes to
6 the point that we are making, Paul and I were
7 making about how you determine what
8 effectiveness is. But going in, you have to
9 have the flexibility within the REMS to not
10 only look at the data you are looking at,
11 looking at the behavior you are trying to
12 change and realize that all risks are not the
13 same. Teratogenicity is not nearly the same
14 as trying to prevent someone co-prescriptioned
15 or someone using something off-label. They
16 are very different risks. Their behavior is
17 going to be different. The solutions may well
18 be different, even though they may share some
19 things in common in relation to education by
20 the patients or prescribers or dispensers.

21 MS. TOIGO: You mentioned that
22 there is a lot of data on notifications. If

1 it something you are willing to the docket
2 that we may be haven't --

3 DR. GOLDMAN: I will send you my
4 preprints.

5 MS. TOIGO: -- seen yet, then
6 please consider including that with your
7 slides.

8 DR. GOLDMAN: Sure.

9 MS. TOIGO: Claudia and then
10 Elaine.

11 DR. MANZO: My question is for
12 Jim. You mentioned that there were certain
13 REMS requirements that didn't integrate well
14 into pharmacy systems. And I wondered if you
15 could I guess again describe sort of the
16 requirements that you think might be best
17 integrated into retail settings versus maybe
18 specialty pharmacies or mail order pharmacies.

19 MR. DEVITA: I think for the
20 retail community pharmacy environment that the
21 requirements that fit well into workflow that
22 leverage the technology that is available, the

1 ePrescribing systems, the physicians' health
2 record, electronic health record, and the
3 claims adjudication system as well. Like the
4 TIRF program is really working out well.
5 There is really no manual process associated
6 with that. It is part of the normal workflow
7 and we get information on eligibility and so
8 forth before the prescription is even filled
9 for the patient.

10 So things that work into the
11 workflow work best for retail that limits the
12 technology.

13 The other REMS requirements that
14 are more complex that are more time consuming
15 such as extensive counseling for patients may
16 fit better outside of community pharmacy.

17 MS. TOIGO: Thanks, Jim. Elaine?

18 MS. LIPPMANN: Yes, thanks. I
19 have a question for Brian.

20 You seem to be suggesting that FDA
21 should be involved in the process of
22 determining some of the more logistical

1 aspects of the single shared system. Like you
2 mentioned liability and insurance costs and
3 shared access to data, that sort of thing. I
4 just want to get a better understanding of how
5 you see, how you envision FDA' role in those
6 kinds of decision-making in the development of
7 the single shared system. How far you think
8 that the role should be extending into those
9 kinds of decisions.

10 MR. MALKIN: So I would imagine
11 this would come through in a notice of
12 rulemaking comment sort of procedure where
13 both the reference-listed drug, the
14 innovators, and the generic drug manufacturers
15 sort of talk about these different costs and
16 the controls and what is entailed and what
17 would be an expectation.

18 So for example, if there is a
19 particular development cost for a REMS and
20 that is -- it is able to be quantified by the
21 innovator that the generics agree that they
22 are going to all pay into that, that there

1 would be this pot of money -- that whatever
2 that cost was, depending upon how many members
3 are now in that program, they all sort of
4 share the cost for that development cost or
5 the maintenance costs for the program or what
6 additional costs that need to be run into it
7 in order for it to make sense, for them to
8 share the program, versus having two
9 independent programs which, as we were talking
10 about earlier today, just makes things more
11 complicated. I mean and now there is a
12 situation where there is going to be
13 innovators and the group of generics having
14 the buprenorphine program that is more
15 complicated. There are two programs to keep
16 straight versus there being one program.

17 MS. LIPPMANN: Thanks.

18 MS. TOIGO: Thank you. Anyone --
19 Adam.

20 MR. KROETSCH: Hi. A couple of
21 you mentioned that or suggested that we look
22 into using real-time portals, web-based

1 portals, shared databases that could be used,
2 I think, to track things like certification
3 and provide real-time approvals to distribute
4 drugs, for example. And one of the questions
5 that we asked in the Federal Register Notice
6 is who you might envision implementing
7 something like that and how exactly it would
8 work across a range of different REMS. So did
9 you have any thoughts on that?

10 I can mention I know Paul, you
11 were one of the people on that.

12 MR. SELIGMAN: Since I mentioned
13 it, I should actually reply.

14 So I think there are a number of
15 options to consider. Clearly, the first
16 organization that comes to mind, of course, is
17 the FDA or an organization on contract to the
18 FDA. Particularly when it comes to developing
19 a shared resource for access to various
20 prescriber and patient tools, I think that
21 would be a great resource.

22 I think you heard very cogently

1 this morning from the University of Illinois
2 Hospital System how they effectively manage
3 healthcare using their own internal
4 information systems. And again, I think that
5 a resource either at the federal level or a
6 contract managed at the federal level would
7 provide those kinds of tools to, for example,
8 other kinds of healthcare systems that want to
9 effectively manage their risks I think would
10 be probably the best place for that, best
11 locus for that kind of system.

12 MS. TOIGO: Thanks, Paul. Megan.

13 MS. MONCUR: I have a question for
14 Dr. Goldman. In one of your observations you
15 mentioned how the perceived burden of REMS or
16 a REMS program, a particular REMS program
17 changes when there is an understanding of the
18 rationale for the REMS and what it makes
19 possible in terms of availability.

20 Why do you think that that is
21 something that isn't more well-known and how
22 can we make that better understood?

1 DR. GOLDMAN: Do you really want
2 to know?

3 (Laughter.)

4 DR. GOLDMAN: Sub-optimal
5 education by the FDA, by the industry, by the
6 healthcare professional groups across the
7 board, quite frankly.

8 As a physician, I would say
9 physicians are among the ones. Pharmacists
10 can be more tuned in in relation to that. I
11 was doing work with ASHP. I think that tells
12 you something in relation to that.

13 I think I was encouraged over the
14 year that I did the work because healthcare
15 professionals advocate for their patients.
16 That is why we are here. I am first and
17 foremost a clinician. And when you explained
18 first of all the rationale for REMS, the fact
19 that most drugs don't have REMS as we talked
20 about, and again, that is why I advocate for
21 the safety specification pharmacovigilance
22 plan because most drugs are not going to

1 require that.

2 When I actually explained to I
3 think these were pharmacists around the
4 country, explaining why you have to have this;
5 how the data was being used; the fact that it
6 was feeding into a system that would then
7 possibly revise the plan in relation to that;
8 that is exactly the kind of work we do when we
9 talk about post-marketing surveillance and
10 adverse event reporting.

11 So I think -- and again, I
12 appreciate your questions because it is
13 obviously one I have thought a lot about. It
14 has to be a coordinated effort. And it is not
15 just one group. That is one of the things we
16 said in 1999. There is a lot of stakeholders
17 when it comes to risk. It is not just a
18 regulator. It is not just a regulator
19 industry. It is healthcare professional
20 groups. It is patients themselves in relation
21 to that.

22 But you have to explain. You

1 can't roll out a program that is going to be
2 administered by healthcare professionals
3 without first of all talking to the healthcare
4 professionals themselves. You have got to
5 look at the disease state in particular. And
6 again, I have been involved with several
7 different REMS and risk matters, and they are
8 very different. And the behaviors are very
9 different and the goals are going to be very
10 different in relation to that but the bottom
11 line is all the same. Keeping a product that
12 is effective but that poses particular risk on
13 the market, making sure that patients still
14 have access to it.

15 If you make that clear from the
16 beginning, I think people will accept more of
17 a burden in relation to that because that is
18 what they are said to do. That is what they
19 sign on to do when they go to medical school,
20 dental school, and nursing school and pharmacy
21 school. You accept that going in.

22 I think if we made that clearer I

1 think there would be a lot more acceptance,
2 frankly, of REMS.

3 MS. TOIGO: Go ahead.

4 MR. SELIGMAN: Actually I have a
5 really comment to the previous question that
6 Adam raised. In your presentation you talked
7 about the structured product label and the
8 DailyMed. There is another potential place
9 for such access to that information.

10 Sorry about that.

11 MR. KROETSCH: Yes and one of the
12 -- I agree completely. But I think one of our
13 concerns is that that is a source of
14 information about different REMS programs and
15 what the requirements might be. But it sounds
16 like what I hear regarding portals is this
17 idea of some sort of shared database two-way
18 communication which is beyond, I think, what
19 SPL would be capable of doing.

20 DR. GOLDMAN: May I make a point
21 about labeling? Because Paul, that is a very
22 good point.

1 The issues about changes being
2 affected as opposed to approved labeling is
3 obviously a major concern that people have.

4 You know I was the Medical
5 Director of MedWatch, the first one we had.
6 And we spent a lot of time changing labeling,
7 posting labeling revisions which now has been
8 an ongoing program, knowing where to find
9 the data on the DailyMed and others. There
10 are things separate from REMS that are clearly
11 risk mitigation. And again, it goes to the
12 label. It goes to knowing about the latest
13 labeling and those aren't labeling changes.

14 If I were to advocate for looking
15 at that, perhaps even separate than what you
16 do with a REMS, might be helpful in terms of
17 trying to determine what it is that we are
18 trying to get across and how peoples'
19 behaviors are changed based on the fact that
20 they know what the latest safety information
21 is. I do think it is part of the mix.

22 MS. TOIGO: Megan, did you have a

1 follow-up? And then that will be the last for
2 this.

3 MS. MONCUR: Okay. It is actually
4 not a follow-up question. It is a question
5 for Jim Devita. And you mentioned that the
6 TIRF program is working well for you and in
7 particular because it is an automated program.
8 But one aspect of that program that is not
9 automated and we have referred to it before,
10 if for some reason certification cannot be
11 verified, if somebody hasn't enrolled.

12 Do you have any best practices or
13 have you received any feedback on how that can
14 be handled more efficiently?

15 MR. DEVITA: I haven't received
16 any direct feedback to that nature. The
17 feedback that I have received about TIRF is
18 when the pharmacist compared to essentially
19 all the other REMS programs, which is multiple
20 manual processes and they are very different
21 in obtaining a stick or there is a form you
22 have to fax that you have to call. Another

1 one is you have to access a website. They are
2 all very different. And relying on
3 pharmacists remembering to do it correctly,
4 although they are being trained, it is still
5 relying on them following the process the way
6 they were trained and it could be months
7 later.

8 The TIRF program is integrated
9 into the system. It goes out through the
10 claims adjudication process. And if there is
11 an issue they get a claims rejection with a
12 message as to what the specific issue is and
13 they can address it from there.

14 MS. MONCUR: Okay.

15 MS. TOIGO: Thank you.

16 MR. DEVITA: You're welcome.

17 MS. TOIGO: So thank you to our
18 panel members. And again, if you are willing
19 to submit your slides to the docket, that
20 would be great. We heard the references to
21 suboptimal communication. If you have some
22 examples of optimal or even better than

1 optimal communication or things that have
2 worked well and you want to share those
3 examples, I would encourage you to do that in
4 the docket as well.

5 So thank you very much. And we
6 will line our up our next panel, which is
7 prescriber and patient directed tools. So we
8 have Ann Karty, Murray Kopelow, Andrew
9 Kolodny, and Natalie O'Donnell.

10 Hopefully the temperature is
11 better in here. We heard a lot of complaints.
12 We have been trying to adjust the temperature
13 to the extent that we can in this room. So
14 hopefully those that were cold are okay. And
15 if not, tomorrow please bring a blanket.

16 Okay, so our first speaker for
17 this panel is Ann Karty from the American
18 Academy of Family Physicians.

19 DR. KARTY: Hi. Good afternoon.

20 I am Karty and I am the Medical
21 Director in the Continuing Medical Education
22 Division at the American Academy of Family

1 Physicians. I am a family physician. I
2 maintain a clinical practice and I see
3 patients in an outpatient clinic.

4 On behalf of the American Academy
5 of Family Physicians, about 111,000 family
6 physicians and medical students, I appreciate
7 that the FDA is holding this two-day meeting
8 to discuss issues and challenges associated
9 with standardization and assessment of Risk
10 Evaluation and Mitigation Strategies.

11 The AAFP has submitted written
12 comments to the FDA in response to the Notice
13 of the Public Meeting from the AAFP Board
14 Chair, Glen Stream, and I have copies that are
15 also available but they have already been
16 provided.

17 I represent the AAFP as a
18 registered speaker for this meeting and the
19 displayed link actually goes straight to the
20 written comments that were provided to the
21 FDA.

22 Because this is the first REMS

1 that has continuing medical education
2 integrated into it and it also -- my approach
3 to these comments is actually as a case study
4 to demonstrate that there really is a broad-
5 based approach to many multiple medical issues
6 and just to remind everybody that when this
7 first CME introduction happened, there were
8 many administrative initiatives that were
9 happening in parallel. And they were related
10 to not just administrative issues but other
11 medical issues that we had also self-
12 identified that were necessary for our
13 patients.

14 Pain management and opioid abuse
15 are serious public health concerns and the
16 AAFP shares with the FDA commitment to making
17 sure that patients continue to have access to
18 appropriate pain medications and that all
19 opioid products are used safely and
20 effectively.

21 The AAFP remains dedicated to
22 finding solutions to the crisis of pain

1 management and opioid abuse and released a
2 position paper titled pain management and
3 opioid abuse, a public health concern.

4 Integrated into this position
5 paper there are several key recommendations,
6 including advocacy, clinical improvement, and
7 maintenance of function for patients,
8 evidence-based physician education, and
9 collaboration with other organizations. As
10 such, the position paper urges states to
11 obtain physician input when considering pain
12 management regulation and legislation; urging
13 all states to implement prescription drug
14 monitoring programs; opposition to mandatory
15 CME as a prerequisite for DEA or other
16 licensure; supporting the development of
17 education to ensure the safest and most
18 effective use of long-acting and extended
19 release opioids; and to increase national
20 funding to support research into evidence-
21 based strategies for optimal pain management
22 and incorporation into the patient-center

1 medical home model.

2 Again, this hyperlink directs to
3 the position paper and I have extra hard
4 copies that I can share.

5 The AAFP is also pleased that the
6 FDA and the White House Office of National
7 Drug Control Policy continues to address this
8 ongoing public health crisis, resulting in the
9 latest report titled "Epidemic: Responding to
10 America's Prescription Drug Abuse Crisis."

11 Family physicians and other
12 primary care physicians and clinicians play a
13 vital role in effective pain management, which
14 includes prescribing opioid analgesics. The
15 AAFP remains concerned with any policies that
16 would create additional prescribing barriers
17 for primary care physicians, since
18 professional judgment and clinical experience
19 determine, along with patients, the need for
20 pain relief.

21 The AAFP fully supports voluntary
22 participation.

1 In particular, the AAFP is a
2 continuing medical education and national CME
3 provider. We continue to be involved in
4 conversations with the FDA and REMS program
5 committee, other credit systems and other CME
6 provider organizations. We are pleased to
7 support CME that addresses educational goals
8 identified in the FDA CME/CE extended release
9 long-acting opioid REMS blueprint. And the
10 blueprint details core messages to be covered
11 in educational offerings for prescribers of
12 the ER/LA opioids.

13 Education is foundational to
14 family physicians striving to perform the best
15 patient care possible and to educate family
16 physicians about this growing epidemic, the
17 AAFP continues to offer dedicated CME.

18 The AAFP is developing live online
19 and self-study CME activities that align with
20 educational goals set forth by the FDA
21 blueprint. The CME offerings are in
22 compliance with relevant accreditation

1 guidelines and they ensure validity. And
2 again, the AAFP would not support mandates
3 that require physicians to complete the CME
4 because the AAFP believes that voluntary
5 education helps to address the growing problem
6 of prescription drug use and misuse.

7 The AAFP also offers CME
8 opportunities beyond information that area
9 actually embedded in the FDA blueprint. We
10 have an upcoming webinar called Chronic Pain
11 and the Safe Use of Opioids that focuses on
12 educating family physicians about chronic
13 nonmalignant pain and encourages physicians to
14 talk with patients about past or present risk
15 factors. It is important to note that the
16 curriculum that this particular upcoming
17 program is based on is from information
18 gleaned last fall at one of our annual
19 assembly meetings. So it is always to build
20 your education on outcomes-based research when
21 you are developing new programs.

22 There are future programs for CME

1 about REMS that will be integrated where
2 appropriate in the development of educational
3 plans. And the intent also is that there will
4 be additive activities to extend educational
5 experiences to impact and improve patient
6 outcomes.

7 I have a few summary bullets. As
8 a family physician, it is important to address
9 the dual issue of the pain crisis with
10 appropriate pain management for patients and
11 opioid abuse. Voluntary education is
12 preferred, not to make mandatory additional
13 restrictions to impact the ability to practice
14 medicine or licensure. The AAFP supports
15 meeting and exceeding the FDA targets for this
16 training.

17 The AAFP as a credit system openly
18 supports the CMSS code and the ACCME standards
19 for commercial support and is successfully
20 working with the RPC and the IWG Industry
21 Working Group to make sure that these REMS
22 work within the rules and follow within the

1 rules of all of the credit systems.

2 Within the broad scope of
3 medicine, and specifically family medicine,
4 there continue to be recommendations that the
5 FDA hopefully consider when there are other
6 considerations for CME.

7 Prescribing is already integrated
8 into physician education when discussing
9 specific clinic topics and CME is designed on
10 evidence-based needs assessments and formal
11 gap analysis. Therefore, gaps in knowledge,
12 practice, skills, and attitudes also exist in
13 new technologies, innovative drug treatments,
14 changes in treatment algorithms, and actually
15 practicing hands-on procedural skills
16 acquisition, as well as important patient-
17 based skills, including communication,
18 cultural competency, attention to health
19 disparities, and end of life issues.

20 When CME is being considered as a
21 REMS, it may be important to consider reading
22 recommendations of specific topics or formats

1 to those subject matter experts actually
2 preparing the content and the formal
3 educational design of the activity to those
4 with some adult education experience to meet
5 the specific outcomes of the training. And
6 that goes back to the earlier conversation
7 about knowing the metrics on the front end.
8 That really would depend on what the issue is,
9 what the topic is, and what the outcome is.

10 Continuing to encourage
11 technology, including integration of
12 electronic health record data, to add patient
13 outcomes and garner information for CME
14 activities, one format which includes
15 performance improvement CME, which is already
16 in existence for measuring physician pre-
17 assessment intervention and post-assessment
18 data, which is a required component of board
19 certification and most states' licensure.

20 It is also important to remember
21 that PICME or education at this level, it
22 takes time to show change. It is extremely

1 expensive. And pulling the de-identified data
2 reports and publishing it, again, will take
3 time.

4 Thank you.

5 MS. TOIGO: Thank you, Ann. Next
6 we will hear from Murray Kopelow from the
7 ACCME.

8 DR. KOPELOW: Thank you, very
9 much. It is an honor to be here. I speak in
10 support of accredited prescriber education and
11 in support of REMS. The Accreditation Counsel
12 for Continuing Medical Education was created
13 by the National Organizations of Medicine in
14 1980 and we accredit the continuing medical
15 education enterprise on their behalf.

16 The scope of the accredited
17 continuing medical education enterprise that
18 is available to the FDA in the REMS programs
19 for prescriber education is massive. There
20 are 24 million registrants in accredited
21 continuing medical education within the ACCME
22 system in 2012; there were 133,000 activities;

1 almost a million hours of instruction. There
2 are 2,000 accredited providers between our
3 system and the state medical society's system
4 that covers the country and that is available
5 to the initiatives for prescriber education.

6 The system has a long experience
7 with population in a community health-base
8 needs. Our system addresses regional
9 variation. It addresses variation within
10 medical problems and their care as described
11 by McGlinnis in 2002 in the New England
12 Journal.

13 Our system addresses the racial
14 disparity issues as is manifest in the issue
15 of the disparity in healthcare. Survival
16 between black women and white women with
17 breast cancer, for an example. And we have
18 for several years, our system has been
19 addressing the issues that this long-acting
20 sustained release opioid REMS has addressed.

21 When you look at the factors that
22 predict or increase the probability of change

1 through education, our system creates the
2 facilitating conditions for change through
3 predisposing, enabling, or reinforcing the
4 professionals to practice.

5 It is our system's simple
6 requirements are that the education needs to
7 be based on professional practice gaps. We
8 need to understand the needs that underlie
9 those gaps. They need to address a specific
10 competency within the framework of medicine.
11 They need to use the appropriate educational
12 format and they need to measure for success in
13 change. Those are the constructs that come
14 along with accredited continuing medical
15 education.

16 Tom Frieden, the Director of CDC
17 has acknowledged our system's responsiveness
18 to addressing public health issues, the same
19 kind of public health issues that the REMS
20 address.

21 Now with respect to integration of
22 REMS into the healthcare system, it is

1 important to recognize that education
2 developed and delivered by manufacturers is
3 outside the professional practice systems of
4 physicians and is avoided by physicians.

5 A prescriber education developed
6 and delivered by manufacturers does not meet
7 the medical profession self-regulation
8 standards for independence from ACCME-defined
9 commercial interest as articulated in the
10 ACCME standards for commercial support.

11 So we say stay the course. Use
12 accredited continuing medical education for
13 prescriber education in your REMS.

14 With respect to standardization,
15 it is important to recognize that an option is
16 the standardization of process, not the
17 standardization of content as to be delivered
18 in the education, that our process ensures
19 that the basis for educational content is the
20 needs that underlie the professional practice
21 gap. We ensure that the scope of evaluation
22 of effectiveness is always the change in

1 competence performance or patient outcome and
2 all of our providers measure change in these
3 parameters. And that the data system or the
4 data set describing accredited CME is
5 standardized by the accreditors a priori.

6 In addition, there is a rigorous
7 management of the boundary issues created by
8 the presence of manufacturers and their funds
9 in the process. The ACCME standards of
10 commercial support that were first articulated
11 in 1992 and then revised in 2004 provide for
12 independence, provide for the resolution of
13 personal conflicts of interest, ensure the
14 management of commercial support is
15 appropriate, that there is a separation of
16 promotion for education, that there is absence
17 of bias, and there is the disclosure to
18 learners of relevant financial relationships
19 in the presence of money.

20 It is ironic that these parameters
21 were created by the Food and Drug
22 Administration in your guidances to the CME

1 industry in 1997 and these are manifestations
2 of the CME system's implementation of what is
3 important to the Food and Drug Administration.

4 A way to standardize contents, one
5 is through blueprinting. But blueprinting may
6 be the enemy of integration, as prescribers
7 are living in a world of practice-based
8 learning and change and of reflective self-
9 assessment. Continued professional
10 development systems that REMS prescriber
11 education wishes to integrate into are now
12 based on the individual's own knowledge, their
13 own confidence, or their own performance.

14 Variants in the overall content is
15 a strength of the CME system. And doing the
16 same continuing education over and over again
17 to every audience is somewhat like a watch
18 that doesn't move. It is perfectly accurate
19 twice a day but otherwise, it is not very
20 useful.

21 Prescriber education that is
22 defined and based on the individuals' needs

1 reflects the true variation of the needs
2 within the physician community. The physician
3 community is not a homogeneous group.
4 Physicians are at various stages of either
5 knowing or at various stages of changing. And
6 the continuing medical education enterprise
7 and the evolving and emerging continuing
8 professional development systems like
9 maintenance of licensure and maintenance of
10 certification are based on understanding that
11 individual variation and having the education
12 be responsive to it.

13 So if you want education that goes
14 beyond the requirements of the drug prescriber
15 information, we can do it if accredited
16 education is left to be responsive to the
17 information on professional practice gaps, the
18 needs that underlie these gaps. And the FDA
19 and the FDA's processes would be a great
20 source of what those gaps are.

21 Does the accredited prescriber
22 education teach us how to manage serious risks

1 associated with the drugs? Yes, if the
2 accredited CME is allowed to be responsive to
3 the stage of change and levels of knowing that
4 the people in the room and not dealing with
5 all of the physicians as a single homogeneous
6 group.

7 The less the FDA dictates the
8 content, the further beyond the requirements
9 of the drug information the CME system will
10 probably go and the more likely we will be to
11 address all of the individuals' needs who are
12 taking care of patients.

13 The prescriber education -- the
14 effectiveness also could be measured simply by
15 its effectiveness in promoting access to
16 education for physicians that didn't have
17 before. By mobilizing the education community
18 to an issue could be an effectiveness of REMS.
19 And drawing the profession's attention to the
20 problem would be another parameter through
21 which the effectiveness of REMS could be
22 measured.

1 Going forward, we think we should
2 be promoting the integration of REMS into the
3 fabric of accredited continuing medical
4 education. We should value addressing many
5 people's measured and individuals' needs and
6 that could be the focus. We could value the
7 evidence of change and not just the evidence
8 of reach to the learners. And we could
9 promote reliable recognition of prior learning
10 that if people do know what the risks are, if
11 people do know how to use it, then maybe those
12 people don't need to have additional
13 education.

14 And the other is that perhaps the
15 route to safety for the patients is not solely
16 through education to the prescribers but maybe
17 to the physicians who are not prescribing
18 these products.

19 Thank you very much.

20 MS. TOIGO: Thank you, Murray.

21 Our next presenter is Andre Kolodny from the
22 Physicians for Responsible Opioid Prescribing.

1 DR. KOLODNY: Thank you. It is a
2 pleasure to be here today. My name is Andrew
3 Kolodny. I am president of PROP, Physicians
4 for Responsible Opioid Prescribing. It is an
5 organization with a mission to reduce
6 morbidity and mortality from opioid analgesics
7 and to encourage more cautious prescribing of
8 opioids. I am going to share with you our
9 organization's perspective on the ER/LA opioid
10 REMS.

11 The United States is facing an
12 epidemic of opioid addiction, opioid analgesic
13 addiction to be specific. The epidemic began
14 in the late 1990s and this rate shows you
15 rates of people seeking treatment for pain
16 killer addiction in the late 1990s, just when
17 the epidemic was beginning. And what you see
18 is that states that are showing up as red or
19 maroon are the states with the greatest rate
20 of people seeking treatment for pain killer
21 addiction. I would like you to watch what
22 happens to the color of the map as we go

1 forward in time. This is 1999. This is 2005
2 and you can see that much of the map has
3 turned red. Almost the entire east coast has
4 had a sharp increase in people seeking
5 treatment for pain killer addiction. And by
6 2009, you see that just about every single
7 state in the country experienced a sharp
8 increase in people seeking treatment for pain
9 killer addiction. And this is how you would
10 define an epidemic when you have a sharp
11 increase in the prevalence of a disease over
12 a short period of time.

13 It is important to recognize that
14 people get this disease in pretty much one of
15 two ways. You become addicted to pain killers
16 either through non-medical use, so for example
17 a young person finding leftover pills in a
18 medicine chest; experimenting with them,
19 enjoying them, and then becoming hooked. Or
20 a patient can become addicted through medical
21 use of opioid analgesics, starting off by
22 taking the pills as prescribed and then

1 developing the disease of addiction.

2 One of the unfortunate but common
3 outcomes for people who develop this disease
4 is that many of them die of overdose deaths.
5 And what we have seen over this period of time
6 since the beginning of the epidemic, we have
7 seen a sharp increase in people dying from
8 pain killer overdose deaths indicated in red.
9 We actually have more people dying from pain
10 killer overdoses than dying from heroin and
11 cocaine combined. And for drug overdose
12 deaths in general, we now have more people in
13 the United States dying from drug overdose
14 deaths than dying from car crashes.

15 This is a CDC slide and the CDC
16 has been showing this slide to try and be as
17 clear as they possibly can about what they
18 think is causing this epidemic. The green
19 line represents cells for opioid analgesics,
20 basically the increase in consumption of
21 opioids. And what the CDC is arguing is that
22 the sharp increase in prescribing of opioid

1 analgesics beginning in the late 1990s is
2 causing this epidemic and it is leading to
3 parallel increases in overdose deaths,
4 represented in the red line and in addition
5 or people seeking treatment for addiction to
6 pain killers represented by the blue line.

7 As you look at this graph, one
8 thing that is important for you to recognize
9 is that this change in prescribing practices,
10 what caused this green line to shoot up was
11 not some new evidence that opioids were safe
12 and effective, what caused the change in
13 prescribing practices was an industry-funded
14 campaign that misled the medical community to
15 believe that the risks of opioid analgesics
16 were far lower than they actually are. In
17 particular, we were misled to believe that we
18 shouldn't worry about addiction. And the
19 benefits of opioids, particularly for chronic
20 non-cancer pain were exaggerated.

21 The opioid REMS, FDAs plan to have
22 an opioid REMS was released in February 2009.

1 And when there was the first announcement that
2 FDA was planning to do this, there were many
3 in the advocacy community who had very high
4 hopes for this REMS. And some of the early
5 communications about the REMS led us to
6 believe that FDA might be interested in having
7 a registry for chronic pain patients who were
8 on opioids that could ensure that the patients
9 are being properly monitored, that could
10 ensure that they are not doctor shopping, or
11 even reduce the risk of diversion of pills to
12 the black market. We were also hopeful that
13 FDA would be introducing mandatory education
14 so that prescribers of opioid analgesics might
15 be required before prescribing opioids for low
16 back pain, for common chronic conditions long-
17 term that you might require some mandatory
18 education for prescribers like we have for
19 buprenorphine when used for addiction
20 treatment. And we understand that
21 buprenorphine has a significantly lower risk
22 of addiction and abuse potential than the

1 other opioids.

2 Between the first announcement of
3 an FDA opioid REMS and the plan that was
4 presented to an advisory committee in July
5 2010, there were multiple meetings and
6 multiple opportunities for stakeholder input.
7 And on my slide I put stakeholder in quotes
8 because I think that FDA was most influenced
9 by organizations that I probably would not
10 characterize as legitimate stakeholders.

11 So for example, the American Pain
12 Foundation, which is an organization that
13 closed down last year when the Senate Finance
14 Committee announced an investigation of its
15 influence on opioid prescribing, that is an
16 organization that had received about 90
17 percent of its income from opioid
18 manufacturers. That organization which
19 presented itself as a grassroots organization
20 representing the interests of patients in pain
21 but probably better characterized as an
22 AstroTurf organization, artificial meant to

1 look like grassroots, the American Pain
2 Foundation told the FDA that patient
3 registries would stigmatize patients, would be
4 bad for pain patients. And other
5 organizations, along with the American Pain
6 Foundation, convinced FDA to gut the plan that
7 had initially been proposed.

8 When the final REMS was presented
9 to an advisory committee in July of 2010, the
10 committee voted it down 25 to 10. And what
11 they said was that this REMS has no teeth in
12 it. This was the coverage of that meeting in
13 the press, FDA News. Class-wide opioid REMS
14 lacks teeth to tackle abuse. FDA advisors
15 reject Agency plan to control opioid use as
16 too soft. FDA panel rejects REMS for opioids
17 says current plan inadequate.

18 Why did FDA listen to the American
19 Pain Foundation and to the other
20 organizations? And why did we wind up with
21 such a weak REMS program? I think if we would
22 give FDA the benefit of the doubt, I think

1 that they bought this argument and this is the
2 argument that pain organizations made. They
3 argued that there are millions of pain
4 patients who need ready access to opioids
5 because they are being helped by them and then
6 there are the drug abusers who are being
7 harmed by opioids and they said don't have a
8 REMS that is so strict that you are trying to
9 stop drug abusers but making pain patients pay
10 the price for the bad behavior of drug
11 abusers.

12 But that is really a false
13 dichotomy because what we do know is that we
14 don't have two distinct populations. We don't
15 have pain patients who are all being helped
16 and drug abusers who are being harmed. We
17 know that abhorrent drug use behaviors are
18 extremely common in pain patients.

19 We know that 35 percent of
20 patients on long-term opioids meet criteria
21 for opioid addiction. And in a recent study
22 of overdose death victims that came out of

1 Utah, they found that 92 percent of the people
2 dying of opioid overdoses were having opioids
3 prescribed to them for a diagnosis of chronic
4 pain. Probably many of them were addicted but
5 they were having opioids prescribed to them
6 supposedly for legitimate pain.

7 After the FDA plan for an opioid
8 REMS was voted down, we had the release of a
9 blueprint curriculum for voluntary education
10 programs. And then finally in April 2013, FDA
11 issued the final curriculum and there was the
12 final plan for the opioid REMS, which was the
13 exact same plan that the advisory committee
14 had voted down.

15 When comments to the draft
16 curriculum were sought, my organization
17 submitted a letter to FDA expressing our
18 concern about the curriculum that was going to
19 be used for voluntary education programs
20 sponsored by industry. And I suppose to many
21 of you this is just a list of names but this
22 list includes some of the most prominent pain

1 specialists in the world. Some of the experts
2 on opioid use. It includes some of the
3 leading experts in the country on addiction,
4 including the former Deputy Drug Czar. It
5 includes leaders in the field of public
6 health, including health commissioners who
7 signed this letter.

8 What we told FDA in our comment on
9 the curriculum that was being proposed was
10 that we were worried that the curriculum would
11 potentially cause more harm than good, that
12 the curriculum would suggest to prescribers
13 that opioids are safe and effective for
14 chronic pain if certain rules are followed.
15 What we wanted were education programs that
16 would present what the medical community is
17 beginning to realize, which is that when you
18 treat chronic non-cancer pain with opioids,
19 with long-term opioids, that you are harming
20 far more chronic pain patients than you are
21 helping. What we wanted was an education
22 program that would communicate to prescribers

1 that treating chronic pain with opioids is
2 often a very bad idea.

3 Instead, what we have is a
4 curriculum that teaches what the industry
5 would call the new paradigm and what I would
6 call the emperor's new paradigm because I
7 think in many ways it is a hoax. Instead
8 teaching that opioids are a poor choice for
9 fibromyalgia or headache or low back pain,
10 which is about 90 percent of people with
11 chronic non-cancer pain, instead what is
12 taught is that if you use certain risk
13 assessment tools that will help you identify
14 somebody's risk of becoming addicted and then
15 you stratify them on the basis of that risk
16 and monitor them closely, that somehow this
17 turns the treatment into something that is
18 safe and effective, which we know is not true.

19 So the opioid REMS included more
20 than just the education which we were opposed
21 to because it was voluntary industry-paid-for
22 education which is what caused that green line

1 to shoot up in the first place, but also there
2 were other elements of the REMS which could
3 have been effective if done properly.

4 What I have just passed out would
5 be what is called the Patient Counseling
6 Document. And according to the description of
7 the document and FDA briefing materials, the
8 document was intended to encourage a
9 conversation between patients and their
10 prescribers about the risks of opioids that
11 would have been an opportunity for a
12 prescriber who he or she himself may not be
13 well-informed about opioid risks to go over
14 some of these and provide a patient with
15 informed consent.

16 If you look at this document -- I
17 am going to finish up here -- but what is
18 missing from that document is any counseling
19 on the risk of addiction with opioids. And
20 according to the FDA, there was no mention of
21 risk of addiction because they prefer to have
22 blank space on that document where doctors

1 could put in information specific to their
2 patients.

3 I am going to wrap up here. What
4 we wound up at the end of the day was an
5 opioid REMS that would in no way jeopardize
6 this green line from continuing to go straight
7 up, which is exactly what the industry wanted.

8 And unless we begin to see that
9 green line begin to come down, it is unlikely
10 that we are going to be able to have an impact
11 on this epidemic.

12 Thank you.

13 MS. TOIGO: Thank you. Next we
14 will hear from Natalie O'Donnell from United
15 BioSource Corporation.

16 MS. O'DONNELL: Hello. My name is
17 Natalie O'Donnell and I am the Director of
18 Risk Management at United BioSource or UBC.
19 UBC has been working in the area of risk
20 management since 1999. We have been involved
21 in many RiskMAPs and REMS. Today, I am going
22 to be talking about patient-directed REMS

1 tools, which include patient counseling and
2 discussions around benefits and risks of drug
3 or biologic, as well as instructions on how to
4 use drugs safely. I am going to be speaking
5 about this in relation to the patient.

6 So we have talked a lot about
7 PDUFA V today and the goal to examine the need
8 to reduce burden in the healthcare system. We
9 know the mission of the FDA to protect public
10 health and ensure safety. And when we
11 consider REMS in place to ensure that the
12 benefit of drugs outweigh the risks, all those
13 important factors together are very important
14 and why we are here today.

15 However, I want to ensure that
16 through this examination, this meeting today,
17 and the docket in the future, that we don't
18 decrease the focus on patients and patient
19 education. I think instead, let's move
20 towards a greater efficiency. It would be
21 efficient to use our existing healthcare
22 system to manage patient safety.

1 While we believe that REMS has
2 been effective in minimizing risk, we want to
3 continue to expand their role in other
4 healthcare professionals to further strengthen
5 REMS. Although REMS requirements have never
6 prohibited nurses or pharmacists from being
7 key stakeholders, the primary focus has
8 typically been on physicians or prescribers.

9 I would like to comment today on
10 the need to better recognize the role that
11 pharmacists and nurses play in the education
12 and interactions with patients. In current
13 REMS programs, it is unusual for nurses or
14 pharmacists to be specifically included in
15 REMS training and enrollment requirements. In
16 fact, when reviewing REMS with elements to
17 assure safe use, about only half of them even
18 have outreached to nurses or nurse
19 practitioners.

20 Currently, there are over 2.6
21 million practicing nurses, including 250,000
22 advanced practice nurses and 2.1 full-time

1 practicing pharmacists in the United States.

2 The nurses are responsible for primary direct
3 patient care in many settings, including
4 medical offices, hospitals, long-term care
5 facilities, and pharmacists are interacting
6 patients in pharmacies, hospitals, grocery
7 stores, other retail and healthcare
8 environments, as we have talked about today.

9 Considering the timing and
10 frequency of patient counseling, the initial
11 dialogue occurs between the prescriber and the
12 patient. I understand this relationship is
13 the cornerstone of an informed treatment
14 decision. Additional downstream safety nets
15 exist within our current healthcare delivery
16 system. We won't be over-educating our
17 patients by building a model of reinforcement.
18 Data indicates that when patients are provided
19 solid knowledge base about their disease
20 process and treatment, the outcome for
21 patients is more favorable.

22 After a prescribing decision is

1 made between the patient and physician, the
2 nurse and nurse practitioner have the
3 opportunity in many of the settings I have
4 already discussed to reinforce, further
5 educate the patient on the risk and benefit of
6 the product. Then the pharmacists has the
7 opportunity to further reinforce early
8 teachings, as well as cross-check medications
9 on the patient's profile.

10 In particular with many complex
11 REMS involving specialty pharmacy, there is a
12 natural opportunity for pharmacists to serve
13 as the bridge between the patient and
14 prescriber. REMS are a central part of the
15 specialty pharmacy model. Processes in the
16 specialty pharmacy allow for regular
17 monitoring of patients and adherence to
18 treatment regimens. Specialty pharmacies have
19 the ability to identify in real time patients
20 exposed to medications and engage with them
21 directly. In both the retail and specialty
22 pharmacy settings, pharmacy management systems

1 can provide messaging to the pharmacist about
2 specific educational messages related to REMS
3 while confirming that the appropriate patient
4 is authorized to receive the medication and
5 those who do not meet the REMS requirement do
6 not receive the medication.

7 There does not seem to be a
8 downside to leveraging the current health
9 system. This does not increase burden but
10 rather redistributes the important components
11 of educating patients.

12 With the Affordable Healthcare Act
13 on the horizon, it is anticipated that an
14 additional 32 million Americans will have
15 access to healthcare. The timing is right.
16 Engaging more healthcare professionals already
17 key to patient education will help us ensure
18 the goal of the FDA, PDUFA V and REMS.
19 Together, we cast a safety net ensuring the
20 right patients receive the right products. We
21 reduce adverse events and hopefully prevent
22 death.

1 In summary, REMS required training
2 should and could include nurses and
3 pharmacists. While the decision about the
4 appropriate treatment takes place between the
5 prescriber and the patient, education is an
6 iterative process, building the bridge between
7 the patient and the prescriber with the
8 support of nurses and pharmacists creates a
9 solid foundation REMS can build upon.

10 Thank you.

11 MS. TOIGO: Thank you, Natalie.
12 That concludes this panel. And we have time
13 for about ten minutes of FDA questions. So
14 who on the panel wants to start this session?

15 Gary.

16 DR. SLATKO: So my question is to
17 Natalie.

18 One of the things that we have
19 heard from stakeholders is that, particularly
20 those in closed systems and government
21 healthcare organizations, that the specialty
22 pharmacy, they have a barrier to getting

1 access to products if they are distributed
2 through specialty pharmacy mechanism
3 exclusively.

4 So do you have any thoughts about
5 a way to make those products that are
6 distributed through a specialty pharmacy also
7 available through these organizations?

8 MS. O'DONNELL: I should have said
9 I am a nurse not a pharmacist. I don't --
10 actually our organization has some knowledge
11 about that, it is not my area of expertise.
12 I would be misleading you if I tried to answer
13 that honestly. I'm sorry.

14 MS. TOIGO: Kate?

15 MS. OSWELL: This question is for
16 Murray. You had spoken about accredited CME
17 and allowing them to be responsive to
18 knowledge gaps and the stages of change to
19 address individual needs.

20 Could you expand a little bit
21 about how the knowledge gaps are determined
22 and developed, actually, in the CME?

1 DR. KOPELOW: Thank you. It
2 starts with a professional practice gap. It
3 starts with the difference between what people
4 are doing either as individuals, communities,
5 or populations, between what they are doing
6 and what they should be doing. That data
7 comes from you, from industry, from patients
8 of those who are observing directly what is
9 going on.

10 The reason for that is the need,
11 either a knowledge need, a strategy need, a
12 performance need that underlies that gap. The
13 incidence, the prevalence of substance abuse
14 in the population of the United States is 1 in
15 12 I was taught when I was at ONDCP. The
16 incidence or prevalence of physicians -- of
17 patients in physicians' practices ranges
18 dramatically from zero to 1 in 12.

19 And the need that underlies that
20 professional practice gap might be that the
21 physicians don't understand or know about the
22 epidemiology of the disease. They don't

1 understand the use or misuse of products.
 2 They don't have the strategies to ask the
 3 question. They don't have the ability. They
 4 don't know what question to ask. They don't
 5 have the expert kind of tools available to
 6 them to use to screen.

7 There is a range of what the needs
 8 are that underlie those gaps and they are as
 9 heterogeneous as the physician population.

10 It is limited. We have heard some
 11 on both sides that describe some of them. And
 12 it is that variation that is the richness of
 13 the continuing education enterprise.

14 Did that answer your question?
 15 Thank you.

16 MS. TOIGO: Ann, did you want to
 17 add anything to that? Knowledge gaps, how
 18 AAFP may look at when you are developing your
 19 educational programs?

20 DR. KARTY: Our process is very
 21 similar. And actually AAFP wears a unique hat
 22 because not only are we one of the three

1 credit systems, the AMA, the AOA, and the
2 AAFP, we are actually an accredited provider
3 of ACCME credit as well. So we have several
4 different hats.

5 But as far as creation of
6 identification of need assessments and gaps in
7 physician practice, it is a very similar
8 process. I would say opioids are one that
9 doesn't have as distinct a performance measure
10 as diabetes, for example, where there are
11 specific blood tests or specific tools that
12 can be or pieces of information that can be
13 garnered from electronic records to see if
14 physicians are doing them on appropriate
15 times.

16 And then the whole concept and the
17 notion of peer review and comparing yourself
18 to your geographic location to those in other
19 practices. Sometimes gaps are found based on
20 zip code and practice performance.

21 MS. TOIGO: Mwango.

22 DR. KASHOKI: Hi. My question is

1 for Ann as well. And I don't know if this is
2 what you meant to imply in your presentation
3 but you talked about the voluntary
4 participation in education or training is
5 effective, so to speak.

6 I know you talked about some of
7 the limitations you have thus far with regard
8 to training in opioids and the opioid REMS, et
9 cetera.

10 But I was wondering if you have
11 any general information that compares
12 effectiveness of a voluntary education program
13 for any other kind of learning against
14 something that was required, whether it was a
15 guideline or whatever, in order to give some
16 context for how useful voluntary participation
17 in a training is.

18 DR. KARTY: I am going to give a
19 couple different pieces of background. I
20 think the concept of voluntary education
21 versus mandatory education specifically in
22 family medicine with pain management, it is

1 concerning that things that are more
2 restrictive on any type of practice has the
3 potential for physicians to choose not to do
4 that in their practice and for physicians that
5 are in rural practices where they may be the
6 only prescriber to be able to write opioids,
7 should they not take the mandatory education,
8 there is the potential to impact patient
9 outcomes. It becomes an access problem.

10 And so as much as one can
11 encourage voluntary participation, I mean I
12 think that is the preferred route to go. And
13 I am not representing the licensing boards,
14 although I have a few extra comments that I
15 can provide from our meeting earlier in the
16 week, but there are several municipalities
17 from a prescriber and a physician licensing
18 piece that there are over 40 of the 46 states,
19 I think, that actually have CME requirements
20 globally for a certain number of hours,
21 certain number of credits per year to maintain
22 licensing. And physicians on average have

1 multiple licenses, two to four licenses I
2 think are the most recent statistics I have
3 heard.

4 So each state has different
5 requirements and may have different numeric of
6 20, 40, 60 credits globally. And there are I
7 think 16 municipalities that have topic-
8 specific requirements of which I think 14
9 involve some opioid piece of that.

10 So you can envision somebody who
11 has four different licenses with many
12 different requirements not only to hit a
13 certain credit number to maintain those
14 licenses, which probably are reciprocal, but
15 if there are multiple states that have
16 different topic-specific CME and now there are
17 REMS-required CMEs, that that really eats into
18 the overall 40 credits per year, whatever that
19 would look like. Because each one is
20 different.

21 So that whole notion of required
22 versus voluntary for family physicians, it

1 definitely would be an access concern.

2 For the question of is there a
3 difference between voluntary education and
4 mandatory education, I am not sure I have that
5 data or that I can provide comment on that.

6 MS. TOIGO: Anyone else on the
7 panel with a question?

8 MR. KROETSCH: So I think I have
9 questions about the idea that the training is
10 designed to address these gaps in knowledge
11 and in practice. And that if we were to be
12 able to supply that list of gaps that CME
13 providers could build training that addressed
14 that and customize that training to different
15 prescriber needs. Is that the -- did I get
16 that right?

17 DR. KOPELOW: Right, that is the
18 current system and we have data to show that
19 when presented with these gaps, the CME system
20 does translate them into education and does
21 translate that into evaluation.

22 MR. KROETSCH: Yes, and actually

1 it was that translation that I am curious
2 about. I would be interested in understanding
3 better what kind of evidence you use to track
4 that sort of translation and how you might --
5 that is how you know retrospectively that that
6 has been successful. And then in the future
7 if we were interested in a REMS to understand
8 how those gaps were translated into say
9 messages that are delivered in the education
10 and then ultimately into behaviors. Do you
11 have systems that can help track how that
12 happens?

13 And I think even in addition to
14 that, is there a way to track what the
15 baseline level of knowledge was and what the
16 sort of customizations that were made to
17 account for any of the unique needs of
18 prescribers?

19 DR. KOPELOW: You know, it is okay
20 to ask a one-part question, --

21 (Laughter.)

22 DR. KOPELOW: -- especially to

1 someone old who has trouble remembering.

2 An assumption in your question is
3 that a knowledge deficit is the cause of a
4 patient outcome. And that is a testable
5 hypothesis.

6 Our system of accreditation has
7 the data you seek about whether or not the
8 providers have based their education on
9 professional practice gaps because our system
10 does that in the determination. Then have
11 they translated or not translated but deduced
12 what the needs are from that gap? We have
13 that data. That is our compliance data and
14 our providers are operating at an 80 or 90
15 percent compliance rate for that. That is the
16 process that I was speaking of that you have
17 access to.

18 We do not have data -- we have the
19 information but we have not pulled it out of
20 the information what the prevalence of
21 education is on the substance abuse issues and
22 that range. We have recently done that for

1 NIH for genomics to look at the range of
2 education that is on genetics and genetic
3 testing. And we can do that within our
4 system.

5 So we have that data. We have
6 that information. We do know with the
7 certainty of the accreditation process that
8 the educators can translate professional
9 practice gaps into needs and needs into
10 education and we have a requirement that you
11 use the appropriate format.

12 The quality of the education is as
13 good as the accuracy of those professional
14 practice gaps. And what Dr. Kolodny talks
15 about about the inaccuracy of what is right
16 and what is wrong, that needs to be
17 reconciled. That needs to be reconciled.

18 We need to say that having a zero
19 percent of patients in your practice with
20 substance abuse is, in itself a professional
21 practice gap. We need to be able to say that
22 your use of products and your manner of using

1 them is at variance from what is in the best
2 interest of the nation.

3 That is the professional practice
4 gap that we need. That is what we need from
5 you because that determines the precision and
6 the accuracy and the reliability of the
7 education that follows.

8 MS. TOIGO: So I think Dr. Kolodny
9 wanted to add something to that comment, Adam.

10 DR. KOLODNY: Yes, I see it a
11 little differently from Dr. Kopelow. So I
12 think your question may be assuming that if we
13 teach doctors the right way to treat chronic
14 pain with opioids, for example, if they are
15 taught to use risk assessment tools, stratify
16 a patient's risk of addiction, monitor them
17 accordingly, that it can turn out safe and
18 effective in the end. And there is really no
19 evidence that that is the case. There is
20 increasing evidence that using these
21 medications, extended-release opioids for non-
22 cancer pain long-term is a really bad idea.

1 And so the real gap in
2 understanding for prescribers is that these
3 medications are highly addictive, not that
4 there is just one small percentage of our
5 population at risk of getting addicted. That
6 is not really true. With highly addictive
7 drugs, if you expose people long-term, a good
8 number of people will develop that disease.

9 So the gap in understanding is
10 that the drugs are very dangerous and that
11 evidence of long-term benefit is very weak.
12 And in fact, there is increasing evidence that
13 patients do poorly long-term because of
14 tolerance to analgesia.

15 So the education programs that we
16 have that are getting accreditation are
17 teaching to use these practice tools and this
18 is the safe and effective way to do it but the
19 evidence does not support that.

20 MS. TOIGO: Well in the interest
21 of time, we are running a little bit over but
22 I wanted to make sure that we had an

1 opportunity for questions on this panel.

2 So we will take a break. We will
3 take a full 15-minute break and we will be
4 back at five after three o'clock.

5 The unfortunate thing is we didn't
6 have enough time during this panel to really
7 explore more about how CME, the process worked
8 with the ER/LA opioids but we would spend a
9 half hour on that. So I can't ask my
10 question. Sorry.

11 (Whereupon, the foregoing
12 proceeding went off the record at 2:54 p.m.
13 and went back on the record at 3:11 p.m.)

14 MS. TOIGO: Okay, we're going to
15 get started with our last panel for today.
16 And this is our speakers are going to address
17 REMS tools in dispensing settings. And so we
18 have multiple representatives from diverse
19 pharmacy practice settings that are going to
20 speak to us today about tools and dispensing
21 settings.

22 And we are going to start off with

1 Kevin Nicholson from the National Association
2 of Chain Drug Stores.

3 MR. NICHOLSON: All right, thank
4 you. Good afternoon and thank you for the
5 opportunity to share the perspective of chain
6 pharmacy on the issues and challenges
7 associated with the standardization and
8 assessment of Risk Evaluation and Mitigation
9 Strategies.

10 I am Kevin Nicholson, Vice
11 President Public Policy and Regulatory Affairs
12 for the National Association of Chain Drug
13 Stores. NACDS represents traditional drug
14 stores, supermarkets, and mass merchants with
15 pharmacies from regional chains with four
16 stores to national companies. Our members
17 operate more than 41,000 pharmacies and employ
18 more than 3.8 million employees, including the
19 132,000 pharmacists. They fill over 2.7
20 billion prescriptions annually, which is more
21 than 72 percent of annual prescriptions in the
22 U.S.

1 We commend FDA for looking for
2 ways to standardize and assess REMS to better
3 integrate them into existing and evolving
4 healthcare systems with a goal of reducing any
5 associated burdens. Streamlining REMS will
6 assure that healthcare providers can focus on
7 the provision of health -- provision of
8 patient care while still meeting underlying
9 REMS goals. We support FDA's work to this
10 end.

11 From our members perspective there
12 are a number of ways that FDA could work with
13 stakeholders to standardize and improve REMS.
14 We strongly urge FDA to elevate in priority
15 the adoption of a single patient medication
16 information document that is standardized with
17 respect to format and content, referred to as
18 the one-document solution.

19 The one-document solution would
20 improve the effectiveness of information
21 provided for REMS drugs, enhance pharmacists'
22 ability to consultations on those drugs, and

1 streamline provision of that information into
2 pharmacy management systems.

3 Currently, patients are given
4 numerous written materials, including
5 Medication Guides, patient package inserts,
6 and other consumer medication information in
7 myriad formats when they receive their filled
8 prescriptions from their pharmacies.

9 Patients need a useful document
10 designed and written for them in a manner that
11 recognizes their information needs that
12 provides both concise and critical
13 information. This is especially important for
14 REMS drugs where over-saturating patients with
15 confusing lengthy documents can lead to
16 patient oversight of critical information,
17 which could have severe health consequences.

18 A single, concise, and well-
19 designed patient medication information
20 document could be used by pharmacies as a tool
21 in their counseling sessions with patients to
22 highlight and clearly delineate any critical

1 information about a prescription. This
2 document would also serve as an important
3 resource for patients to take away from the
4 counseling session, reinforcing the key
5 information that they learned from their
6 pharmacist about their medication.

7 Where a patient is interested in
8 more detailed information, this should be
9 obtainable through an FDA-provided or
10 manufacturer-provided consumer-friendly
11 website, which we suggest that either FDA work
12 to create or that FDA develop standards for
13 the creation of websites by manufacturers.

14 Additionally, patients would be
15 well served by more in-depth MTM services for
16 REMS drugs. Reimbursing pharmacies for
17 providing enhanced MTM sessions would further
18 facilitate patient understanding. To this
19 end, models for pharmacist reimbursement
20 should be considered when designing REMS.

21 Beyond consolidating the format of
22 written information via the one-document

1 solution, there are other ways to improve the
2 provision of information to patients to meet
3 REMS requirements. With more patients relying
4 on mobile and other technologies, patients
5 should have the option of receiving medication
6 information in a written document,
7 electronically via email, through a stable
8 website, or through applications on mobile
9 devices.

10 Additionally patients with low
11 literacy or visual impairment should have the
12 option of toll-free numbers so that
13 prescription information can be orally
14 communicated.

15 To facilitate these various
16 multiple media solutions, FDA could create or
17 approve source documents for each medication
18 that would be used for the development of
19 electronic and paper media. The source
20 document would serve as the most authoritative
21 reference.

22 To further improve organized,

1 standardized, and centralized REMS, REMS
2 information and any associated processes and
3 requirements, NACDS urges FDA to continue to
4 work with the National Council for
5 Prescription Drug Programs, NCPDP, to
6 integrate REMS into the standard product
7 labeling standard known as SPL. And this has
8 been mentioned by other speakers today. So we
9 support that. We support the SPL standard as
10 well.

11 Integrating REMS into SPL will
12 yield uniform format and content for REMS
13 information that is easily accessible for
14 practitioners, along with other product
15 labeling information in one centralized
16 resource. This is notably in line with the
17 one-document solution that we continue to
18 advocate for. Doing so will facilitate the
19 integration of REMS into the prescribing and
20 dispensing processes via the ePrescribing
21 systems used by prescribers and the pharmacy
22 management systems used by pharmacies, which

1 will ultimately streamline the process for
2 practitioners to complete any REMS
3 requirements for a particular medication.

4 We believe that FDA could also
5 improve REMS by establishing a single web
6 portal to act as a repository for standardized
7 REMS tools and materials and to serve as a
8 central information or reference source for
9 REMS stakeholders. We strongly urge FDA to
10 work with a strategic partner with experience
11 necessary to design such a resource for this
12 purpose.

13 FDA should also work on developing
14 a uniform standard for REMS that include
15 elements to assure safe use, the ETASU. For
16 these REMS in particular, standardization of
17 the now varied approaches that can include
18 patient registries and/or attestation, and
19 special processes for practitioner enrollment
20 and training will streamline processes and
21 minimize associated compliance challenges for
22 patients and practitioners.

1 In general, the TIRF REMS serves
2 as a good example for standardizing and
3 integrating REMS with ETASU into healthcare
4 delivery systems. The TIRF REMS effectively
5 incorporates training and certification
6 requirements for patients, prescribers, and
7 dispensers into the dispensing process and
8 into existing pharmacy adjudication systems.
9 This approach allows dispensers to effectively
10 ensure that any safe use conditions are met
11 prior to dispensing.

12 This is a much more efficient
13 approach than the patient registry requirement
14 under other programs, such as the iPLEDGE
15 program. Where training enrollment is
16 necessary for prescribers and/or dispensers
17 under particular REMS, this should be made
18 available online. Doing so provides a
19 convenient and faster way to enroll and meet
20 particular REMS requirements. With respect to
21 certification of pharmacists and pharmacies,
22 in the pharmacy setting, additional

1 certification for pharmacists would be
2 unnecessary. We are required, pharmacies are
3 already certified and there are trigger points
4 in place operationally to alert dispensing
5 pharmacists if there are any REMS requirements
6 that must be met for a specific medication.

7 Moreover, by virtue of their
8 education, all licensed pharmacists are
9 medication experts who know the risks of
10 various drugs. So we feel that additional
11 certification for pharmacists would be
12 unwarranted. Notably, it would be extremely
13 challenging for a pharmacy chain to ensure
14 that every single pharmacist is current with
15 their certification. There is a strong
16 probability that this would lead to patient
17 access issues as most likely only certain
18 pharmacists in certain locations would be
19 certified.

20 Additionally, we believe that a
21 workable certification process can be created
22 for certifying a chain pharmacy as a whole, as

1 opposed to individual pharmacy locations. We
2 believe appropriate policies and procedures
3 can be implemented to ensure that
4 certification requirements are followed chain-
5 wide.

6 Finally when evaluating REMS, FDA
7 should consider that certain REMS requirements
8 can make it difficult for authorized
9 dispensers to obtain drugs to meet their
10 patients' needs. For example, REMS that have
11 limited distribution place an undue burden on
12 patient access. Additionally, where REMS
13 requirements are onerous and unique, this, in
14 some case, has caused particular pharmacies
15 not to carry the product, which also impacts
16 patient access. Improved standardization
17 could help address these issues.

18 Thank you again for the
19 opportunity to speak with you today and convey
20 our members' input on the topic of REMS
21 standardization. I would be happy to answer
22 any questions.

1 MS. TOIGO: Thank you, Kevin.
2 Next we will hear from Stacie Maass from the
3 American Pharmacists Association, not the
4 American Public Health Association.

5 MS. MAASS: Thank you. Good
6 afternoon. I am Stacie Maass, Senior Vice
7 President for Pharmacy Practice and Government
8 Affairs with the American Pharmacists
9 Association or APhA.

10 APhA represents more than 62,000
11 pharmacists, pharmaceutical sciences, and
12 pharmacist technicians in all practice
13 settings.

14 Pharmacists, due to their
15 medication expertise, play an essential role
16 in the safe use of medications and effective
17 implementation of REMS programs. APhA would
18 like to take this opportunity to thank the FDA
19 for the significant investment of your time
20 and resources in the improvement of the REMS
21 program. We are especially gratified that
22 FDA's current questions reflect the progress

1 made and the input by APhA and other
2 stakeholders over the past few years. So,
3 thank you.

4 APhA continues to support efforts
5 to standardize REMS. With a wide variety of
6 REMS programs, each with its own particular
7 components, compliance can be very daunting.
8 However, moving forward standard REMS programs
9 will contribute to the efficiencies by
10 ensuring that patients not only have access to
11 medications but take those medications safely,
12 while reducing the administrative burden on
13 providers.

14 As stated by many speakers today,
15 REMS should be incorporated into existing
16 prescriber and dispenser workflows to the
17 greatest extent possible. Leveraging existing
18 technologies and infrastructures, including
19 electronic health records, ePrescribing
20 systems and pharmacy management systems
21 creates the possibility of interoperability
22 among providers, as well as information

1 sharing, without the necessity of expensive,
2 new information technology.

3 New options for integration should
4 be evaluated in pilot programs, allowing
5 front-line providers to offer feedback and
6 suggestions for improvement, as well as time
7 for providers to prepare for and adapt to
8 changes.

9 As the entire healthcare system
10 becomes more coordinated, the opportunities
11 for centralizing REMS and effectively sharing
12 information increases. We urge the FDA to
13 consider centralizing all REMS information,
14 making education material, training, and
15 registration information available on one
16 site.

17 Further we suggest that FDA
18 continue to examine the possibility of
19 organizing REMS programs based on tiers or
20 levels, perhaps similar to the schedules for
21 controlled substances. The structure of each
22 level could consist of a standard set of

1 components that may be applied based on the
2 level of risk associated with the medication.
3 Such an approach would offer manufacturers
4 some flexibility in constructing REMS programs
5 but would also provide baseline consistency
6 that would make management of numerous REMS
7 programs easier, as well as decreasing the
8 burden on prescribers and dispensers.

9 By integrating REMS processes into
10 regular operations, prescribers, dispensers,
11 and patients are able to maximize
12 communication, leading to improved patient
13 experiences, fewer adverse effects, and less
14 time handling paperwork.

15 APhA appreciates FDA's ongoing
16 effort to improve patient education and the
17 outreach regarding REMS programs. In a
18 perfect world, all discussions of REMS
19 medications would involve a provider
20 intervention. However, the cost associated
21 with such an approach would make it
22 infeasible. As such, we support the

1 simplification of the education materials so
2 that patients are not confronted with the
3 overwhelming amounts of information.

4 For instance, each REMS medication
5 could have a one-pager of the risks and
6 benefits, followed up with additional
7 information separate and apart with more of
8 the technical or scientific information.

9 Further, in some instances it may
10 be helpful to take advantage of technology
11 solutions, such as online learning modules
12 that guide patients through the medication
13 information or a smartphone app that you could
14 push safety reminders, along with reminders to
15 take medications. These innovations, though
16 should only supplement communication with a
17 provider, not supplant that communication.

18 Patients, like most people, have a
19 limited capacity for taking in and retaining
20 highly technical information. In many
21 instances, medication discussions comes at the
22 end of an appointment, by which point the

1 patient may have already reached his or her
2 medical information saturation limit. I think
3 that something that probably all of us in this
4 room maybe are experiencing at this hour. And
5 I am sure you are all wishing for a one-pager
6 but sorry.

7 Thus, APhA recommends that FDA and
8 stakeholders consider solutions that result in
9 face-to-face and telehealth consultations as
10 key elements of REMS programs, incorporating
11 human interaction into the REMS process
12 improves patient safety and allows for a
13 provider to gauge patient comprehension.

14 For example, many states embraced
15 medication therapy management or MTM as an
16 essential tool for adherence or safe use of
17 medications. We suggest one possible REMS
18 patient education be folded into such MTM
19 programs. In addition to the benefits to the
20 patient, MTM programs provides an opportunity
21 to provide data, relevant data regarding REMS
22 and MTM allows patient monitoring, produces

1 data on patient usage in adverse events, which
2 could be highly beneficial in assessing the
3 relevant effectiveness and impact of REMS
4 programs on patient medication usage.

5 APhA believes that with the
6 appropriate application of time and resources
7 direct intervention REMS element would allow
8 pharmacists to improve program effectiveness,
9 patient safety, and the public health.

10 I touched on earlier the
11 development of a standards repository for
12 REMS-related information would greatly
13 pharmacists. A REMS clearinghouse would allow
14 pharmacists to complete certification
15 education requirements under a single system,
16 rather than across multiple program-specific
17 platforms.

18 Pharmacists could use a national
19 provider identifier, such as NPIs, to access
20 REMS verification and education requirements
21 as required for certification. Attestation of
22 the successful completion of the program could

1 be sent electronically and verified through a
2 seamless electronic process claims
3 adjudication process.

4 Additionally, we believe this
5 electronic verification would cut down on the
6 administrative work for pharmacists and
7 improve communication across the whole
8 healthcare team. This worked well for TIRF
9 products and it could be translated into
10 additional medication that is suggested by
11 others.

12 APhA suggests that FDA and
13 stakeholders continue to work cooperatively to
14 identify opportunities for effective
15 integration across providers and systems.

16 In closing, we thank FDA and
17 stakeholders for their dedication time and
18 resources to this effort in acknowledging the
19 essential role of pharmacists and pharmacies
20 in REMS standardization and implementation.
21 While FDA does not regulate the practice of
22 pharmacy, the decisions you make definitely

1 affect our practice. If appropriate time and
2 resources are invested, pharmacists can
3 further improve public health and education
4 regarding REMS medications. We look forward
5 to working with FDA, manufacturers,
6 prescribers, pharmacists, and other
7 stakeholders to identify solutions, evaluate
8 options for REMS standardization and
9 implementation. Thank you.

10 MS. TOIGO: Thank you, Stacie.

11 Our next speaker is Carolyn Ha from the
12 National Community Pharmacists Association.

13 DR. HA: Thank you, Terry. Good
14 afternoon and thank you for allowing me this
15 opportunity to share community Pharmacies'
16 perspective regarding issues and challenges
17 associated with the development,
18 standardization, and implementation of REMS.

19 I am Carolyn Ha, Director of
20 Professional Affairs of the National Community
21 Pharmacists Association. NCPA represents
22 America's community pharmacists, including the

1 owners of more than 23,000 community
2 pharmacies, pharmacy franchises and chains.

3 First we would like to applaud the
4 FDA for making the process that has led to
5 this public meeting a transparent one and we
6 appreciate another opportunity to publicly
7 comment on FDA's efforts to standardize and
8 assess REMS and the impact of such programs on
9 community pharmacists and the patients they
10 serve.

11 We would like to reiterate,
12 however, that state boards of pharmacy
13 regulate the practice of pharmacy and also
14 would caution that REMS programs have the
15 potential to interfere with that role if they
16 are used too frequently and without
17 coordination with existing regulatory
18 requirements.

19 Pharmacists take seriously their
20 role as a primary source of drug information
21 for their patients. Pharmacists provide both
22 lifesaving medications to their patients, as

1 well as critical written and verbal drug
2 information and counseling that allow
3 medications to be used most appropriately and
4 safely.

5 Recent studies have shown that
6 patients recognize the value of and are
7 willing to receive pharmacist provided care.
8 Ideally, that care is delivered by a
9 pharmacists with whom a patient has had an
10 established and trusted relationship. While
11 other approaches to delivering these services
12 exist, studies continue to show that community
13 pharmacists providing face-to-face patient
14 interactions may have a greater impact on
15 patient behavior and adherence, compared to
16 other methods of service delivery. Such
17 patient counseling services that are based on
18 a medication therapy management model could be
19 utilized to meet the goals of a REMS program.

20 It is important to note that in
21 the provision of care processes, pharmacists
22 have standard workflow procedures that ensure

1 prescription medications are safely delivered
2 to their patients. The absence of such
3 standardization of REMS processes creates
4 unnecessary workflow and workload burdens and
5 eventually hinders patient care.

6 To date, community pharmacies
7 experience with REMS continue to be
8 challenging due to the lack of a common design
9 or platform surrounding such programs.
10 Medication Guides have not provided the
11 solution that some had hoped and that is why
12 NCPA is a strong advocate for the creation and
13 use of a single FDA-approved language document
14 to replace existing written information that
15 is currently distributed by pharmacies.

16 We greatly appreciate the Agency's
17 movement in this direction and additionally we
18 are encouraged by the Agency's approval of a
19 classified REMS for long-acting and extended
20 release opioids, which provides for a
21 consistent framework for all stakeholders
22 while addressing FDA's REMS requirements.

1 As previously mentioned, community
2 pharmacies are highly regulated in each state
3 by Boards of Pharmacies and the Drug
4 Enforcement Administration. It is, therefore,
5 NCPA's position that any state and DEA-
6 licensed pharmacy should be eligible to
7 dispense specific REMS products. Not only do
8 restricted distribution programs interfere
9 with patient access to prescribed therapies,
10 they may limit legitimate access to certain
11 therapies as well.

12 As an example, NCPA does not
13 support REMS for products which are dispensed
14 through a sole channel distribution such as
15 specialty or mail order pharmacy. Based on
16 studies and experience, we know that direct
17 face-to-face counseling is more effective than
18 a restricted programs method of shipment via
19 courier service to the home and counseling
20 those provided by a call center phone bank
21 from an unknown individual. This submits the
22 necessary pharmacist patient contact, which

1 can lead to greater risk in patient safety.

2 NCPA contends that many
3 independent pharmacies can meet stringent REMS
4 requirements, such as being on-call 24-hours
5 a day, as this is the level of service many of
6 our members currently offer to their patients,
7 regardless of REMS requirements.

8 The independent community
9 pharmacists who choose to participate in a
10 given REMS program and can meet all of their
11 requirements should be allowed to do so and
12 not be restricted by a special arrangement
13 between the manufacturer and its specialty
14 firms provider or any issues surrounding the
15 ability of drug wholesalers to only distribute
16 product to specific pharmacies. This is a
17 service that NCPA believes wholesalers have
18 the ability to provide on a daily basis
19 currently.

20 Therefore, NCPA respectfully
21 requests that FDA verify that REMS elements
22 will not impede patient access to lifesaving

1 medications by placing products in a
2 restricted distribution program. In instances
3 where products have been placed in such a
4 program, NCPA would respectfully request that
5 FDA study the prescribing patterns for these
6 products where oftentimes prescription volume
7 could significantly decrease, thereby reducing
8 patient benefits from these products. It also
9 limits the ability for the pharmacist to
10 manage the patient's entire drug therapy
11 through multiple dispensing site.

12 Regarding certification of
13 pharmacists or pharmacies to dispense certain
14 drugs with REMS, the education of pharmacists
15 to ensure understanding of these products,
16 NCPA asserts that self-attestation of
17 completion of education should serve as
18 confirmation of receipt of training.
19 Certification of individual pharmacists is not
20 necessary. Certification at the pharmacy
21 level should be sufficient, as long as there
22 is an authorized pharmacist such as a

1 pharmacists in charge who, on behalf of the
2 pharmacy, can attest that any required
3 training will occur for all pharmacy staff
4 involved in the dispensing of a REMS product.

5 If additional education is
6 required, any provider of continuing pharmacy
7 education should be accredited by the
8 accreditation counsel for pharmacy education.
9 Furthermore, this education should be allowed
10 to be provided by entities such as national,
11 state, or local pharmacy associations, or
12 schools of pharmacy who are experts in the
13 development of pharmacy-specific training and
14 certification programs.

15 For pharmacists to receive the
16 certification of completion awarding CPE
17 credits for home study programs, they must
18 review the content of the activity and
19 successfully complete a post-test before their
20 statement of credit is issued.

21 Any REMS-related CPE programs
22 offered by an ACP-accredited provider would be

1 required to follow this process. In addition,
2 the CPE provider could track which pharmacist
3 had completed a given program, if it is
4 necessary to specifically track completion of
5 training.

6 NCPA cannot stress enough that any
7 REMS system be created using a standardized
8 platform. As stated before, and as many of my
9 other pharmacy colleagues have pointed out,
10 workflow standardization is an important
11 component of safely filling prescriptions. A
12 standardized REMS process that can be
13 integrated within existing pharmacy workflow
14 is critical to the successful execution of the
15 program.

16 If the need for verification of
17 certain elements to assure safe use does
18 exist, we would urge FDA manufacturers to
19 utilize existing nationwide technologies that
20 provide automation scale and efficiency in the
21 transmission of electronic or hand-written
22 prescriptions, ePrescribing, any registry the

1 pharmacy management system and technology used
2 to document patient understanding at the point
3 of dispensing, should all work together and be
4 interoperable.

5 For example, as mentioned this
6 morning by the panel and you will hear more
7 about it tomorrow, there is currently work
8 underway from the National Counsel for
9 Prescription Drug Programs, an accredited
10 standards development organization looking at
11 the development of a template for codified
12 submission of REMS information in a
13 centralized repository within FDA's SPL.
14 Additionally, we would recommend a centralized
15 website with a secure login portal that could
16 significantly ease the process for patients,
17 prescribers, and pharmacies to carry out the
18 necessary registration, enrollment, and
19 certification required for varying REMS
20 programs.

21 REMS should be monitored and
22 assessed frequently enough to evaluate

1 effectiveness, as well as to evaluate overall
2 burden on the healthcare system. For example,
3 the number of minutes a healthcare provider
4 dedicates to each component of a given REMS
5 should be captured and evaluated. In certain
6 instances, this information may be collected
7 by online methods, especially as it relates to
8 provider training or enrollment of patients in
9 a specific REMS program.

10 In other instances, methods should
11 be developed or expanded that will allow for
12 a capture of time spent by a provider with
13 their patient discussing elements that are
14 associated with REMS.

15 Metrics for determining the
16 effectiveness of REMS should be specified, as
17 has been noted today at the time that REMS are
18 approved on the front-end of the process.
19 NCPA recommends that efforts to create REMS
20 are equally matched by efforts to evaluate the
21 effectiveness and outcomes of a given REMS and
22 its individual components.

1 FDA must ensure that the
2 components of any REMS are proven to be
3 effective in mitigating the specific defined
4 risks and are also workable for patients,
5 prescribers, pharmacists, manufacturers,
6 wholesalers, and technology-assisted vendors.
7 In addition, FDA should make outcomes
8 information available to required participants
9 of any given REMS program, as this applies
10 transparency to the process, so that
11 participants are aware of their contributions
12 to achieving the agreed-upon goals.

13 In order to measure the effect of
14 REMS on health outcomes, we recommend that
15 data could be classified into general
16 categories. Depending on the specific
17 product, these categories could be further
18 defined, such as patient prescriber and
19 pharmacist knowledge, behavior such as
20 inappropriate prescribing and non-medical use
21 and abuse, and outcomes such as serious
22 adverse effects and patient access to care.

1 Though we all admit challenges to
2 trying to measure these outcomes, NCPA
3 believes that through concerted effort to
4 define a set of metrics, REMS will meet the
5 goals of reducing serious adverse outcomes
6 while maintaining patient access to
7 medication.

8 In conclusion, we urge FDA to
9 leverage the value that community pharmacists
10 offer related to proper use of medications and
11 avoidance of costly errors down the road.
12 NCPA encourages the FDA to request stakeholder
13 feedback regarding different approaches to
14 create a standardized REMS process and to
15 support industry-wide efforts to both
16 standardize the REMS process, as well as
17 harmonizing these activities with agency
18 requirements.

19 The NCPA appreciates the
20 opportunity to provide comments on this issue
21 and applauds the FDA for recognizing the
22 important role and involvement of independent

1 community pharmacists in the creation of REMS
2 programs. Thank you for your time.

3 MS. TOIGO: Thank you, Carolyn.
4 Our next speaker is David Chen from ASHP.

5 MR. CHEN: Good afternoon. My
6 name, as mentioned, is David Chen. I am the
7 Director of Pharmacy Practice Sections at the
8 American Society of Health-System Pharmacists.

9 ASHP is the national professional
10 association whose more than 40,000 members
11 include pharmacists, pharmacy technicians, and
12 pharmacy students who provide patient care in
13 hospitals, health systems and ambulatory
14 clinics.

15 For 70 years, the society has been
16 on the forefront of efforts to improve
17 medication use and enhance patient safety.
18 And again, I appreciate the opportunity to
19 present our views to you here today.

20 ASHP is a strong advocate for
21 improving patient safety and medication
22 management. The society believes that the

1 development of consistent evidence-based
2 medication use systems is central to achieving
3 safe medication use. Our members serve as an
4 important patient advocate and the
5 disciplinary care providers helping to ensure
6 the safest use of medications.

7 While ASHP is pleased that the FDA
8 has expanded authority to ensure the safety of
9 drugs through REMS, we still remain concerned
10 about how REMS are applied in the marketplace,
11 the lack of standardization of REMS, and the
12 inability to operationalize REMS without undue
13 administration burden on the medication use
14 system.

15 ASHP believes that through REMS,
16 rather than developing a systematic approach
17 to evidence-based medication use practices, we
18 are seeing a separate medication use system
19 that is being created for each high-risk
20 medication.

21 Before I go into my comments for
22 three facets for dispensing tools related to

1 REMS, I would like to take a moment to
2 acknowledge and recognize the significant
3 number of improvements made to the REMS
4 programs and the FDA resources, since the July
5 2010 FDA meeting. For example, the
6 development of the shared system REMS and the
7 release of the guidance documents for
8 Medication Guides, as well as like today the
9 continued interest in engaging with
10 stakeholders that are taking care of our
11 patients and their medication needs.

12 Our members recognize the
13 potential risk of medications that are
14 inappropriately prescribed, dispensed, and
15 monitored, as well as our own responsibility
16 to provide patients with comprehensible
17 information that is useful both to the patient
18 and the provider. However, ASHP is concerned
19 that current REMS programs are negatively
20 affecting the already limited time that
21 pharmacists have to care for and ensure the
22 safety of their patients. We are also

1 concerned about the fragmentation of the drug
2 supply chain, since any process encouraging a
3 separate distribution system for particular
4 drugs has the potential to increase risk of
5 error and impact continuity of care.

6 Again, we appreciate the
7 opportunity and now I am going to speak about
8 three facets of dispensing relating to REMS
9 that we have been asked to comment on today.

10 Patient education and safety. As
11 noted in the past ASHP comments to the FDA, we
12 believe educating patients is clearly
13 important but there is a lack of research
14 relating to the role, scope, and effect of
15 patient understanding of MedGuides and
16 resulting patient behavior. The usefulness
17 and effectiveness of MedGuides as they are
18 currently written and distributed as tools for
19 counseling patients about serious risks
20 remains to be established through adequate
21 well-designed research.

22 Additionally, FDA should look at

1 the elements of REMS to ensure they are well-
2 founded and effective at mitigating risk. As
3 a member of the National Quality Forum, the
4 ASHP recommends that the FDA look at processes
5 that the NQF uses for the endorsement of
6 quality measures. The process is rigorous in
7 consensus building and can be used by the FDA
8 as a model when developing a process to
9 validate the FDA is actually measuring and
10 achieving what we are hoping to attend to
11 accomplish with particular REMS.

12 Thus, the goals of REMS need to
13 include continued verification and validation
14 that patient knowledge and receipt of
15 information will actually improve outcomes and
16 should include information proving that the
17 MedGuide design is going to reach safety goals
18 and should require the use of established
19 research methods to sample patient populations
20 on behavior modified based on receipt of
21 patient education. This includes the
22 development of appropriate incorporation of

1 health literacy standards.

2 Let's talk a little bit about
3 registration processes in verification. ASHP
4 would like to encourage the FDA to continue
5 working with stakeholders to standardize the
6 different elements of REMS and address the
7 concerns we have heard during this meeting, in
8 order to make this monitoring more efficient
9 and generalizable to future REMS.

10 The core components of REMS are
11 standards. The elements within each component
12 should be analyzed in an effort for
13 standardization. The lack of standardization
14 results in large amounts of duplication within
15 healthcare systems and the lack of
16 centralized or standardized methods of
17 accomplishing the ETASUs collectively for all
18 REMS is a burden. Members share with us that
19 they have had to dedicate specific resources
20 to manage and keep up with the REMS
21 administrative requirements.

22 So we would like the FDA to take

1 into consideration some of ASHP's experiences
2 with our REMS Resource Center for front-line
3 needs when looking at components to consider
4 in a centralized database. In 2009-2010 with
5 advice of members, we created this Resource
6 Center to find the answers for pharmacist
7 providers. The litmus test was to ask what
8 was necessary at 6:00 p.m. on a Friday to
9 manage a patient admitted on a REMS drug. The
10 resulting Resource Center attempts to answer -
11 - well actually it answers 12 questions for
12 each drug. And we took the time to go into
13 the source documents to help providers go to
14 the original information.

15 These questions: Why is the REMS
16 required? Does the hospital or pharmacy have
17 to register? And take them to the according
18 link. Does patient have to register? Does
19 the prescriber have to enroll? Do I have to
20 verify patient/prescriber are enrolled? Do I
21 have to provide MedGuide? Is there specific
22 monitoring involved? Can I order medication

1 through a usual supplier? What do I have to
2 document? Am I required to complete CE? Are
3 there any restrictions on dispensing amounts?
4 And am I subject to an audit?

5 We find that this has been helpful
6 for members as they start building their
7 internal SOPs and other procedures to help
8 operationalize the management of patients on
9 REMS and ensuring that they are compliant with
10 all the components of REMS.

11 So the ASHP encourages the FDA to
12 work towards a centralized, electronic means
13 for all REMS in the various registration,
14 provider education, and patient documentation
15 requirements in an effort to eliminate
16 redundancies that exist and the need to
17 maintain separate paper record-keeping in the
18 thousands of patient care settings. This
19 should include mechanisms to routinely and
20 proactively inform practitioners on changes to
21 the REMS programs.

22 Most importantly, it is to ensure

1 stakeholders from all size settings and
2 geographic regions for future FDA work groups
3 as you are developing practitioner tools
4 discuss medication access and continuity of
5 care.

6 Hospitals and health systems have
7 a unique charge in that we have to provide and
8 obtain all the medications for our patients
9 while under our care. Introducing systems
10 that require patients to bring in their own
11 medications or require multiple supply chain
12 channels to purchase medications introduces a
13 growing number of variables, variables that
14 consume time, raise risks to health systems'
15 medication use systems.

16 The ASHP encourages the FDA to
17 continue open dialogue with providers,
18 including hospital and health system-based
19 pharmacists and providers and considerations
20 for a stakeholder group that has all health
21 system providers at the table to conduct a
22 critical analysis on how and where patients

1 initiate REMS medication therapies and the
2 transitions of care that occur where providers
3 need to obtain access to a REMS drug to manage
4 the patient in a particular setting, with a
5 focus on the IT interfaces between these
6 settings to eliminate as much redundancy as
7 possible and enable or create a vehicle
8 allowing the data and the drug to be
9 accessible to all provider settings.

10 Centralization of REMS information
11 and data needs to become part of ePrescribing
12 systems and means developed to integrate into
13 electronic health records. Additionally, the
14 FDA should require provider input in the
15 development and refinement of existing REMS on
16 a routine basis. This would provide valuable
17 input to ensure the REMS is effective, has not
18 caused undue burden, and addresses the need of
19 the various practice setting REMS drugs must
20 be obtained and administered, while continuing
21 to safeguard our patients.

22 So in conclusion, ASHP appreciates

1 the opportunity to comment and participate on
2 the further improvement of REMS programs and
3 we appreciate the FDA's efforts to engage
4 stakeholders in the process.

5 Thank you very much.

6 MS. TOIGO: Thank you, David.

7 Next we will hear from Mary Jo Carden of the
8 Academy of Managed Care Pharmacy.

9 MS. CARDEN: Good afternoon. My
10 name is Mary Jo Carden and I am the Director
11 of Regulatory Affairs for the Academy of
12 Managed Care Pharmacy.

13 AMCP would like to thank FDA for
14 hosting this meeting today and tomorrow to
15 continue to improve the REMS process. And we
16 are particularly thankful that over the years
17 FDA has reevaluated existing REMS programs,
18 particularly those with Medication Guide only
19 and released some of those REMS because they
20 were overly burdensome. This is particularly
21 important to continue as programs become more
22 complex, based on new medications and

1 particularly specialty medications that are
2 introduced to the market. And as biosimilar
3 come onboard, we will have as an industry and
4 as patients, to look at those medications and
5 look at REMS and look at other means to ensure
6 safe and effective use. So continuously
7 examining REMS programs and determining their
8 efficacy is continually important. AMCP
9 members play a big role in managing REMS
10 programs, particularly in the specialty area.

11 Today I will talk about the impact
12 of REMS on the responsibility of managed care
13 pharmacies. This is true of many pharmacies.
14 And, as already stated, there are ways that
15 this can be streamlined, the REMS process, to
16 ensure that workload is appropriate but also
17 to ensure that REMS programs and REMS
18 protocols actually improve patient outcomes
19 and patient safety.

20 We also provide recommendations
21 for standard electronic processes to ensure
22 consistency when implementing REMS programs.

1 And finally, AMCP will provide recommendations
2 for integration into the healthcare system.

3 One of the biggest areas that AMCP believes is
4 important for REMS programs is to evaluate
5 actual patient health outcomes and if the REMS
6 program is actually having an impact on
7 positive patient care and overall improvement
8 of healthcare in this system.

9 We have already kind of discussed
10 the issue of the primary role of pharmacy.
11 Oftentimes, the pharmacist and the pharmacy
12 are the last entity to touch the medication
13 and to interact with the patient. And as a
14 result, the pharmacy has quite a role in
15 interaction with patients and in administering
16 the REMS program. This can result in a burden
17 in some cases if in fact REMS programs are
18 duplicative of utilization management tools
19 that are designed to ensure that patients
20 receive appropriate medications. In some
21 cases the REMS programs may be duplicative of
22 those and, therefore, it is important to

1 evaluate whether or not the REMS program is
2 actually effective or that other means
3 implemented by managed care organizations and
4 other entities for ensuring patient safety can
5 actually be better.

6 And of course, as discussed, this
7 results in administrative and financial
8 burdens for pharmacies that should be examined
9 and should be streamlined as REMS programs
10 evolve.

11 AMCP would like to recommend a
12 standard electronic process for REMS programs
13 but not recommend a single regulatory approach
14 for REMS programs design. AMCP understands
15 and appreciates the need for a streamlined
16 workflow in the pharmacy for managing REMS.
17 However, as mentioned previously, a one size
18 fits all approach for a REMS protocol may not
19 be effective for drugs that we have yet to see
20 and those in the future. And therefore, a
21 rigid regulatory standard would make
22 compliance more difficult as these new

1 approaches evolve.

2 I am not going to explain this
3 slide. As Carolyn Ha mentioned, tomorrow
4 there will be quite a bit of discussion on the
5 NCPDP standard. This is an illustration of it
6 that will be integrated into electronic health
7 records and into pharmacy systems that can
8 manage and help manage the workflow and allow
9 pharmacists to interact clinically with
10 patients and better understand the REMS
11 protocols so that they can in fact communicate
12 that information with patients.

13 And finally, AMCP would like to
14 recommend that managed care organizations that
15 have access to rich data, patient data, as
16 well as access to patients themselves and
17 particularly in the issue of specialty
18 pharmacies to conduct research both that is
19 required by the FDA.

20 As mentioned previously the Office
21 of the Inspector General has noted that FDA
22 has not completed the federally-required

1 evaluations for most drugs with ETASUs. AMCP
2 believes that managed care organizations can
3 help in this process and also more
4 importantly, that managed care organizations
5 can take data and analyze it. The data is out
6 there. It is existing. And we can analyze it
7 and look at how REMS programs are affecting
8 outcomes overall, which is very important in
9 today's new marketplace.

10 So thank you very much. AMCP
11 looks forward to continuing to work with FDA
12 on the REMS program.

13 MS. TOIGO: Thank you, Mary Jo.

14 Our next presenter is Lindsey
15 Kelley from the University of Michigan Health
16 System.

17 DR. KELLEY: Hello. Thank you all
18 for allowing us the time to speak this
19 afternoon and we will try and move you along
20 as quickly as possible.

21 My name is Lindsey Kelley. I am a
22 pharmacist and an administrator at the

1 University of Michigan Hospitals and Health
2 Systems as well as Cancer Center in Ann Arbor,
3 Michigan.

4 I have experienced David's 6:00
5 p.m. call for we have a REMS drug and how do
6 I get that to a patient. I am speaking to you
7 on behalf of myself in that role as well as
8 University Health Systems across the nation as
9 we look towards how we solve this problem and
10 the best way to move forward.

11 The impact of Risk Evaluation and
12 Mitigation Strategies as well as their
13 standardization and limited distribution on
14 hospitals and health systems is important.
15 And it is important to the patients we care
16 for. And it is important looking forward into
17 the future at accountable care organizations
18 and how we make those successful.

19 When we think about academic
20 medical centers and the types of patients that
21 we care for, they are complex patient
22 populations. They are patients who often have

1 high illness severity and they are patients
2 who are often recipients of specialty
3 medications and the medications that have REMS
4 requirements. And although many of the
5 medications that received those REMS
6 requirements are tested in our university
7 health systems, once those drugs are approved,
8 we do not have access to those medications.
9 We are denied access to provide the care and,
10 as JoAnn spoke to earlier, these medications,
11 even though we have the ability to provide
12 that safe care, we can access the medical
13 record, we have developed protocols within our
14 health systems to ensure that patient's
15 safety, we simply cannot get the drug or we
16 are creating or taking part in a duplicative
17 process just so that we can gain access and
18 provide that care.

19 These can be due to a REMS program
20 through the manufacturer. It may also be due
21 to payer carve-out contracts because of the
22 cost of the medications. And either way, this

1 creates a fragmented care system and it makes
2 it difficult for patients to navigate as they
3 try and make their way through.

4 Academic medical centers are
5 uniquely positioned with a highly qualified
6 and well-trained workforce, including
7 pharmacists and nurses as was alluded to
8 earlier. And we are able to take care of
9 these patients.

10 When we think about the
11 considerations of REMS, and I want to make
12 sure that we focus on the solution and not too
13 much on the problem, the considerations are a
14 logistical burden in the unintentional
15 fragmentation of care. When I think about
16 what this means on the patient perspective --
17 we have a cancer center at the University of
18 Michigan. It is a nationally recognized
19 comprehensive cancer center. It provides to
20 patients in a very well-equipped system.

21 We created an entire program
22 around oral chemotherapy as one example of

1 REMS and how they impact our care. The focus
2 of that program was to review the treatment
3 that was prescribed to the patient. It was to
4 look at the profile and ensure that it was
5 safe and appropriate, and then to provide
6 education and communication, very similar to
7 what these programs are trying to do
8 themselves.

9 When we looked at what quality
10 that was impacting, we looked at adherence.
11 We looked at patient knowledge. We looked at
12 communication. Most importantly, we looked at
13 safety to our patients. We put together a
14 proposal to do this in a standard way for all
15 of the patients coming into our health system.
16 We took it forward. We got it approved. And
17 at the end of day when that program was
18 approved, we were spending seven hours of
19 every workday working through the access
20 components for those patients. Seven hours of
21 every workday, a pharmacist was figuring out
22 how to gain access, how to get a patient able

1 to provide it or pay for it, and simply just
2 getting access to the drug in a way that
3 didn't delay therapy.

4 To me this is troubling and so
5 when I look at this, I want to focus on
6 solutions that solve that problem for our
7 patients and for our providers and health
8 systems.

9 When we think about the logistical
10 burden, additional record keeping and storage
11 is something that we have talked about and I
12 fully support any electronic method or
13 centralized system that would decrease the
14 burden this puts on our health systems.

15 When we think about the
16 requirements that our colleagues of NCPA have
17 talked about in terms of state requirements
18 and the national requirements that we are
19 already encouraged to meet and forced to meet,
20 the additional record keeping can be
21 burdensome.

22 When we think about the

1 certification of pharmacists, I agree with my
2 colleagues that we are already medication
3 experts and that there really is very little
4 role to certify an individual pharmacist. And
5 I would support us moving towards some kind of
6 system that certifies a group or a system of
7 pharmacies so that we don't have to go through
8 these for individual pharmacists, thereby
9 limiting the access a patient has.

10 When a patient comes into our
11 system, we have three pharmacies within the
12 University of Michigan. That patient may come
13 to any of our pharmacies. And in certain
14 instances, we are only allowed to provide a
15 medication or to provide certain education
16 requirements out of one of our three
17 pharmacies, although we operate out of a pool
18 of pharmacists and we fulfill all the
19 requirements based on a health system stance
20 and perspective.

21 Because of the REMS requirements,
22 we can only send that patient to one pharmacy.

1 That patient must go there. And for our
2 patients, many of them have access issues in
3 terms of transportation and that may be a
4 problem.

5 When we talk about access to
6 medications and the inability to procure
7 these, I have spoken a little bit about the
8 logistical burden but it also has incredible
9 impact on patients in terms of confusion and
10 frustration.

11 As an example, there was a
12 medication recently released that was for
13 multiple myeloma. The patient was seen in our
14 clinic, in our cancer center clinic. The
15 provider identified the therapy as being
16 appropriate and sent the patient home with a
17 prescription for this medication. The
18 medication that the patient needed was not
19 able to be procured from the pharmacy the
20 patient went to. The patient was given the
21 prescription back and said you need to go
22 through a separate process. There are only

1 certain pharmacies where this medication can
2 be provided to you.

3 And while I understand the REMS
4 and I appreciate the safety and that patient
5 safety is paramount, from that patient
6 perspective, I don't believe that they are
7 truly being served. They are confused and
8 they are frustrated and they don't understand.
9 And I think we can do a better job.

10 Let's assume the pharmacy had
11 access and was able to get that drug, as one
12 of ours does. They come down, the patient
13 gets the drug. Well what happens when that
14 patient is admitted to the hospital? We can
15 no longer provide that drug from an inpatient
16 stance. It is only given in that one
17 outpatient pharmacy.

18 And for many university health
19 systems across the country, this is a very
20 real situation. At that point, we turn to the
21 patient to coordinate their own care. We say
22 to the patient, we cannot get this drug for

1 you and you need to bring in what is called
2 patient-owned med. You bring it in and we
3 provide it to you out of your own supply.

4 You can imagine from a patient
5 perspective and from a healthcare perspective
6 that we can do a better job in their eyes.
7 And I would tend to agree.

8 So access to these drugs has a
9 crucial impact on our ability to provide care
10 to these patients and to impact the decrease
11 in delay for their care.

12 When we think about the actions we
13 can take, REMS must be standardized in all
14 instances where possible and appropriate. And
15 I would agree with the statements regarding
16 process versus any other approach. Anytime we
17 can make it easier through a standardized
18 approach, I agree.

19 Additionally, it is crucial that
20 hospitals and health systems, in particular
21 university health systems have access to
22 limited distribution drugs where we can

1 provide a safe and meaningful care for those
2 patients in a way that is very similar to what
3 the REMS themselves are trying to approach.

4 In 2010 an NCCN white paper stated
5 that as the new REMS paradigm developed that
6 practical implications of the policies and
7 processes must be carefully considered so that
8 REMS are implemented in a feasible manner that
9 allows patients to have access to innovative
10 drugs and biologics. And colleagues today
11 have stated the same thing. This statement
12 has never been more relevant than today.

13 A gentleman earlier recommended
14 better patient access. And the colleague just
15 recently from NCPA talked about the importance
16 of existing and trusted relationships with
17 pharmacists.

18 We believe that in university
19 health systems, pharmacists are highly
20 qualified without certification. They have
21 meaningful dynamic relationships with both
22 patients and providers and we collaborate to

1 communicate a cohesive and similar message to
2 patients around their medications. We
3 understand and we have access to the data that
4 is needed to care for and monitor safely for
5 our patients these medications.

6 Our access to these drugs is
7 crucial and the reasonable standardization is
8 imperative.

9 Thank you for your energies so far
10 to the FDA and to all of my colleagues in the
11 room. And thank you for the work that you are
12 doing now.

13 You will hear more from a
14 colleague tomorrow from UIC regarding a
15 process that they have implemented there. In
16 addition, the University HealthSystem
17 Consortium has a voluntary committee that is
18 focused on solving these issues for university
19 health systems. They have developed an
20 approach and I would be more than happy to
21 submit their approach to the docket for your
22 consideration. I think it is a reasonable

1 approach for university health systems.

2 Again, thank you for your time.

3 MS. TOIGO: Thank you, Lindsey.

4 And yes, I encourage you to submit that to the
5 docket.

6 Our last speaker today is Katie
7 Stabi from the Cleveland Clinic.

8 DR. STABI: Good afternoon My
9 name is Katie Stabi and I am the REMS Drug
10 Information Pharmacist from the Cleveland
11 Clinic Health System.

12 I oversee the implementation and
13 management of REMS programs in our inpatient
14 and outpatient pharmacies and I assist with it
15 with our outpatient clinics.

16 I would like to thank the FDA for
17 allowing me to address questions posed in the
18 REMS tools in dispensing settings.

19 The Cleveland Clinic Health System
20 is primarily located within Northeast Ohio but
21 has facilities in Florida, Nevada, and
22 internationally. Our 44,000 plus caregivers

1 care for thousands of patients annually in our
2 hospitals and clinics. For your reference, I
3 will be addressing these following topics
4 posed in the Federal Register.

5 The caregivers at the Cleveland
6 Clinic are able to provide care to a large
7 number of patients, due to our integrated
8 healthcare system. Our 1,400-bed main campus
9 interacts with our nine community hospitals,
10 over 170 outpatient clinics, and 15 outpatient
11 pharmacies. Since each of these areas has
12 access to the patient's medical record, they
13 are able to better communicate and provide
14 care through each transition of care.

15 When REMS programs restrict use of
16 medications in any of these areas, it can
17 become more difficult to ensure complete
18 patient care. This is why REMS drugs are
19 better managed within a healthcare system and
20 should not be restricted.

21 One of the questions posed was
22 whether or not individual pharmacies should be

1 certified or if health system certification
2 should exist. This health system
3 certification would be of great benefit.

4 These benefits include managing
5 patient care within a system in which all
6 caregivers have access to the patient's
7 medical record. This can increase patient
8 safety. Contraindications to medications,
9 drug-drug interactions, and disease state
10 concerns can be easily identified.

11 This is opposed to a patient
12 filling one prescription in an outside
13 pharmacy that does not have access to any of
14 the patient's medical record. A health system
15 certification would increase access to
16 restricted REMS drugs. I have a detailed
17 example on the next slide that displays this.

18 A single certification for health
19 system would also decrease the current burden
20 of REMS programs. As of right now, I enroll
21 25 pharmacies in a REMS program when this is
22 a requirement, just because the health system

1 certification does not yet exist.

2 One concern with the single
3 certification system is if one pharmacy is
4 found noncompliant, it would mean that every
5 single pharmacy within that master
6 certification is noncompliant.

7 We would want to limit the
8 possibility of a medication to be removed from
9 all pharmacies just because one pharmacy was
10 potentially noncompliant.

11 I do have an example of a patient
12 that could have benefited from a health system
13 certification. I do not want to name the
14 specific REMS program, so some of the details
15 are vague.

16 We had a patient that ran out of a
17 restricted distribution REMS drug. Since this
18 drug does require specific laboratory
19 monitoring, the patient saw the physician in
20 the office to have the medication refilled.
21 Our outpatient pharmacy is attached to this
22 physician office and did have access to the

1 patient's medical record.

2 The pharmacist was able to verify
3 that all the REMS requirements had been met.
4 However, the pharmacist could not fill the
5 prescription because the prescription is not
6 stocked in that pharmacy. However, the
7 medication is stocked in our inpatient
8 pharmacy, which is in the attached building.

9 The REMS program was called to
10 discuss what could be done for the patient to
11 receive his maintenance medication. The
12 pharmacist was advised by the REMS program
13 that no dosage should be dispensed from our
14 inpatient pharmacy. Instead, it was advised
15 to admit the patient for care in order to
16 receive their maintenance therapy or to have
17 them go without until the pharmacy that only
18 carried this medication could actually fill
19 the prescription after verifying the REMS
20 requirements and ship the drug to the
21 patient's home.

22 If a single certification was in

1 place that enables all pharmacies in an
2 integrated system to have access to a drug,
3 this patient would have had immediate access
4 to the medication that was needed. And this
5 could potentially prevent costly hospital
6 admissions in order for patients to receive
7 maintenance therapy.

8 For your reference, I have
9 summarized my main points on this slide but in
10 the interest of time, I will move on.

11 Standardizing REMS is a difficult
12 task, since there are so many different
13 patient scenarios that must be addressed.
14 Currently, most REMS programs address
15 outpatient scenarios and leave the inpatient
16 management open to interpretation by the
17 hospital designee. It would be very helpful
18 to create standardization or require REMS
19 programs to address inpatient and outpatient
20 processes. Similar to what everyone has been
21 speaking to, the TIRF share system REMS.

22 Also, the burden of the REMS

1 requirements on the dispensing setting should
2 be considered. We are very much familiar with
3 the iPLEDGE program and REMS programs that
4 have similar prescription window requirements.

5 The iPLEDGE program is used as an
6 example for restricted access and burden for
7 inpatient dispensing. This program explicitly
8 states that inpatient pharmacies are able to
9 dispense the medication but the pharmacy
10 cannot dispense a partial prescription or
11 break the blister pack. This process is
12 burdensome for inpatient dispensing, since we
13 write orders and not prescriptions for a 30-
14 day supply and we dispense doses individually
15 that are unit-dosed for patients.

16 Due to these requirements, we have
17 a process in place for patients to provide
18 their own home therapy. This can create a
19 challenge if the patient does not have the
20 drug readily available. Therefore, it would
21 be helpful if REMS programs considered the
22 different dispensing settings and therapy

1 initiation versus continuation when creating
2 REMS tools and processes.

3 For example, if a REMS program is
4 in place that requires monthly monitoring and
5 a certified prescriber is required for
6 outpatient use but is also required for
7 inpatient prescribing, it would be helpful to
8 allow an non-certified prescriber order the
9 medication for an inpatient admission when all
10 documentation of the REMS program's
11 requirements have been met. This could
12 prevent a delay of therapy while a certified
13 prescriber is being found within the hospital
14 system to assess the patient and order the
15 drug.

16 The REMS requirements also need to
17 be transparent. For example, a REMS program
18 states a drug must be logged each time it is
19 dispensed and the pharmacy must report to the
20 REMS program daily. However, when the REMS
21 program is called, the caller is informed that
22 this requirement is only for the outpatient

1 pharmacy and not the inpatient pharmacy.

2 There are several challenges of
3 potential authorized dispensers to obtain
4 access to drugs and provide care for patients.
5 Our outpatient pharmacies very often ask a
6 specialty pharmacy, since they are in a
7 specialized physician clinic. Medication that
8 have similar REMS programs, such as Thalomid,
9 Pomalyst and Revlimid are not all available at
10 our pharmacies but some of them are.

11 Therefore, requirements for access should be
12 standardized, especially when programs are so
13 similar.

14 As I discussed previously,
15 sometimes inpatient pharmacy has access to the
16 drug but due to the dispensing requirements,
17 is not able to provide the medication to the
18 patient.

19 Another frustration is that REMS
20 programs have outlined pharmacy enrollment
21 requirements. However, it does not always
22 allow pharmacies to enroll in the program and

1 have access to the drug. This emphasizes the
2 requirements need to be transparent and
3 addressed by dispensing setting.

4 Our primary concern about
5 difficulties obtaining and dispensing a
6 restricted REMS drug is when access is
7 permitted to select hospitals. There is
8 currently a trial program for a REMS drug that
9 allows pharmacies to stock the drug for new
10 starts only. This can create an ethical
11 dilemma for the pharmacist who is not able to
12 dispense the drug to a patient for
13 continuation of therapy, despite documentation
14 of all REMS requirements because the patient
15 may have left the drug at home. Instead,
16 therapy is to be delayed for this patient
17 until an emergency supply can be received by
18 the specialty pharmacy.

19 In these situations, it would be
20 best if medications were made available to
21 hospitals to care for all patients. There
22 also needs to be exceptions addressed in order

1 to best care for patients.

2 Tikosyn is a medication with many
3 safety concerns and the REMS programs really
4 does address these concerns well. However,
5 there is also a patient safety concern if more
6 than two doses of this medication is missed,
7 in which case, the patient would then have to
8 go through re-initiation of therapy, which is
9 a three-day hospital admission.

10 By allowing an exception in this
11 case when a patient may have not taken their
12 doses at home and a certified prescriber is
13 not readily available on-site, it would be
14 appropriate to let a non-certified prescriber
15 continue therapy and have a certified
16 prescriber follow-up as soon as possible.
17 This could potentially decrease medication
18 delays and unneeded increased lengths of stay.

19 And once again, I have summarized
20 my main points on this slide for your
21 reference. The effectiveness of REMS can be
22 improved and burden-reduced by interfacing

1 REMS programs with existing technologies.
2 Currently, it is up to each dispensing setting
3 to create processes to ensure REMS
4 requirements are met before dispensing a drug.
5 We have heard several places explain what
6 their process is and one of the examples that
7 we have done in the Cleveland Clinic includes
8 creating a list of all of our certified
9 prescribers in our system so that pharmacists
10 do not have to verify and look up at each REMS
11 program the requirements that the prescriber
12 is truly certified.

13 It would also be helpful to have
14 all REMS information accessible in one
15 location, as opposed to individual sites
16 having to store forms and verify patient and
17 prescriber enrollment. A centralized online
18 database that stores this information could be
19 a possibility and only accessible by
20 registered prescribers and pharmacies.
21 Overall, information needs to be more
22 centralized.

1 My current process to find
2 information includes starting with the FDA
3 website, then calling the REMS program, and
4 finally -- starts with the FDA website, excuse
5 me, and then the REMS program's specific
6 website, and then I will call the REMS program
7 for clarification. It is not uncommon to find
8 contradicting and missing information between
9 these three sources. This causes frustration
10 and burden to the dispensing setting because
11 these requirements really should be more
12 straightforward, since REMS programs are here
13 and designed for patient safety

14 And finally, it would be helpful
15 to have more shared system REMS for programs
16 with similar requirements. An example of this
17 includes a centralized clozapine registry
18 instead of each manufacturer having their own
19 registry.

20 To conclude, I believe REMS
21 programs should be standardized based upon the
22 dispensing setting. This includes inpatient

1 versus outpatient and sometimes initiation
2 versus continuation of therapy.

3 Patient care should be maintained
4 within a healthcare system and a single
5 certification may assist with this. Access to
6 REMS medications need to be increased and
7 technology should be better utilized.

8 Also, a centralized website or
9 database would decrease burden on the health
10 system, as well as increasing the number of
11 shared systems REMS that have similar
12 requirements.

13 And thank you for your time.

14 MS. TOIGO: Thank you, Katie. So
15 we have about ten minutes or so for questions
16 from the FDA panel. Anyone to start? No
17 questions? Adam, I know you have a question.

18 (Laughter.)

19 MR. KROETSCH: So a few of you
20 mentioned challenges getting access to
21 medications for drugs with REMS. And I think
22 I heard a few words or terms used restricted

1 distribution, restrictions, limited
2 distribution. Could I get a sense of what
3 exactly do you mean when you say that as far
4 as what are the challenges that are preventing
5 you from being able to obtain those drugs?
6 What kind of barriers are you running into?

7 DR. KELLEY: I'll go ahead and
8 start and then I suppose Katie will have
9 something to add.

10 At least for us within our health
11 system it can mean a variety of things. It
12 can mean that we can't get the medication
13 through our primary wholesaler, as JoAnn spoke
14 to earlier, so we have to go to a separate
15 wholesaler. That wholesaler may have its own
16 accounts that we have to create, which may
17 take time to set up. It may be an entirely
18 different distribution process or distribution
19 center that we would have to receive the drug
20 from and so that may delay patient care. I
21 would say that is probably a good instance.

22 In other instances, it may mean

1 that we do not have access to the drug; that
2 they only provide it to a limited number of
3 sites throughout the country and that we would
4 have to either send our patient to that site
5 or wait for that site to coordinate with us,
6 which some sites do.

7 In the worst case scenario, a
8 patient would have to then mail their
9 prescription to the site and wait for the site
10 to return the product to them or get it from
11 the manufacturer directly.

12 MR. KROETSCH: Thanks. And do the
13 others who mentioned those sorts of issues, is
14 that generally what you have experienced as
15 well?

16 MR. NICHOLSON: Yes, what we
17 experience when I refer to patient access
18 issues or restriction distribution,
19 specifically we are referring to products,
20 medications that are only available to certain
21 locations, certain pharmacy sites throughout
22 the country. One of the main components of

1 the REMS is that it is only available through
2 a certain wholesaler to certain pharmacies.

3 MS. TOIGO: Mwango?

4 DR. KASHOKI: Yes, I would like
5 some clarification. I think an assertion I
6 heard a couple of people make that with regard
7 to individual pharmacist certification there
8 seemed to be an assertion made that
9 pharmacists are highly trained, they are
10 highly capable, et cetera. It may not be
11 necessary to certify the individual pharmacist
12 but maybe the pharmacy or even if we go a
13 level higher, the system in which they are
14 practicing.

15 So I would like some information
16 about what specific aspects of the pharmacist
17 training and/or way in which they practice are
18 indicators of sufficiency that certification
19 may not be needed. Because you could make
20 that argument, I guess, of all healthcare
21 providers.

22 And this is coming from a

1 perspective of trying to understand when would
2 a REMS with all of its various interventions
3 be needed. And so if we make the assertion
4 that a REMS would be needed when benefits
5 outweigh risks because we are making an
6 assumption that either the way the drug will
7 be used, where it will be used, who it will be
8 used by will not be sufficient to manage the
9 risk.

10 And so I am coming back that to
11 what I heard was the assertion that no, you
12 may not need to certify us as part of a REMS
13 intervention because we already know, we are
14 already doing. So I would like some more
15 information about what are the indicators
16 because that would inform our thoughts about
17 when would a REMS be needed or a specific
18 intervention needed.

19 MR. NICHOLSON: I'll jump in
20 first. This is Kevin with NACDS. As a
21 pharmacist myself, I personally having
22 practiced as a pharmacist for a number of

1 years, pharmacists are trained. They go
2 through extensive training. Right now
3 pharmacists are required to go through a
4 minimum of six years of education, many of
5 that is clinical rotations and very detailed
6 information on drug, drug use, drug risks,
7 drug benefits. And I would -- there really
8 are no other healthcare providers in the
9 healthcare system that are trained on the
10 level of drug, prescription drug,
11 pharmacokinetics, contraindications,
12 indications than your pharmacists.

13 And so we don't really see any
14 additional certification -- we don't see that
15 certification would provide any additional
16 benefit to the healthcare system.

17 If there are specific elements
18 within a REMS that require pharmacists to do
19 something in particular, then the chain
20 pharmacies, they will set up systems in the
21 pharmacies, within the pharmacy operational
22 system either operationally or within the

1 technology system to make sure that those
2 steps are taken.

3 So while there may be within REMS
4 a necessity to make sure that certain steps
5 are taken, we feel that the base knowledge
6 that that pharmacist comes out of school with
7 -- pharmacists are also required to take
8 continuing education. And just by virtue of
9 the fact that they work with these medications
10 -- work with medications on an ongoing basis
11 and it is part of their professional duty to
12 make sure that they are current on the latest
13 therapies.

14 So again, we feel that they --
15 again, while there may be processes and steps,
16 checks that make sure that there are certain
17 procedures that they follow, we feel that
18 pharmacists have the -- they come out of
19 school with the information that is required
20 in order for them to practice but also they
21 also have the aptitude to grow with their
22 profession and making sure that they are

1 certified for what particular medication or
2 another particular medication really doesn't
3 provide any additional benefit.

4 MR. CHEN: David Chen, ASHP. And
5 I will just add to that I would agree. At the
6 end of the day, pharmacists are medication use
7 experts and I think that every drug that we
8 handle has the potential to have unintended,
9 undesirable outcome. I think that the
10 challenge that you have heard through this
11 whole day today is that REMS addresses
12 significant drugs that have higher risk. Some
13 of the challenges that we face are just all
14 the various administrative burdens. But at
15 the end of the day, pharmacists, what we do in
16 evaluating the safety monitoring and
17 appropriate dispensing practices is what we do
18 with every medication.

19 And so I think the other elements
20 to help ensure that certain steps are taken
21 because they are known to help improve, if the
22 evidence is there. That is the other thing we

1 are asking is if the evidence is there that
2 certain additional steps will help improve
3 better management across the continuum of
4 drugs. I think that is definitely a plus
5 through the REMS process. I think that would
6 be an additional administrative burden on top
7 of all the other pieces of administrative
8 requirements for documentation with a
9 profession where that is what we do with every
10 medication we handle is make sure that it is
11 handled, safely, effectively, and appropriate
12 for our patients.

13 MS. TOIGO: Other questions? So I
14 have one and I don't remember whether it was
15 Katie or Lindsey that mentioned the University
16 Health Systems Consortia. Could you elaborate
17 a little bit on that on what that is?

18 DR. KELLEY: Not being a paid
19 representative of UHC, I will do my best as a
20 member.

21 The University HealthSystem
22 Consortium is a group of academic medical

1 centers that belong to -- it doesn't serve
2 just pharmacists but much larger, the academic
3 medical centers as a whole. They provide many
4 services.

5 The one that we are currently
6 involved in as it pertains to this is a
7 subcommittee of UHC focused on how we
8 successfully navigate the waters that REMS has
9 created within the health system. One of the
10 ideas that we have brought together centers
11 around the idea of consistent care across all
12 of the health systems throughout the nation in
13 a way that would provide a certification
14 somewhat like a systems-wide REMS and allow us
15 to meet the needs of the manufacturers in
16 terms of postmarketing surveillance but also
17 allow us to provide the care to our patients.

18 I think the unique components of
19 the UHC members or of any academic medical
20 center or hospital and health system is the
21 access to the electronic medical record and
22 our ability to leverage that, to look at

1 postmarketing data and to furthermore utilize
2 that to do research was mentioned by some of
3 my colleagues on the outcomes of those
4 medications to ensure that the REMS are
5 meeting the means that we have set them out to
6 do.

7 The organization itself is, again,
8 beyond my scope. But that is the role of the
9 committee that we are on currently.

10 MS. TOIGO: Thank you. I didn't
11 catch the committee name. So that is very
12 helpful. There is a group that if we are
13 looking for some listening sessions, it sounds
14 like it would be a good group for us to set up
15 a listening session to get some better
16 detailed information.

17 DR. KELLEY: Absolutely. We would
18 be more than happy to help.

19 MS. TOIGO: Thank you.

20 Claudia.

21 DR. MANZO: So I heard
22 recommendations that rather than certifying

1 individual hospitals or settings that an
2 entire health system would be certified. And
3 I think to some extent we are attempting to
4 minimize burden by eliminating some of the
5 requirements on the inpatient setting side
6 because in those types of settings patients
7 are monitored very closely.

8 So now I guess we are hearing a
9 little bit more that that causes possible
10 access problems and it increases burden with
11 regard to having all those different sites and
12 roles.

13 So I guess I am just wondering how
14 a healthcare setting could carry out the
15 requirements of both the in and the outpatient
16 setting. On the inpatient setting we usually
17 have one person who is the authorized
18 representative that would ensure that all of
19 the sites -- all of the other staff were aware
20 of the requirements. How would this occur in
21 a hospital system?

22 DR. STABI: I guess I will start.

1 So my position, Katie Stabi from the Cleveland
2 Clinic, is I am the REMS pharmacist for the
3 whole health system. In other words, I was
4 specifically hired to help manage the REMS
5 programs for ten hospitals and our outpatient
6 pharmacies.

7 And so every time a new REMS
8 program comes to fruition, I have a process in
9 place to review the REMS program and make sure
10 that all of our pharmacies are enrolled if
11 that is needed. That education is sent out to
12 all of our pharmacists or the specific
13 prescriber groups, as needed.

14 So with the health system
15 certification in regards to access is that
16 since there isn't one certification, our
17 inpatient pharmacies kind of have one set of
18 rules and our outpatient pharmacies have
19 another set. And so my thoughts with the
20 health system certification is to kind of blur
21 those lines a little bit and we would all have
22 access to the medication.

1 Because right now, sometimes our
2 outpatient pharmacy can have it but our
3 inpatient pharmacy is not allowed to stock
4 that medication, and vice-versa.

5 MS. TOIGO: Megan and Gary, and
6 then we are done.

7 (Laughter.)

8 MS. MONCUR: Let's see, I think my
9 question is for Katie.

10 David mentioned that they had
11 these 12 questions that summarizes kind of the
12 requirements for pharmacists. Do you have
13 something similar? And if you do, how do you
14 develop that?

15 DR. STABI: I do have something
16 similar. When I first started my position, I
17 actually created a four-page checklist in
18 regards to REMS programs and the different
19 requirements. I have used this when I review
20 a REMS program to see that I am not missing
21 something. So our processes in place include
22 making sure that we know prescribers need to

1 be certified.

2 Do I need to update our electronic
3 medical record with alerts for our
4 prescribers? Do I need to create a process so
5 that we can store the patient-physician
6 agreement forms in our electronic medical
7 record?

8 So I do have that checklist. That
9 is available and I have shared it with other
10 facilities when they have asked. And in
11 regards to that process, that is how I also
12 communicate with all of our REMS
13 representatives, as I call them, a pharmacist
14 at each facility that I work with and each
15 outpatient pharmacy that I have communication
16 with to be able to share the REMS
17 requirements.

18 MS. TOIGO: Is that something
19 that you would submit to the docket?

20 DR. STABI: I can definitely
21 submit that.

22 MS. TOIGO: Thank you.

1 MR. KROETSCH: And just to butt in
2 for a moment, I think I would want to repeat
3 what I suggested this morning, which is these
4 are the sorts of tools that when you share
5 them with us, it is really helpful. So if you
6 are familiar with other people in your
7 organizations who have tools like this that
8 you would be willing to share on the docket,
9 that would be really helpful.

10 MS. MONCUR: And Katie, the other
11 thing that I wanted to add, any feedback that
12 you can give us that would help somebody who
13 is in your position more efficiently pull that
14 information, that essential information from
15 a REMS so that we make it easier to convey
16 would be very welcome.

17 DR. STABI: Yes, I can definitely
18 submit different example and suggestions to
19 the docket. I think what comes with it is
20 just experience of having to implement so many
21 different REMS programs you kind of learn the
22 ins and the outs and the very pointed

1 questions to ask in order to get the details.

2 MR. CHEN: If I could add to that,
3 when we built our Resource Center and actually
4 I commend the FDA's web resources are much
5 improved since 2009-2010, it was the struggle
6 of actually even finding where to go in the
7 REMS documents themselves. So our REMS
8 Resource is open to the public. And could
9 almost envision that the portal to answer the
10 question if it actually went to a centralized
11 database once the information was complete, it
12 would just be a seamless environment.

13 But we have found that those were,
14 at least when we started, sort of the starting
15 point questions just so you can get your head
16 around what you need to do to take care of a
17 patient that was being admitted to a hospital.

18 DR. SLATKO: So several of you
19 mentioned MTM in your presentations. And we
20 have talked about this internally and
21 contemplated it as a possible innovative
22 approach to providing counseling to patients.

1 My question is, can you give me a
2 sense of how -- is this becoming a standard
3 practice or is it the exception rather than
4 the rule? Because we are trying to get a
5 sense of what can count on or what can we look
6 at as existing platforms that we can leverage
7 to not disrupt the workflow but rather
8 capitalize on what is already happening.

9 So give me a sense of if that
10 practice is actually already happening and how
11 extensively it is happening. Can anybody? I
12 can do it sidebar. It's fine. I just was
13 curious.

14 MR. NICHOLSON: As far as MTM is
15 something that is growing. It is something
16 that the pharmacy profession has taken and is
17 making sure that basically the educators and
18 the profession itself is looking for more
19 opportunities to utilize.

20 Pharmacists are certainly capable
21 of MTM services. The challenge is that often
22 MTM services are not reimbursed. And so that

1 is -- so one of our goals is moving towards a
 2 system where payers and basically healthcare
 3 payers are willing -- you know, understand the
 4 benefits of MTM and are willing to provide
 5 payment and reimbursement for those services.

6 So at NACDS that is one of our
 7 major initiatives is to work legislatively and
 8 otherwise to expand the opportunities for MTM
 9 services.

10 And so with respect to your
 11 question on how widespread it is, it is not as
 12 widespread as we would like it to be but it is
 13 definitely a very high priority for us. And
 14 we are continuing to pursue opportunities to
 15 expand the provision of MTM services.

16 DR. SLATKO: Thank you.

17 MS. TOIGO: Okay, my watch says a
 18 little after 4:30.

19 But looking ahead to tomorrow, the
 20 morning session will be mostly presentations
 21 on the question in the Federal Register
 22 related to projects and then a few speakers in

1 there that didn't fit in the other panels that
2 will speak there.

3 Then we will have time for an open
4 public hearing. And if we don't have a lot
5 people who have signed up, we might do some
6 playing with the agenda tomorrow.

7 We have then two presentations on
8 evaluation. Gary Slatko will talk about --
9 Mary Willy will talk first about experiences
10 with REMS assessments to date and then Gary
11 Slatko will do some looking forward on REMS
12 assessments.

13 And then in the afternoon, we will
14 have the evaluation speaker session. And then
15 questions and the evaluation public hearing.

16 So that is how tomorrow will go.
17 It looks to me like we may end early tomorrow;
18 so if you are trying to do some planning.

19 So in closing, thank you everyone
20 for a productive day and thank you to our last
21 panel and to all the panel member who actually
22 have to spend a lot of time preparing for

1 this. And we don't always know until close to
2 the end, close to when the meeting time is,
3 how much time you are going to actually be
4 allotted. So we appreciate the willingness to
5 work with the system and still come and
6 present.

7 To our participants here and on
8 the webcast, thank you for sticking it out
9 through the day; to FDA panel members for
10 listening.

11 And nobody held their BlackBerry
12 out, I think. Everybody followed the rules.
13 So good on that. We were attentive listeners
14 from our FDA panel.

15 And then two special people to
16 thank. For those of you who are presenters
17 you probably through the REMS standardization
18 mailbox, you interacted with Michie Hunt and
19 Randi Clark. But they are much more than the
20 REMS standardization mailbox. They did a lot
21 to keep all the meeting preparation stuff in
22 line and then they actually held the program

1 together and made sure we all did what we had
2 to do and got done what we needed. So thank
3 you to Michie and Randi and many other people
4 that are not here but a lot of work goes into
5 planning this. And the people do need to be
6 recognize because it is beyond their regular
7 jobs and not with any PDUFA funding that was
8 sort of to accompany this process.

9 So again, transcription probably
10 available within 60 days. The slides, the FDA
11 slides probably early next week, I would say.
12 It depends. We have to look at them and make
13 sure that they are ready for posting.

14 But just check the meeting page
15 and we will be sure to get those up. And then
16 lastly, if you want to speak tomorrow, please
17 make sure you sign up.

18 Actually not lastly because that
19 won't be your last opportunity. The docket is
20 open indefinitely, except we need to hear from
21 you by September 16th if you want us to be
22 considering it for the report or for any of

1 the projects.

2 So that is it. Thank you. We
3 start at 8:30 tomorrow. And again, enjoy the
4 lovely weather.

5 (Whereupon, at 4:37 p.m., the
6 foregoing proceeding was adjourned to
7 reconvene at 8:30 a.m. on Friday, July 26,
8 2013.)

9
10
11
12
13
14
15
16
17
18
19
20
21
22

A				
AAFP 236:11,13	academia 162:3	353:4,11,15 354:1	accuracy 105:15	actual 46:11
236:17 237:16,21	academic 91:20	354:6 358:5,20	283:13 284:6	100:15 148:2
239:15,21 240:1	161:9 178:20	360:1,17 367:21	accurate 96:8	330:5
240:17,18 241:2,4	334:19 336:4	369:10 370:15,22	191:21 250:18	ad 109:13 117:2
241:7 242:14,17	366:22 367:2,19	accessed 65:14	achieve 86:11	Adam 1:22 4:5
275:18,21 276:2	Academy 3:2,17	174:7	112:11 141:6	13:14 25:18 29:14
abbreviation 203:5	235:18,22 236:4	accessible 134:20	217:21	29:20 57:3 77:20
abhorrent 261:17	328:8,11	292:13 327:9	achieved 96:14	121:21 148:14
ability 56:8 130:17	accept 230:16,21	356:14,19	97:8 172:3 193:2	150:2 225:19
142:2 156:3	acceptable 135:13	ACCME 242:18	achieving 105:2	231:6 284:9
191:11 196:12	acceptance 231:1	245:7,21 248:10	188:15 189:17	358:17
242:13 270:19	accepted 184:9,9	249:9 276:3	191:2 216:16	adapt 36:14 80:4
275:3 288:22	187:20	ACCME-defined	316:12 319:2	194:18 299:7
310:15,18 311:9	access 16:6 19:15	248:8	322:10	adaptation 114:10
335:11 342:9	38:17 47:21 60:17	accommodate	acknowledge 11:3	adapted 111:4
367:22	60:18 84:21 90:6	165:18	18:10 320:2	add 152:6,18 187:2
able 9:21 20:9	92:20 101:21	accompany 379:8	acknowledged	191:16 244:12
32:14 34:8 40:21	120:15 121:3	accomplish 9:22	20:15 100:17	275:17 284:9
45:19 47:20,22	123:14 124:9,12	322:11	247:17	359:9 365:5
51:5 54:6 56:2	125:22 126:7,13	accomplishing	acknowledging	373:11 374:2
73:1 107:1 140:17	126:16 127:3,21	323:17	161:1 304:18	added 154:12
140:18 142:5	134:17 136:22	account 25:8	acknowledgments	addicted 255:15,20
149:8 159:17	139:7,11 140:17	281:17	61:19 67:18	262:4 264:14
219:14 224:20	149:19 162:18	accountability	acne 138:5	285:5
266:10 278:6	171:16 172:1	195:1	ACOs 192:12	addiction 254:12
280:12 283:21	178:4 209:14	accountable 105:7	ACP-accredited	254:13,16,21
300:11 336:8	214:1,1,3,5,5,8,15	334:17	312:22	255:5,9 256:1
337:22 340:19	224:3 226:19	accounting 210:13	acquisition 191:5	257:4,5,18 258:19
341:11 346:6,13	230:14 231:9	accounts 359:16	191:20 243:16	258:22 261:21
349:2 351:8	234:1 237:17	accredit 245:14	act 16:5 115:11	263:3 265:19,21
353:17 354:11	252:15 261:4	accreditation 3:3	135:17 136:18	284:16
359:5 372:16	271:15 273:1	87:2 187:18	188:17 271:12	addictive 285:3,6
absence 103:6	278:9 280:1	240:22 245:11	293:6	adding 88:21
249:16 308:2	282:17 295:17	282:6 283:7	action 141:15	191:17 219:9
absolute 92:9	296:12,16 298:10	285:16 312:8	actions 61:13	addition 68:22
215:12	303:19 309:9,10	accredited 245:10	342:12	124:5 132:19
absolutely 148:12	310:22 316:22	245:16,20 246:2	actively 192:5	140:18 249:6
368:17	317:6 326:4 327:3	247:14 248:12	activities 24:21	281:13 302:19
abuse 237:14 238:1	332:15,16 335:8,9	249:4 251:15,21	98:1 106:14 110:6	313:1 316:7
238:3 239:10	335:12,17 337:19	252:2 253:3	175:16 190:7	344:16
242:11 258:22	337:22 338:2	273:16 276:2	240:19 242:4	additional 15:21
260:14 274:13	339:9 340:2,5	312:7 314:9	244:14 245:22	20:22 23:3 58:17
282:21 283:20	341:11 342:8,21	accreditors 249:5	317:17	60:21 82:18
316:21	343:9,14 344:3,6	Accredo 211:11	activity 24:9 26:8	124:21 161:22
abusers 261:6,9,11	346:12 347:6,13	212:21	106:19 244:3	166:16 171:14
261:16	347:15 348:22	accumulating	312:18	186:21 212:4
	350:2,3 351:6	184:21	acts 141:18	225:6 239:16

242:12 253:12 269:14 271:14 294:22 295:10 301:6 304:10 312:5 338:10,20 363:14,15 365:3 366:2,6 additionally 72:10 75:1 79:1,19 97:1 177:19 290:14 291:10 295:20 296:12 304:4 308:17 314:14 321:22 327:13 342:19 additive 242:4 address 22:1 25:14 33:4,5 34:18 60:22 85:19 86:14 99:4 117:10 147:19 188:9 190:10 191:6 215:3 234:13 239:7 241:5 242:8 247:9,20 252:11 273:19 280:10 286:16 296:17 323:6 345:17 350:14,19 355:4 addressed 55:14 59:19 79:12 95:14 103:18 117:9 138:1 246:20 280:13 350:13 354:3,22 addresses 240:7 246:8,9,13 327:18 365:11 addressing 37:20 83:1 246:19 247:18 253:4 308:22 346:3 adds 178:2 adequate 94:21 148:10 218:12 321:20 adequately 144:1	adhere 61:21 176:7 212:1 adherence 101:3 270:17 302:16 307:15 337:10 adjourned 380:6 adjudication 174:8 175:20 223:3 234:10 294:8 304:3 Adjunct 109:2 adjust 235:12 adjustments 88:18 administer 76:5 140:18 154:7 192:10,21 administered 71:17 97:3 230:2 327:20 administering 330:15 administration 1:1 16:4 61:14 107:3 135:17 136:17 212:15 249:22 250:3 309:4 319:13 administrative 88:17 169:8 173:11,18 177:1 184:10 237:8,10 298:12 304:6 323:21 331:7 365:14 366:6,7 administrator 333:22 administrators 188:2 admission 352:9 355:9 admissions 350:6 admit 317:1 349:15 admitted 324:9 341:14 374:17 adopt 111:18 adopted 112:6 adoption 288:15 adult 114:20	117:16 244:4 advance 34:7 196:13 advanced 111:4 268:22 advancements 99:15 advantage 123:12 301:10 advantages 106:22 107:5 adverse 61:5 76:14 76:15 133:20 146:19 187:12 212:8 219:17 229:10 271:21 300:13 303:1 316:22 317:5 adversely 133:3 advertising 59:15 advice 324:5 advise 141:13 advised 349:12,14 advisors 260:14 advisory 17:17 259:4 260:9 262:13 advocacy 131:22 138:3 139:10 238:6 258:3 advocate 185:17 228:15,20 232:14 292:18 308:12 318:20 319:4 advocated 92:2 132:10 advocating 113:12 114:1 aerospace 111:2 Affairs 287:11 297:8 305:20 328:11 affect 305:1 Affordable 271:12 aforementioned 190:11 AFP 239:5	afraid 19:1 159:1 African 120:4 afternoon 7:15 85:9 164:20 169:17 188:6 197:18 211:6 235:19 287:4 297:6 305:14 318:5 328:9 333:19 345:8 377:13 agency 69:3 91:1 93:1,5 144:19 167:3 168:1 188:22 193:3 260:15 317:17 agency's 25:10 85:9 308:16,18 agenda 7:8 9:6 11:22 12:5 377:6 aggregate 44:18 ago 133:18 183:1 220:4 agree 16:13 224:21 231:12 339:1 342:7,15,18 365:5 agreed 210:17 agreed-upon 316:12 agreement 10:1 44:15 64:21,22 67:1,3,7 68:5 69:8 99:22 100:2 173:5 202:22 372:6 agreements 44:12 44:13 61:20 62:5 67:18 205:12 ahead 112:13 158:20 231:3 359:7 376:19 aircraft 111:9 alert 89:17 295:4 alerts 107:2 108:6 372:3 algorithms 243:14 align 95:11 240:19 aligned 55:8 195:4	200:19 aligns 173:19 alike 183:10 alleviating 118:4 allied 213:7 allotted 83:4 378:4 allow 51:8 62:1,3 67:21 84:4 87:12 88:15 115:2 174:17 193:7 270:16 303:7,13 307:2 315:11 332:8 352:8 353:22 367:14,17 allowed 207:17 212:5 252:2 310:11 312:9 339:14 371:3 allowing 126:15 127:20 128:13 149:19 165:7 176:18 197:8 273:17 299:4 305:14 327:8 333:18 345:17 355:10 allows 47:19 48:22 50:2 294:9 302:12 302:22 343:9 354:9 alluded 205:18 336:7 altering 89:1 alternative 21:22 22:2 24:16 AMA 276:1 ambulatory 318:13 AMCP 328:13 329:8 330:1,3 331:11,14 332:13 333:1,10 amenable 86:4 amend 203:14 amended 90:8 147:12 Amendment 135:17
--	--	---	--	---

amendments 16:5 188:17 209:19	201:2,4 204:20	304:12	112:9 116:3 117:3	207:4 210:18
America 2:12	Andre 253:21	app 90:17 301:13	135:21 139:4	212:5 215:9
American 3:2,10	Andrew 2:13 3:4	appeared 207:21	170:10 193:7	308:18
3:15 120:4 183:12	4:14 5:5 91:5	appears 207:8	196:7 219:4 237:2	approvals 226:3
235:17,22 236:4	102:15 142:13	214:20	237:5 294:9,13	approve 16:6
259:11 260:1,5,18	148:13 235:8	Appio 2:19 4:21	300:3,21 319:16	129:10 136:15
297:3,4,8 318:8	254:2	164:18,20	331:13,18 342:16	291:17
Americans 211:14	and/or 26:21	applaud 134:12	342:18 343:3	approved 17:7 28:1
271:14	170:14 195:21	306:3	344:20,21 345:1	47:15 90:8 95:15
America's 239:10	214:15 293:18	applauds 317:21	374:22	95:20 96:2 107:13
305:22	294:16 361:17	applicable 200:1	approached 135:4	129:16 131:7
Amgen 2:22 188:5	anemia 122:20	applicant 200:3	approaches 40:9	152:12 166:13
188:8,13 197:8	123:4	applicants 177:12	55:7 56:3 79:11	173:13 207:1,3
Amgen's 189:8	anger 183:14,17	201:11 202:21	85:7 88:11 89:8	212:6 232:2
amounts 301:3	animal 180:5	application 95:11	92:19 97:15	315:18 335:7
323:14 325:3	Ann 3:2 5:4 235:8	95:13 132:22	104:10 109:13	337:16,18
Ana 13:20 63:20	235:17 245:5	202:1,4,6 303:6	293:17 307:11	approving 210:9
Anahita 2:8 4:9	275:16 277:1	applications 17:11	317:13 332:1	approximately
analgesia 113:14	334:2	88:1 112:21 116:8	approaching 44:20	84:8
285:14	announced 259:14	116:11 291:8	appropriate 11:6	apps 68:19
analgesic 254:12	announcement	applied 116:18	21:22 23:2 25:13	April 262:10
analgesics 239:14	258:1 259:2	152:11 153:3,6	33:4 51:3 61:11	aptitude 364:21
254:6 255:21	annual 182:10	201:3 300:1	69:2 84:21 85:19	Araujo 1:18 14:15
256:19 257:1,15	241:18 287:21	319:10	90:14 92:13,20	14:16
258:14	annually 170:15	applies 25:3 213:17	98:8 113:5 176:8	Arbor 334:2
analyses 194:4	287:20 346:1	316:9	176:20 191:1	area 39:6 41:19
analysis 1:23 13:16	answer 156:10	apply 57:22 58:1	219:20 237:18	50:13 51:13 52:3
51:7 108:3 112:9	162:15 273:12	115:2	242:2,10 247:11	119:18 165:1
113:4,20 114:6	275:14 296:21	appointment	249:15 271:3	218:1 241:8
115:5 132:17	324:10 374:9	301:22	272:4 276:14	266:19 273:11
136:12 243:11	answering 53:4	appreciate 85:1	283:11 296:2	329:10
326:22	56:22	109:4 132:5	303:6 305:1	areas 31:12 36:5
analyst 1:19,23 2:2	answers 324:6,11	229:12 236:6	322:22 329:16	51:17 53:13 60:18
2:4,8 13:18,22	anticipate 111:5	306:6 308:16	330:20 337:5	89:8 143:13 190:9
14:3 57:6 63:21	anticipated 194:19	318:18 321:6	340:16 342:14	193:21 196:10
analytically 51:9	271:13	328:3 341:4 378:4	355:14 365:17	330:3 346:11,16
85:7	anticipates 112:13	appreciated 160:6	366:11	arena 182:21
analyze 333:5,6	anticipation 23:20	160:14	appropriated	argued 261:3
analyzed 113:13	anybody 149:6	appreciates 84:16	99:10	arguing 256:21
194:3 323:12	156:6 375:11	90:19 102:6	appropriately	argument 261:1,2
analyzing 105:2	anymore 206:17	300:15 317:19	100:4 105:7 144:2	361:20
112:10	Anytime 342:16	327:22 331:15	208:1,2 307:3	arrangement
ANDA 200:3,11,17	AOA 276:1	approach 37:16	approvable 16:9	310:12
200:21 201:11,16	apart 301:7	39:3 53:4 85:11	approval 88:16	art 180:17 181:1
202:5,8 204:8	APhA 297:9,10,17	92:3,5 99:18	92:22 132:11	182:1
ANDAs 17:12	298:1,4 300:15	100:22 104:15	136:13 166:16	arthritis 166:13
	302:7 303:5	108:1 110:13	195:19 202:4,7	articulate 87:4

216:3 articulated 190:20 248:9 249:10 articulation 192:3 artificial 259:22 ascertain 168:8 ASHP 228:11 318:4,9,20 319:7 319:15 320:18 321:11 322:4 323:3 325:11 326:16 327:22 365:4 ASHP's 324:1 aside 161:6 asked 34:6 43:22 51:17 52:1,4,11 53:15 57:1 65:19 74:12 75:1 93:5 162:20 168:2 226:5 321:9 372:10 asking 150:20 158:2 217:11 220:6 366:1 aspect 199:22 233:8 aspects 147:1,2 179:15 186:4 224:1 361:16 assembly 241:19 assertion 118:15 144:4 361:5,8 362:3,11 asserts 311:16 assess 33:21 51:2 94:16 99:9 127:1 130:18,19 146:7 152:17 203:13 288:2 306:8 352:14 assessed 95:6 104:22 314:22 assessing 9:14 100:18 303:2 assessment 23:8,11 24:5,17,18 25:9	34:1 91:12 99:21 100:2,8,19,22 101:8 103:2 112:1 121:5 126:21 127:4,16 128:14 130:21 147:21 153:17 165:21 166:1 179:20 186:15 188:12 205:20 236:9 244:17 250:9 264:13 284:15 287:8 assessments 93:19 130:3 142:21 146:3,8,13 147:19 193:6 194:2 209:18 210:12,14 210:20,22 243:10 276:6 377:10,12 assist 89:11 345:14 358:5 Assistant 83:20 119:4 assistants 58:5 assisting 211:21 associate 1:16,21 6:11 14:9 23:14 associated 21:15 91:11 98:18 99:5 177:11 180:13 223:5 236:8 252:1 287:7 288:5 292:2 293:21 300:2,20 305:17 315:14 association 3:9,11 3:13 84:1 287:1 287:12 297:3,4,9 305:12,21 318:10 associations 312:11 assume 176:12 341:10 assuming 284:12 assumption 131:7 282:2 362:6 assurance 170:1 187:17	assure 42:14 65:17 76:9 93:12 95:19 103:12 138:10 143:7 144:7 174:2 175:12 190:2 196:17 199:14 200:1 268:17 288:6 293:15 313:17 assuring 95:12 asterisk 202:12 AstroTurf 259:22 attached 348:21 349:8 attachments 42:4 attain 189:19 attempted 125:17 attempting 125:8 369:3 attempts 122:5 324:10 attend 322:10 attention 97:21 153:10 243:18 252:19 attentive 378:13 attest 312:2 attestation 293:18 303:21 attestations 191:15 attitudes 243:12 attorney 198:7 attorneys 198:15 attributable 114:12 attributes 112:12 audience 59:3 250:17 audiences 117:18 audio 60:13 audit 62:4 325:4 audits 75:10 Australia 181:13 authoritative 291:20 authorities 91:2 authority 16:3,5 35:19 137:14	319:8 authorization 176:6 authorizations 214:10 authorized 73:12 271:4 296:8 311:22 353:3 369:17 automated 79:2 233:7,9 automatically 76:20 79:22 automating 173:11 automation 313:20 availability 100:10 227:19 available 8:19,22 10:15 47:18 74:21 80:13 82:4 87:10 90:10 139:9 149:14 160:10 174:21 187:6 190:4 222:22 236:15 245:18 246:4 273:7 275:5 294:18 299:15 316:8 351:20 353:9 354:20 355:13 360:20 361:1 372:9 379:10 avenue 1:13 159:6 average 278:22 aviation 111:2,7,16 avoid 18:21 112:14 126:17 avoidance 317:11 avoided 116:6 248:4 awarding 312:16 aware 75:11 78:10 161:5 162:8 166:4 167:5,13 219:16 316:11 369:19 awareness 168:6 169:4	A-F-T-E-R-N-O-... 164:1 a.m 1:13 6:2 82:20 82:21 163:4 380:7 <hr/> B back 29:4 51:4 53:6 56:16 82:12,21 115:21 116:4,5 123:10,15 125:14 163:2 164:3,9 186:18 198:4 201:12 217:5 244:6 258:16 264:9 286:4,13 340:21 362:10 background 10:9 10:11 15:11 16:18 26:21 42:2 45:17 45:21 53:3 81:10 82:16 120:6 197:21 198:6 199:9 277:19 bad 19:7 260:4 261:10 264:2 284:22 balance 22:19 89:2 92:13 150:14 balanced 145:1 balancing 78:15 92:10 bank 309:20 barrier 272:22 barriers 239:16 359:6 base 55:10 269:19 364:5 based 10:22 20:14 21:3 69:4 99:14 116:21 132:11,13 156:12 164:14 182:10 190:14 191:14 194:14 210:20 232:19 237:5 238:21 241:17 243:17 247:7 250:12,22
---	---	---	--	---

251:10 276:19	143:12 145:15	302:19 311:8	162:3 177:3 187:5	323:2 332:4 340:7
282:8 299:19	168:14,21 169:13	347:4 362:4 363:7	196:14 213:20	366:17 369:9
300:1 307:17	187:14 189:11	376:4	231:18 241:8	370:21
309:15 322:20	205:9 212:2,7,17	benefitting 61:6	251:14 252:8	black 246:16
328:22 339:19	213:3,5 214:3	benefit-risk 53:17	290:21 368:8	258:12
357:21	215:12 216:8	92:7,13,17 96:13	379:6	BlackBerry 378:11
baseline 281:15	257:15,17 258:6	96:18 97:8,12,16	bias 249:17	blank 265:22
300:5	268:1 293:4	144:15,17 145:4	big 329:9	blanket 235:15
basic 113:7	295:20 296:2	153:14 180:21	biggest 330:3	blind 194:15
basically 122:18	304:4 321:12	182:14	Bill 2:24 4:24 211:3	blister 351:11
123:2,19 256:20	341:6 343:18	best 11:16 22:18,22	211:6 215:17	block 202:3
375:17 376:2	357:20	35:16,20 37:4,7	billion 84:8 170:15	blog 197:20,20
basis 73:4 144:3	believes 15:20	38:11,14 39:12	287:20	blood 276:11
187:14 248:19	85:17 86:6 88:13	40:14 41:5,8	BIO 2:13 91:6,14	blue 257:6
264:15 310:18	89:9 95:17 96:7	50:11 51:21 54:3	91:19 92:2 93:4	blueprint 240:9,10
327:16 364:10	99:20 100:7	54:18 55:16 56:10	95:3,17 96:7,15	240:21 241:9
becoming 120:7	132:16 136:3	93:14 98:17,21	98:7,20 99:12,17	262:9
180:8 255:19	137:5 138:20	99:13 114:15	99:19 100:7 102:6	blueprinting 250:5
264:14 375:2	241:4 303:5	150:15 159:10,18	104:5	250:5
began 254:13	310:17 317:3	160:7,19,21 162:1	biochemistry 198:5	blur 370:20
beginning 103:6	318:22 319:15	162:9 193:4,17	bioequivalence	board 228:7 236:13
120:14 230:16	330:3 333:2	214:15 216:2	137:2	244:18
254:17 256:6	belong 367:1	222:16 223:11	biologic 98:19	boards 278:13
257:1 263:17	beneficial 68:14	227:10,10 233:12	176:11 267:3	306:12 309:3
begun 133:9 182:6	303:2	240:14 284:1	biological 91:13	body 35:10
behalf 91:8 169:18	benefit 16:1 97:16	334:10 354:20	133:10 137:11,16	bone 133:12
198:11,12 236:4	104:14 138:22	355:1 366:19	biologics 92:11	booklets 64:17
245:15 312:1	144:22 153:14,17	better 16:19 17:19	343:10	65:22
334:7	167:1 169:11	18:14 21:11 23:22	Biopharmaceutic...	bottom 219:2,4,7
behavior 23:12	180:12,13 184:19	24:3,16 28:18	102:20	230:10
100:21 148:2	186:16 211:9	45:3 50:21 87:17	biopharmaceutic...	bought 261:1
189:17 191:4	260:22 267:12	93:22 95:6 97:8	84:11	boundary 249:7
221:11,16 261:10	270:5 285:11	112:11 130:7	biosimilar 329:2	box 186:8
307:15 316:19	347:3 363:16	140:15 165:3	BioSource 3:6	boxes 69:14 124:20
321:16 322:20	365:3	168:17 176:2	266:15,18	brain 116:20
behavioral 100:15	benefited 348:12	214:18 223:16	biotechnology 2:13	133:15
behaviors 230:8	benefits 16:8 22:10	224:4 227:22	84:3 91:8,20,21	brainstorming
232:19 261:17	25:5 47:10 61:10	234:22 235:11	birth 218:12	117:20
281:10	67:5 69:16 92:11	259:21 268:10	bit 6:4 15:12,14	brand 89:14,17
belief 134:21	96:9 100:6 103:17	281:3 288:2 331:5	18:6 20:10,19	199:15 202:13
143:20 144:4	104:10 129:12	332:10 341:9	30:11,22 34:11,11	203:21 207:11
believe 113:20	134:18 137:15	342:6 343:14	39:18 42:5 46:10	break 7:14,15 82:2
120:6 121:11	139:12 152:3	346:13,19 358:7	50:7,9 70:13,16	128:10 286:2,3
126:3,7,15 127:12	168:13,20 187:4	366:3 368:15	93:22 120:5 140:1	351:11
127:14 128:6	187:22 191:18	beverages 7:19	140:9,20 143:3	breaking 140:7
131:6 132:13	199:21 257:19	beyond 15:21	199:8 201:21	148:17
133:1 139:1 143:3	267:2 301:6	18:18 49:9 123:20	273:20 285:21	breaks 115:5

breast 246:17	84:20 95:2 98:9	called 24:7 57:20	321:5 325:18	catalogued 45:8
Brian 2:23 4:23	101:9,13,15 102:2	103:10 161:20	326:5,9 327:2	cataloguing 45:16
197:15,18 211:2	102:11 103:21	241:10 265:5	328:8,12 329:12	catalyst 196:8
223:19	105:15 118:4	342:1 349:9	330:7 331:3	catch 368:11
bridge 270:13	121:6 127:7	352:21	332:14 333:2,4	categories 106:1
272:6	128:16 152:15	caller 352:21	334:15,17,21	316:16,17
brief 15:11 115:4	154:3,13 155:13	calling 357:3	335:9,12,18 336:1	category 57:22
129:7	155:14 156:6	campaign 257:14	336:8,15 337:1	158:9 200:10
briefing 265:7	169:8 178:3 183:6	campus 346:8	341:21 342:9,11	caught 42:18
briefly 160:6	184:11 199:20	cancellations 7:7	343:1 344:4 346:1	cause 113:3 135:22
bring 235:15	227:15 230:17	cancer 122:19	346:6,14,14,18	263:11 282:3
326:10 342:1,2	267:8 271:9	246:17 284:22	347:5 349:15	caused 134:4 138:2
broad 112:19 170:9	296:11 298:12	334:2 336:17,19	353:4 354:21	138:7 257:10,12
237:4 243:2	300:8 315:2	340:14	355:1 358:3	264:22 296:14
broadened 185:4	319:13 323:18	capable 190:21	359:20 367:11,17	327:18
broadier 57:22	327:18 330:16	231:19 361:10	374:16	causes 357:9 369:9
broadly 46:13	336:14 338:10,14	375:20	careful 38:6 135:4	causing 256:18
brochures 64:18	340:8 347:19	capacity 92:8	carefully 101:14	257:2
66:1	350:22 351:6	301:19	189:20 343:7	caution 132:22
broken 126:3	357:10 358:9	capitalize 375:8	caregivers 345:22	184:15 306:14
134:19	366:6 369:4,10	CAPT 2:4	346:5 347:6	cautioning 183:9
Brooklyn 181:13	burdens 16:14	capture 45:22 46:5	Caremark 2:21	cautious 254:7
brought 151:2	88:15 130:10	46:14 50:8 100:3	169:16,18 170:3	caveat 89:6
367:10	171:11 191:16	315:12	170:11 171:4	CDC 247:16
Brown 2:16 4:17	288:5 308:4 331:8	captured 315:5	176:21 178:7	256:15,15,21
128:21 129:2,4	365:14	captures 46:11	caring 58:4	CDER 13:13 14:11
build 49:22 50:21	burdensome 38:16	car 256:14	Carolyn 3:12 5:12	CDR 1:18
55:3 56:12 159:9	86:11 93:2 176:3	Carden 3:17 5:15	305:11,19 318:3	CDRH 112:4
241:19 272:9	328:20 338:21	328:7,9,10	332:3	CE 63:8 325:2
280:13	351:12	care 3:18 34:22	carried 349:18	Celgene 2:14
building 1:12 33:7	burden-reduced	48:10 61:3,15	carry 33:13 57:16	102:17,21 103:3,7
47:7 55:9 56:15	355:22	71:20 76:2,9 78:5	296:15 314:17	104:4 105:9,20
159:3,11 269:17	business 20:4	78:7 119:12	369:14	106:12 107:17,20
272:6 322:7 325:6	119:17 211:7	120:13,19 123:19	carve-out 335:21	108:12 141:17
349:8	butt 373:1	125:16,19,20	case 113:13 115:9	200:7 205:9
built 155:19 374:3	B.C.P.S 3:21 5:17	126:14,17 128:18	115:13,19,22	celgeneriskmana...
bullet 142:20	B.S 5:11	136:5 140:16,16	116:15,19 166:2	106:15 140:22
bulleted 65:11 66:8	B.S.N 3:5 5:6	154:14 155:3	168:7 179:16	141:9
66:20 67:12	B.S.Pharm 2:15	170:13 171:17	204:19 237:3	cell 6:17
bullets 142:16	3:10 4:15	174:13 186:1,3	284:19 296:14	cells 256:19
242:7		192:19 212:3	355:7,11 360:7	center 2:16 6:12
buprenorphine	C	239:12,17 240:15	cases 41:22 44:9	59:5 112:22
202:19 207:7	call 115:8 119:7	246:10 252:12	133:1 135:20	119:12 128:22
225:14 258:19,21	156:6 233:22	269:3,4 288:8	138:2 330:17,21	129:4 131:1 198:1
burden 16:10,11	264:5,6 309:20	307:7,8,21 308:5	cast 271:19	309:20 324:2,6,10
21:12 23:3 31:10	334:5 357:6	316:22 318:12	catalogue 40:7 43:3	334:2 336:17,19
62:20 63:4,16	372:13	319:5 320:10,21	46:21	340:14 359:19

367:20 374:3 centered 34:7 centers 91:21 119:10 161:9 334:20 336:4 367:1,3,10 central 172:7 173:13,17 270:14 293:8 319:2 Centralization 327:10 centralized 194:20 292:1,15 314:13 314:14 323:16 324:4 325:12 338:13 356:17,22 357:17 358:8 374:10 centralizing 299:11 299:13 CEO 131:20 certain 16:7 54:12 72:8,11 89:10 104:12 133:14 135:15 147:6 149:16 152:14 222:12 263:14 264:12 278:20,21 279:13 295:17,18 296:7 309:10 311:13 313:17 315:5 339:13,15 341:1 360:20,21 361:2,2 364:4,16 365:20 366:2 certainly 167:8 169:2,11 196:22 212:15 217:20 221:5 375:20 certainty 283:7 certification 52:1,2 52:13 58:18 61:21 62:1,7,12 63:16 75:7 77:9 226:2 233:10 244:19 251:10 294:5,21 295:1,11,15,21	296:4 303:14,21 311:12,19,20 312:14,16 314:19 339:1 343:20 347:1,3,15,18 348:1,3,6,13 349:22 358:5 361:7,18 363:14 363:15 367:13 370:15,16,20 certifications 191:14 certified 45:15 72:6 72:7,17 73:1,10 74:4,11,20 77:10 108:9 295:3,19 347:1 352:5,12 355:12,15 356:8 356:12 365:1 369:2 372:1 certifies 200:4 339:6 certify 339:4 361:11 362:12 certifying 295:22 368:22 cetera 90:18 104:11 277:9 361:10 chain 3:9 77:3 80:21 175:5 287:2 287:5,12 295:13 295:22 296:4 321:2 326:11 363:19 chains 287:15 306:2 chair 1:14,17 6:14 9:7 12:20 15:5,7 27:12 236:14 challenge 351:19 365:10 375:21 challenges 13:4 15:13,15 20:2 21:3,14,21 22:14 23:10,18 26:4 71:12 81:11 91:10	106:8 107:5 175:12 177:11 189:4 192:14 236:8 287:6 293:21 305:16 317:1 353:2 358:20 359:4 365:13 challenging 295:13 308:8 chance 26:14 164:4 164:8 201:15 change 55:17 100:15 134:13 148:3 181:6 184:5 221:12 244:22 246:22 247:2,13 248:22 249:2 250:8 252:3 253:7 257:9,12 273:18 changed 105:22 151:11 152:5 232:19 changes 16:13,16 16:19 28:7 55:12 88:22 106:4,6,9 150:17 151:20 186:9 212:11,18 227:17 232:1,13 243:14 299:8 325:20 changing 232:6 251:5 channel 171:14 309:14 channels 326:12 characteristics 22:4 104:11 characterization 45:16 153:15 characterize 32:16 40:4 41:20 43:3 46:5 51:2 99:9 193:18 259:10 characterized 41:4 45:8 54:5 259:21 characterizing	41:15 Chardae 1:18 14:16 charge 312:1 326:7 check 8:20 123:11 155:22 156:4,7 174:3 379:14 checklist 61:3 68:16 124:15 371:17 372:8 checklists 63:10 124:13 checkpoint 71:16 checks 123:15 158:11,12 364:16 chemical 139:3 chemotherapy 336:22 Chen 3:15 5:13 318:4,5,6 365:4,4 374:2 chest 255:18 Chicago 2:15 119:2 choice 264:8 choices 77:8 96:11 choose 39:3 107:1 142:5 278:3 310:9 chronic 211:15 241:10,12 257:19 258:7,16 262:3 263:14,18,20 264:1,11 284:13 circle 56:16 circumscribed 196:14 circumstance 156:12 circumstances 15:20 87:5 219:19 cited 114:4 166:12 citizen 204:13 claim 175:19 claimed 174:8 200:2 claims 79:21 223:3 234:10,11 304:2 clarification 357:7	361:5 clarify 139:20 147:4 148:22 159:6 clarifying 24:11 49:14 97:2 Clark 378:19 classified 308:19 316:15 class-based 206:22 class-specific 192:16 Class-wide 260:13 Claudia 2:1 14:13 140:4 222:9 368:20 clear 40:10 41:21 42:22 118:9 133:19 147:17 184:2 187:21 189:16 191:18 192:3 230:15 256:17 clearer 230:22 clearinghouse 303:13 clearly 69:16 78:19 136:14 153:2 186:5 190:15 218:19 226:15 232:10 289:22 321:12 Cleveland 3:21 345:7,10,19 346:5 356:7 370:1 click 125:1 client 198:12,13 clinic 3:22 119:19 124:4,5,19 236:3 243:9 340:14,14 345:7,11,19 346:6 353:7 356:7 370:2 clinical 71:10 89:7 109:9 127:9 137:2 179:11 180:6 184:12 185:22 236:2 238:6
--	--	---	--	---

239:18 363:5 clinically 185:17 332:9 clinician 228:17 clinicians 185:9 239:12 clinics 71:6 195:6 318:14 345:15 346:2,10 close 158:20 378:1 378:2 closed 77:15 80:22 119:7 259:13 272:20 closely 29:14 264:16 369:7 closing 138:19 178:7 304:16 377:19 clothes 80:15 cloud-based 195:12 clozapine 122:7 123:17,17 124:9 220:9 357:17 Clozaril 170:21 CME 237:7 238:15 240:2,5,7,17,19 240:21 241:3,7,22 243:6,9,20 244:13 244:15 249:4,22 250:2,15 252:2,9 273:16,22 278:19 279:16 280:12,19 286:7 CMEs 279:17 CME/CE 240:8 CMSS 242:18 coalition 129:6 131:4 coast 255:3 cocaine 256:11 code 242:18 276:20 codified 314:11 coffee 82:4 cogently 226:22 cohesive 344:1 cold 235:14	colitis 166:17 collaborate 101:22 343:22 collaboration 86:18 238:9 collaborations 104:19 196:6 collaboratively 54:16 colleague 343:14 344:14 colleagues 17:21 21:19 25:16 56:19 68:9 71:1 81:20 313:9 338:16 339:2 343:10 344:10 368:3 collect 61:18 197:11 collected 315:6 collecting 102:1 134:22 collection 88:22 101:16 collectively 323:17 colleges 119:11 color 254:22 combination 144:8 combine 198:5 combined 117:14 193:15 256:11 come 9:21 19:13 28:4 45:3 54:13 75:9 83:9,10 145:2 153:20 199:11 201:6 203:4,11 204:21 208:16 224:11 247:13 266:9 329:3 339:12 341:12 364:18 378:5 comes 56:8 208:15 226:16,18 229:17 274:7 301:21 339:10 364:6 370:8 373:19	coming 50:18 166:21 202:22 206:14 337:15 361:22 362:10 commend 132:2 144:11 288:1 374:4 comment 8:5 26:14 85:6,9 87:10 102:7 140:6 150:4 156:21 158:3,3,4 178:14 209:4 224:12 231:5 263:8 268:9 280:5 284:9 306:7 321:9 328:1 comments 8:7,12 8:14,17 11:4 19:20 26:15,16 86:5 89:5 91:10 102:13 117:1 122:15 129:7 132:7 139:14,17 139:21 164:10,14 170:7 215:18 236:12,20 237:3 262:15 278:14 317:20 319:21 321:11 commercial 242:19 248:9,10 249:10 249:14 Commission 113:9 Commissioner 197:22 commissioners 263:6 commitment 9:22 53:12 92:5 103:4 192:5 237:16 commitments 9:19 30:22 31:4,18 40:19 50:14 53:7 84:18 95:12 committed 27:11 31:5,16 53:20 178:8	committee 24:8 27:13 30:7 122:14 170:7 187:17 240:5 259:4,14 260:9,10 262:13 344:17 368:9,11 committees 15:8 17:17 155:3 common 41:21 45:6,18 52:9 56:12 71:15 75:15 78:13 89:10,12 90:4 107:7 117:21 221:19 256:2 258:16 261:18 308:8 communicate 22:7 62:2 77:17 80:18 93:8 94:6 263:22 332:11 344:1 346:13 372:12 communicated 291:14 communicating 96:13 144:22 communication 42:15 89:18 94:9 94:12 95:10 96:4 96:5,19 97:8,9,12 97:17 114:22 143:5,8,13,21 144:10,16,17 145:5,16 174:17 187:9 200:14,16 201:13 231:18 234:21 235:1 243:17 300:12 301:16,17 304:7 337:6,12 372:15 communications 2:3,8 13:18,21 57:5 58:16,19 59:4,7 63:21 89:11,16,21 144:9 145:8 148:2 200:18 258:5 communication-...	95:21 communities 152:14 274:4 community 3:12 119:10 120:2 137:9 138:3 175:13 178:3 193:4 222:20 223:16 246:7 251:2,3 252:17 257:14 258:3 263:16 305:12,15 305:20,22 306:1,9 307:12 308:6 309:1 310:8 317:9 318:1 346:9 companies 20:12 84:3,14 85:13 88:4 91:20 107:13 128:3 130:6,7 211:22 213:19 214:12 287:16 company 20:3,5 102:21 125:7 180:2 comparable 86:8 comparative 142:1 compare 76:10 compared 117:7 233:18 307:15 compares 277:11 comparing 276:17 compatible 38:5 52:17 77:21 80:5 competence 249:1 competency 243:18 247:10 competitors 199:21 complaints 187:9 187:11 235:11 complement 145:13 complementary 96:14 complete 20:8 90:16 95:13 106:18 141:2
--	--	---	---	---

181:5 241:3 293:2 303:14 312:19 325:2 346:17 374:11 completed 68:1 173:5 313:3 332:22 completely 167:5 231:12 completing 41:7 53:21 54:8 214:10 completion 105:14 141:4 303:22 311:17 312:16 313:4 complex 171:3 223:14 270:10 328:22 334:21 compliance 2:5 15:1,2 62:4 73:8 85:16 179:18 180:19 240:22 282:13,15 293:21 298:7 331:22 compliant 325:9 complicated 225:11,15 comply 73:17 complying 177:17 component 58:12 60:13 74:16 244:18 313:11 315:4 323:11 components 60:10 103:19 104:13 172:18 176:14 213:22 271:10 298:7 300:1 315:22 316:2 323:10 324:3 325:10 337:20 360:22 367:18 composed 30:2 composition 133:12 comprehensible 320:16	comprehension 89:12 148:1 302:13 comprehensive 22:15 59:19 93:10 97:18 104:13 106:13 112:15 129:20 142:18 211:12 336:19 comprised 119:8 compromise 135:9 135:11 compromising 139:7 computer 106:2 concept 173:14 179:5 199:11 276:16 277:20 concepts 217:18 concern 136:9 138:2 151:6 183:11 192:21 232:3 238:3 262:18 280:1 348:2 354:4 355:5 concerned 84:19 184:4 239:15 319:9 320:18 321:1 concerning 185:1 278:1 concerns 37:21 52:20 54:20 105:6 131:2,5 136:6,20 189:6 231:13 237:15 323:7 347:10 355:3,4 concerted 317:3 concise 289:12,18 concisely 78:19 conclude 357:20 concludes 70:2 272:12 Concluding 5:21 conclusion 90:19 102:6 128:4 317:8 327:22	concurrent 204:1 conditions 22:8 33:2,14 67:19 72:15 74:8,14 76:21 79:19 80:1 120:6 176:17 190:19 211:15 247:2 258:16 294:10 conduct 87:9 137:2 326:21 332:18 conducted 108:4 193:6 194:6 207:6 Conducting 191:19 confidence 250:13 confirmation 176:5 311:18 confirming 271:3 conflicts 249:13 confronted 301:2 confused 341:7 confusing 44:19 150:18 289:15 confusion 96:20 340:9 Congress 136:19 conjunction 174:15 consensus 322:7 consent 265:15 consequences 139:5 289:17 consider 19:14 20:12 81:1,19 87:21 109:16 132:14 135:7 143:4 147:2 156:18 166:10 167:3,18 178:5 195:9 222:6 226:15 243:5,21 267:11 296:7 299:13 302:8 324:3 consideration 106:7 132:8 135:5 167:10 324:1 344:22	considerations 25:8 243:6 326:19 336:11,13 considered 8:14 26:17 58:9 92:12 167:14 208:6 243:20 290:20 343:7 351:2,21 considering 182:5 238:11 269:9 379:22 considers 106:5 consist 58:15 95:20 299:22 consistency 25:10 172:4 300:5 329:22 consistent 38:2 42:7 48:16 85:10 98:16 150:15 171:22 308:21 319:1 367:11 consistently 49:16 consisting 65:11 66:20 67:11 consists 66:8 consolidated 195:11 consolidating 290:21 Consortia 366:16 Consortium 161:8 344:17 366:22 constantly 109:21 constraints 81:22 constructing 300:4 constructive 90:22 constructs 247:13 consult 177:13 consultant 179:1 consultation 176:4 183:4 185:2 consultations 288:22 302:9 consulting 2:22 185:4 consume 326:14	consumer 64:7 69:4,10 96:22 129:6 131:4 289:6 consumer-friendly 290:10 consumer-patient 129:7 consuming 18:11 223:14 consumption 256:20 contact 141:17 309:22 contain 67:17 173:22 175:18 contained 90:13 contains 44:15 contemplated 374:21 contemporaneous 138:17 contends 310:2 content 47:9 69:17 105:18 111:11 114:22 244:2 248:17,19 250:14 252:8 288:17 292:12 312:18 contents 4:1 5:1 250:4 context 34:22 76:9 97:3,13 133:17 179:16 277:16 continually 329:8 continuation 352:1 354:13 358:2 continue 12:16 90:21 107:8 124:2 166:2 167:21 168:2 169:2 180:14 237:17 240:3 243:4 268:3 292:3,17 299:18 304:13 307:12 308:7 323:4 326:17 328:15,21 355:15
---	---	---	---	---

continued 35:20 250:9 320:9 322:13 continues 91:1 93:1 239:7 240:17 298:4 continuing 3:4 56:7 87:2 102:9 235:21 237:1 240:2 244:10 245:12,14 245:17,21 247:14 248:12 250:16 251:6,7 253:3 266:6 275:13 312:6 327:20 333:11 364:8 376:14 continuity 321:5 326:4 continuous 105:3 152:21 191:10 continuously 56:7 56:17 104:21 329:6 continuum 179:6 179:14 366:3 contract 226:17 227:6 contractor 95:4 contracts 335:21 contradicting 357:8 contraindications 347:8 363:11 contrary 198:14 contribute 174:19 298:9 contributions 316:11 control 101:5 109:9 149:21,21 193:9 206:3 209:14 218:12 239:7 260:15 controlled 119:20 126:6,9 138:12 299:21	controls 52:16 74:3 76:7,13 78:3 80:13 224:16 convene 85:1 convened 1:12 137:18 convenience 212:14 convenient 294:19 convening 132:2 188:10 190:10 196:21 convenor 196:9 conversation 46:2 61:9 162:8 244:6 265:9 conversations 240:4 convey 78:19 144:1 296:19 373:15 conveyed 78:21 convinced 260:6 Con't 5:1 cooperate 204:9,18 cooperatively 304:13 coordinate 165:1 341:21 360:5 coordinated 229:14 299:10 coordinating 199:17 coordination 306:17 cope 110:2 copied 37:3 copies 236:14 239:4 core 240:10 323:10 corner 124:14 cornerstone 269:13 Corporate 76:22 Corporation 2:14 2:20 3:6 102:17 102:21 170:3 266:15 correctly 234:3	cost 127:17 209:15 224:19 225:2,4,4 300:20 335:22 costly 317:11 350:5 costs 137:13 195:6 203:13,15 208:22 209:21 224:2,15 225:5,6 Council 3:3 292:4 counsel 1:24 64:10 66:3,15 83:20 115:10 245:11 312:8 314:8 counseled 213:14 counseling 52:9 57:18 61:8 64:18 65:20 66:13 67:8 68:13 75:3 175:15 223:15 265:5,18 267:1 269:10 289:21 290:4 307:2,17 309:17 309:19 321:19 374:22 count 17:4,5 211:15 375:5 country 211:13 213:16 229:4 246:4 255:7 263:3 341:19 360:3,22 country's 84:1 couple 31:5 153:21 182:12 225:20 277:19 361:6 coupled 213:12 courier 309:19 course 12:3 50:19 62:19 184:11 218:8 226:16 248:11 331:6 Court 186:10 cover 11:4,7 coverage 174:21 214:9 260:12 covered 27:3 75:14 201:4 202:1 240:10	covers 246:4 co-prescription 220:12 co-prescriptioned 221:14 CPE 312:16,21 313:2 crafted 205:13 crafting 189:4 crashes 256:14 create 9:10 73:22 84:20 89:1 171:11 172:14 173:21 189:13 190:4 194:9 196:6 210:10 239:16 290:12 291:16 315:19 317:14 327:7 350:18 351:18 354:10 356:3 359:16 372:4 created 10:12 103:7 159:20 245:12 249:7,21 295:21 313:7 319:19 324:5 336:21 367:9 371:17 creates 117:22 247:1 272:8 298:21 308:3 336:1 creating 172:4,11 173:12 199:20 335:16 352:1 356:8 creation 276:5 290:13 308:12 318:1 creativity 196:19 credit 63:8 240:5 242:17 243:1 276:1,3 279:13 312:20 credits 278:21 279:6,18 312:17	crisis 237:22 239:8 239:10 242:9 criteria 24:12 25:3 207:14 261:20 critical 26:6 28:8 29:3 71:18 94:1 97:22 148:12 174:16 180:9 190:9 196:10 289:12,16,22 307:1 313:14 326:22 cross-check 270:8 cross-disciplinary 94:14 crucial 342:9,19 344:7 cues 141:1 cultural 243:18 curious 150:18 151:3 281:1 375:13 current 25:9 90:7 130:17 135:10 189:7 191:13 194:18 198:21 210:11 213:4 260:17 268:12 269:15 271:8 280:18 295:14 297:22 320:19 347:19 357:1 364:12 currently 63:9 135:10 173:14 195:2 204:6 211:19 268:20 289:3 308:15 310:6,19 314:7 321:18 350:14 354:8 356:2 367:5 368:9 curriculum 241:16 262:9,11,16,18 263:9,10,12 264:4 customers 149:17 customization
--	---	---	--	--

22:20 37:15 80:9 customizations 281:16 customize 22:18 280:14 customized 38:3 79:6 80:14,20 177:2 customizing 81:3 cut 12:17 304:5 CVS 2:21 169:16 169:18 170:2,11 171:3 176:21 178:7 185:1 cycle 93:10 94:12 Czar 263:4	210:9,10 231:17 324:4 356:18 358:9 374:11 databases 226:1 data-driven 132:12 date 15:12 134:10 193:20 205:1 308:6 377:10 daunting 298:7 David 3:15 5:13 318:4,6 328:6 365:4 371:10 David's 334:4 day 9:5 73:4,4 110:11,12 119:16 219:1 250:19 266:4 310:5 337:17 351:14 365:6,11,15 377:20 378:9 days 6:20 8:19 12:4 379:10 de 116:9 180:10 DEA 238:15 309:5 dealing 15:15 51:18 252:4 Dear 59:8 89:22 death 261:22 271:22 deaths 256:4,8,12 256:14 257:3 debate 136:16 decade 133:9 134:6 December 104:6 134:3 decide 33:8 206:18 decision 113:3 125:2,3 132:11 134:12 207:18 269:14,22 272:3 decisionmaking 25:11 decisions 61:7 75:18 100:11 132:14 154:3,16 186:11 224:9 304:22	decision-making 157:3 224:6 decisively 192:9 decks 60:7 declined 214:20 decrease 169:8 267:18 311:7 338:13 342:10 347:19 355:17 358:9 decreased 146:19 decreasing 300:7 dedicate 176:22 323:19 dedicated 59:10 65:2 69:9 84:3 195:13 237:21 240:17 dedicates 315:4 dedication 304:17 deduced 282:11 deemed 103:11 deficit 282:3 define 48:17 50:8 69:14 203:7 255:10 317:4 defined 16:16 69:16 156:12 219:7 250:22 316:3,18 defines 116:3 122:18 defining 216:14 definitely 158:6 198:10 280:1 304:22 366:4 372:20 373:17 376:13 definitions 40:10 41:21 43:16,19 108:14 degree 42:22 112:16 198:5 delay 202:3 338:3 342:11 352:12 359:20 delayed 354:16	delays 126:17 355:18 delineate 289:22 deliver 58:20 192:10 delivered 107:22 108:8 184:22 248:2,6,17 281:9 307:8 308:1 delivering 171:22 307:11 delivers 107:1 delivery 60:9 91:17 95:3 101:10,14,20 102:12 152:16 174:11 184:22 191:17 194:11 269:15 294:4 307:16 demographic 61:18 132:17 demonstrable 191:18 demonstrate 237:4 demonstrated 112:18 116:7 196:12 demonstrates 92:4 demonstrating 191:20 denied 335:9 denominator 107:7 dental 230:20 Department 102:20 depend 244:8 dependent 184:16 depending 17:5 37:12 66:6 192:19 225:2 316:16 depends 7:5 379:12 deployed 87:8 depth 93:22 Deputy 1:18 14:16 263:4 derivatives 151:21 describe 45:4,6	49:16 50:8 59:22 63:12 141:6 145:9 145:10 222:15 275:11 described 157:6,7 200:6,14 202:20 203:12,16 246:10 describing 145:17 216:8 249:4 description 265:6 design 22:12 24:13 29:15 30:4,9 32:6 32:7 38:21,22 51:4,9 86:13 89:14 90:3 93:15 98:21 109:14 116:9 118:9,12,17 147:15 177:14 196:11 205:11 215:11 244:3 293:11 308:8 322:17 331:14 designate 73:12 designated 149:16 designed 34:18 104:18 121:18 180:1,2 187:2 243:9 280:10 289:10,19 330:19 357:13 designee 350:17 designing 24:3 104:15 290:20 designs 104:3 desire 150:16 desired 62:13 103:22 189:17 191:3 desk 8:8 despite 9:20 71:13 354:13 detail 41:17 56:20 detailed 113:19 137:20 157:19 171:5 290:8 347:16 363:5 368:16
---	--	---	---	---

348:14 374:1 detection 179:17 determination 186:19 282:10 determine 23:13,16 25:4 61:11 129:20 153:19 176:19 193:4 220:14,16 221:7 232:17 239:19 determined 75:18 186:17 196:1 273:21 determines 65:7 199:19 284:5 determining 166:10 223:22 315:15 329:7 detrimental 151:19 develop 27:22 32:14 35:20 41:11 48:14,16 50:16 85:6,10 88:10 94:22 96:16 99:13 122:10 129:12 138:15,17 157:11 168:14 173:8 203:13 256:3 285:8 290:12 371:14 developed 46:15 103:8,14 120:10 124:16 195:3 206:22 208:13 209:1 248:2,5 273:22 315:11 327:12 335:13 343:5 344:19 developers 35:9 developing 20:6 24:18 25:1 35:10 53:20 54:9 55:5 84:4,9 86:17,19 158:7 171:1 197:2 213:21 218:3 226:18 240:18 241:21 256:1	275:18 293:13 319:16 322:8 326:3 development 54:22 86:22 93:16 94:4 98:22 99:18 169:20 177:7,14 178:11 190:9 195:9 209:16 211:7 224:6,19 225:4 238:16 242:2 250:10 251:8 291:18 303:11 305:17 312:13 314:10,11 319:1 320:6 322:22 327:15 Developmental 182:8 devices 118:8,18 187:8 291:9 Devita 2:21 4:21 169:16,17,22 222:19 233:5,15 234:16 de-identified 245:1 diabetes 276:10 diagnosis 156:8 262:3 dialogue 94:3 162:14 269:11 326:17 dichotomy 261:13 dictate 168:9 dictates 252:7 die 256:4 differ 183:22 difference 133:6 274:3 280:3 differences 133:11 133:19 134:8,19 215:15 different 20:18 30:3 35:4,5,6,7 37:18 38:12 42:10 42:11 43:21 44:7 44:8 45:1 49:6	56:20 58:7 60:14 60:15 61:10 62:9 62:14 70:14,17,19 71:9,10 75:20,21 78:12 79:7 80:10 81:4 89:7 98:18 121:17,17 135:7 151:17 156:19 165:19 167:5 178:20 181:15 185:12 221:16,17 221:18 224:15 226:8 230:7,8,9 230:10 231:14 233:20 234:2 276:4 277:19 279:4,5,11,12,16 279:20 280:14 317:13 323:6 350:12 351:22 359:18 369:11 371:18 373:18,21 differently 18:6 20:10 284:11 difficult 36:14 43:17 44:20 204:13 205:22 296:8 331:22 336:2 346:17 350:11 difficulties 354:5 digital 68:19 dilemma 354:11 diluted 169:6 dimensions 75:21 direct 13:11 185:22 233:16 269:2 303:7 309:16 directed 3:1 5:3 52:4 57:8 64:15 68:21 150:4 151:1 235:7 direction 134:17 136:1 308:17 directly 76:3 136:10 186:1 192:17 211:16	217:9 270:21 274:8 360:11 Director 1:17,18,21 2:1,6 6:11 14:10 14:13,16,22 119:5 170:1 188:8 232:5 235:21 247:16 266:17 305:19 318:7 328:10 directors 59:6 Director/Medical 2:5 directs 239:2 disappear 120:14 discharge 123:18 124:8,10 126:18 156:2 discharged 124:2 disciplinary 319:5 disciplined 81:21 disciplines 114:12 disclaimer 165:9 disclaimers 198:8 disclosure 249:17 discounts 127:22 discovered 160:20 discovering 84:9 discretionary 206:16 discuss 25:17 57:21 65:3 85:2 147:16 236:8 326:4 349:10 discussed 270:4 330:9 331:6 353:14 discussing 94:19 243:8 315:13 discussion 26:22 67:4 118:10 121:10,21 148:8 148:11,17 155:13 158:16 179:9 332:4 discussions 18:20 19:4 66:4,18 95:7 107:18 154:19,22	155:5 157:13 267:2 300:18 301:21 disease 89:7 104:11 180:8 184:17 185:6,8 213:11,18 230:5 255:11,14 256:1,3 269:19 274:22 285:8 347:9 disparities 243:19 disparity 246:14,15 disperse 72:5 73:1 73:11 74:19 76:3 76:4 107:21 211:16 212:21 309:7 311:13 351:9,10,14 354:12 dispensed 71:4,5 72:11,13 74:7 141:14 309:13 320:14 349:13 352:19 dispenser 72:7,14 72:22 74:4 78:22 101:11 298:16 dispensers 4:10 52:13 58:6 70:9 70:12,20,21 71:15 71:19 73:3,5,7,11 75:5,15 78:13,20 79:8 192:11 221:20 294:7,9,16 296:9 300:8,10 353:3 dispensing 3:7 4:10 5:8 52:12,14,19 60:4 70:9,12,20 71:19 72:5 73:6 74:6 76:2,3 77:1 77:14 78:17 79:7 81:4,18 119:20 123:7 124:18 155:22 160:12,13 170:4 174:22 175:3,17 176:7
--	--	---	---	--

191:3 194:21 286:17,20 292:20 294:7,11 295:4 311:11 312:4 314:3 319:22 321:8 325:3 345:18 351:1,7,12 351:22 353:16 354:3,5 356:2,4 357:10,22 365:17 displayed 236:19 displays 347:17 disproportionate 135:20 137:4 disproportionately 135:2 disrupt 87:19 135:22 150:10 375:7 disseminate 60:9 disseminating 86:20 dissemination 64:8 69:21 70:5 distinct 261:14 276:9 distract 42:19 distribute 195:20 226:3 310:15 distributed 149:22 273:1,6 308:15 321:18 distributing 106:9 distribution 52:16 52:19 74:3 77:22 78:3 96:21 97:10 126:3,6,11 128:12 138:12 140:8,12 140:13 145:10 148:19 149:7 173:6 175:5 195:18,22 204:15 296:11 309:8,14 311:2 321:3 334:13 342:22 348:17 359:1,2,18 359:18 360:18	distributions 149:5 distributors 195:15 diverse 35:13 81:18 98:17 196:9 286:18 diversion 258:11 diversity 71:13 78:12 divide 32:4 divided 9:2,3 division 1:25 2:1,2 2:4,5,8 13:19,22 14:3,14 15:1 19:19 57:6 63:21 70:7 149:3 235:22 divisions 112:4 docket 8:11,17 26:15 102:13 156:21 157:14 162:10,17,19 222:1 234:19 235:4 267:17 344:21 345:5 372:19 373:8,19 379:19 doctor 258:10 doctors 265:22 284:13 document 10:9,11 10:13 26:21 45:10 47:2,14 48:18,22 67:3 74:13 76:21 79:18 81:10 82:16 124:16 190:19 265:6,7,8,16,18 265:22 288:16 289:9,20 290:2 291:6,20 308:13 314:2 325:2 documentation 72:14 74:8 80:1 175:18 176:8 325:14 352:10 354:13 366:8 documents 42:1 43:5,10 45:9 47:1 48:16,21 68:16	125:6 159:13 200:19 203:12 206:8 289:15 291:17 320:7 324:13 374:7 doing 21:10 29:22 30:11 31:3,19 32:5 39:18 41:18 42:20 45:2 46:4 50:13 85:3 117:2 123:11 146:17,22 165:21 181:5 198:9 228:11 231:19 250:15 274:4,5,6 276:14 292:18 294:18 344:12 362:14 door 208:16 doors 7:1 dosage 349:13 dose 134:16 doses 351:14 355:6 355:12 dosing 61:13 134:13 dossiers 181:22 doubt 260:22 downloaded 66:11 downside 271:8 downstream 269:14 Dr 13:10 14:5,8,12 14:15,21 140:5,19 141:20 142:11,12 146:1 164:20 178:18 216:1,4 219:10 220:3 222:3,8,11 227:14 228:1,4 231:20 235:19 245:8 254:1 272:16 274:1 275:20 276:22 277:18 280:17 281:19,22 283:14 284:8,10 284:11 305:13 333:17 345:8	359:7 361:4 366:18 368:17,21 369:22 371:15 372:20 373:17 374:18 376:16 draft 25:1 95:10 184:13 262:15 dramatically 274:18 draw 189:8 drawing 252:19 drawn 39:9 drill 83:8 drills 111:13 drive 110:9 driven 41:20 158:17 driver 158:6,7 drivers 31:2 driving 133:6 144:12 drove 43:3 drug 1:1,17 3:9 6:11,12 15:16 16:4 18:19 22:11 25:6 32:16 35:2 44:1 47:1,15,15 58:3,6,22 60:4 61:1,6,11,13 64:12,13 65:9 66:15,16 67:21 68:3 71:16 72:5 72:10,13 73:1 74:6,19 76:10 86:22 91:13 92:3 92:9,10 96:10 100:5,10 103:17 104:2,10 108:8 110:14 126:4 129:22 134:9 135:22 136:17 137:6,16 138:1,10 157:2 169:1,12 171:2 173:6 175:15 176:16 177:20 179:1 181:12 190:9	194:20 200:2 201:3,8 204:8,11 204:14 205:2,17 205:19 206:1 210:17 214:7 215:15 224:13,14 238:13 239:7,10 241:6 243:13 249:21 250:3 251:14 252:9 256:11,13 261:6,9 261:10,16,17 263:4 267:2 287:2 287:12,13 292:5 306:20 307:1 309:3 310:15 311:10 314:9 321:1 324:9,12 327:3,8 334:5 335:15 338:2 341:11,13,15,22 345:9 348:17,18 349:20 350:2 351:20 352:15,18 353:16 354:1,6,8 354:9,12,15 356:4 359:19 360:1 362:6 363:6,6,6,7 363:10,10 365:7 drugs 1:22 14:10 15:18 16:7 17:10 18:21 25:9 32:9 35:4 44:4 46:14 52:19 69:16 71:4 85:20 94:15 97:13 98:18 104:7 129:10,15 131:6 133:14,21 134:1 135:17 136:9,11 136:13,14,21,22 137:3,7,9,11 138:7 139:12 150:9 151:7,10,22 152:8,9,11,17 154:7 155:9 171:16 173:21 175:7 198:1
---	--	--	--	---

211:17 212:5,22 214:15 215:11 226:4 228:19,22 252:1 267:4,12 285:7,10 288:21 288:22 289:14 290:16 295:10 296:9 311:14 319:9 321:4 327:19 331:19 333:1 335:7 342:8 342:22 343:10 344:6 346:18 347:16 353:4 358:21 359:5 365:12 366:4 drug's 16:1 22:8 67:4 92:16 134:9 144:2 drug-drug 347:9 drug-specific 173:8 175:15 DSUR 182:8 dual 97:16 242:9 due 106:6 119:18 176:2 297:14 308:8 335:19,20 346:7 351:16 353:16 duplication 323:14 duplicative 90:12 330:18,21 335:16 duration 116:16 duty 364:11 DVD 60:12 dying 256:7,9,10 256:13,14 262:2 dynamic 343:21 dysfunctions 203:4 D.C 197:20 D.O 2:4	200:7 205:18 210:8 225:10 244:6 278:15 303:10 335:10 336:8 343:13 359:14 early 82:1 93:9 94:3,13 95:10 177:13 214:18,21 258:4 270:7 377:17 379:11 ease 65:12 67:12 151:16 212:15,16 314:16 easier 19:3 38:2 49:10,21 69:12 85:15 159:8 300:7 342:17 373:15 easily 21:8 89:17 105:17 134:19 292:13 347:10 east 255:3 easy 43:5 eating 19:2 eats 279:17 echoing 146:21 edit 197:20 editorial 88:17 educate 51:21 52:5 57:15 58:8 64:10 240:15 270:5 educating 53:16 106:8 241:12 271:11 321:12 education 3:4 87:3 176:15 191:9 213:6 214:13 221:19 228:5 235:21 237:1 238:8,17 240:2,13 241:5,20 242:11 243:8 244:4,21 245:10,12,15,17 245:19,21 246:5 247:1,6,15 248:1 248:5,12,13,18 249:16 250:11,16	250:21 251:6,11 251:13,16,22 252:13,16,17 253:4,13,16 258:13,18 262:9 262:19 263:15,21 264:20,22 267:19 268:11 271:17 272:5 275:13 277:4,12,20,21 278:7 280:3,4,20 281:9 282:8,21 283:2,10,12 284:7 285:15 295:8 299:14 300:16 301:1 302:18 303:15,20 305:3 311:14,17 312:5,7 312:8,9 321:10 322:21 325:14 337:6 339:15 363:4 364:8 370:11 educational 57:21 58:12 65:5 106:2 106:16 111:11 117:15 176:22 213:22 240:7,11 240:20 242:2,4 244:3 247:11 248:19 271:2 275:19 education-based 219:13 educators 283:8 375:17 effect 101:15 137:4 181:10 217:10 316:13 321:14 effecting 320:20 effective 23:17 38:15 50:21 52:5 65:9 92:18 97:7 105:5 111:19 112:18 131:10 144:22 145:17 147:11 160:2	171:15 178:2 188:16 189:14 194:10 215:14 217:3 220:5,5,16 221:3 230:12 238:18 239:13 257:12 263:13 264:18 265:3 268:2 277:5 284:18 285:18 297:16 304:14 309:17 316:3 322:2 327:17 329:6 331:2,19 effectively 95:16 96:13 142:10 188:19 189:5 199:3 227:2,9 237:20 294:4,9 299:11 366:11 effectiveness 21:11 85:11 93:19 99:19 101:12 108:17 142:21 143:20 146:7,15 175:6 185:21 214:19 216:16 220:15,22 221:8 248:22 252:14,15,18,21 277:12 288:20 303:3,8 315:1,16 315:21 321:17 355:21 effects 51:7 112:8 114:6 133:21 134:9 151:19 300:13 316:22 efficacious 92:20 efficacy 103:20 329:8 efficiencies 172:3 298:9 efficiency 16:14 97:5 267:20 313:20 efficient 48:21 52:5 89:1 97:7 189:14	194:9 267:21 294:12 323:8 efficiently 95:16 142:10 233:14 373:13 effort 29:11 138:21 208:14 229:14 300:16 304:18 317:3 323:12 325:15 efforts 26:2 49:4 84:17 85:6,10 88:8 90:20 93:2 93:11 95:17 97:19 98:7 142:18 143:5 143:8,21 150:8 188:15 193:8,8 216:7 217:7 298:4 306:7 315:19,20 317:15 318:16 328:3 EHR 121:20 EHRs 121:17 128:10 eight 65:10 83:8 134:3 189:2 eighteen 66:6 eighth 105:18 either 8:14 76:21 78:8 79:18 122:2 139:19 141:13 154:4 155:16,19 167:11 169:6 181:20 204:18 218:7,12 227:5 251:4 255:16 274:4,11 290:11 335:22 360:4 362:6 363:22 elaborate 24:21 140:8 155:7 366:16 Elaine 1:24 14:19 222:10 223:17 electronic 47:4 48:5 50:4 59:14 60:11 76:17,18
--	---	---	--	---

121:14 122:3,21 123:10 127:1 140:21 155:19 172:9,10 174:19 194:21,21 197:6 223:2 244:12 276:13 291:19 298:19 304:2,5 313:21 325:12 327:13 329:21 331:12 332:6 338:12 367:21 372:2,6 electronically 291:7 304:1 elegance 116:2 element 142:6 190:11 191:22 193:10 194:17 196:4 199:14 202:6 206:16 303:7 elements 42:14 65:17 86:3,9,10 86:14 89:10,12 90:2 93:12 95:19 96:4 98:6 103:12 108:4 143:7 144:7 145:9,18,21 152:15 174:1 175:11 189:11,15 190:2 196:17 199:22 203:9,18 204:4,9 205:10 206:3,10,12,15,18 210:11,16 218:20 265:2 268:16 293:15 302:10 310:21 313:17 315:13 322:1 323:6,11 363:17 365:19 elevate 288:14 eligibility 223:7 eligible 309:6 eliminate 15:18 90:12 98:13	114:14 325:15 327:6 eliminating 369:4 email 90:17 291:7 emails 59:9 embed 192:1 embedded 194:10 197:2 241:9 embedding 189:18 embrace 113:21 embraced 302:14 emergency 354:17 emerging 251:7 Emmett 2:13 4:14 91:6,7 142:13 144:5 147:5 152:6 emperor's 264:6 emphasis 124:9 134:7 emphasize 134:14 emphasized 184:7 emphasizes 354:1 employ 25:13 170:15 287:17 employees 287:18 empower 100:11 EMR 123:14 EMRs 88:4 enable 111:12 154:6 327:7 enables 16:5 118:18 350:1 enabling 61:2 115:1,21 117:15 247:3 encounter 75:15 encourage 10:12 12:15 27:1,5 45:20 56:2 66:17 69:21 82:17 97:6 162:7,16 213:19 235:3 244:10 254:7 265:8 278:11 323:4 345:4 encouraged 214:13 228:13 308:18	338:19 encourages 87:21 241:13 317:12 325:11 326:16 encouraging 321:2 endorsement 322:5 enemy 250:6 energies 344:9 enforceable 130:21 enforcement 138:18 309:4 engage 26:3 192:5 270:20 328:3 engaged 102:9 engagement 26:8 94:14 101:2 engagements 196:5 engaging 271:16 320:9 engine 17:2 Engineering 109:3 engines 111:9 England 246:11 enhance 175:6 180:18 288:21 318:17 enhanced 23:2 290:17 enhancements 105:4 213:3 enhancing 84:15 97:16 enjoy 164:4 380:3 enjoying 255:19 enroll 61:17 67:19 73:12,15 75:8 294:19 324:19 347:20 353:22 enrolled 68:2 72:18 141:11 233:11 324:20 370:10 enrolling 72:9 enrollment 44:11 52:2 58:18 61:16 61:22 62:17 63:3 65:1 67:17,21 68:3 80:20 88:20	90:12 105:12,16 106:17 172:5 174:3,4 217:12,13 268:15 293:19 294:15 314:18 315:8 353:20 356:17 enrollments 44:13 ensure 16:1 22:10 24:10 25:5 57:16 64:12 67:22 73:14 95:15 99:14 100:5 101:5 103:17 105:5,17 136:4 137:15 144:21 146:13 169:3 178:1 218:10,13 238:17 241:1 248:21 249:13 258:8,10 267:10 267:11,15 271:17 294:10 295:13 296:3 307:22 311:15 316:1 319:5,8 320:21 322:1 325:22 327:17 329:5,16 329:17,21 330:19 335:14 337:4 346:17 356:3 365:20 368:4 369:18 ensures 248:18 ensuring 27:13 105:1 135:1 176:8 212:13 218:5,11 218:21 271:19 298:10 325:9 331:4 entailed 224:16 entered 47:16 107:21 123:1 enterprise 245:15 245:17 251:6 275:13 entire 35:11 43:13 130:10 149:19	179:10,19 196:19 255:3 299:9 311:10 336:21 369:2 entirely 158:17 191:11 359:17 entirety 122:14 entities 139:3 151:17 153:4 312:10 331:4 entity 148:20 149:1 330:12 entry 122:21 155:20 environment 106:6 106:21 176:2 222:20 374:12 environments 269:8 envision 224:5 226:6 279:10 374:9 epidemic 239:9 240:16 254:12,13 254:17 255:10 256:6,18 257:2 266:11 epidemiology 64:1 94:16 180:7 274:22 ePrescribing 48:6 172:13 174:8 175:19 223:1 292:20 298:19 313:22 327:11 ePrescriptions 108:8 equally 315:20 era 214:5 error 2:6 13:12 321:5 errors 317:11 ER/LA 240:12 254:9 286:8 ESAs 122:6,12,18 123:1 especially 52:6
---	--	---	--	--

78:1 100:19 127:9 133:20 155:1 165:4 281:22 289:13 297:21 315:7 353:12 essential 68:20 129:13 195:16 206:3 210:15 218:15 297:15 302:16 304:19 373:14 essentially 219:7 233:18 establish 73:16 214:15 established 24:7 39:12 52:18 106:10 149:21 179:5 188:18 307:10 321:20 322:18 establishing 38:14 93:14 124:9 133:17 172:6,7 293:5 et 90:17 104:11 277:8 361:10 ETASU 42:14 95:22 96:2 97:9 97:13,19 98:6 126:5 142:19 143:7 145:9,17,21 148:18 199:13 201:4 202:2 204:16 205:22 206:4,5,13 210:15 211:18 214:10 293:15 294:3 ETASUs 65:17 186:20 190:3 323:17 333:1 ethical 354:10 ETSU 95:20 Europe 181:5,11 181:19 182:2 evaluate 93:19 97:7 100:8 111:5	113:16 127:2 132:3,14 138:16 142:22 146:3 147:10 305:7 314:22 315:1,20 330:4 331:1 evaluated 299:4 315:5 evaluating 1:3 85:11 95:9 102:1 105:4 146:15 166:8 296:6 365:16 evaluation 1:3 6:7 6:12 21:16 24:15 24:17 25:21 26:19 55:4 56:15 91:12 92:6 93:17 95:5 99:1 110:22 111:20 113:1 114:2 120:17 121:6 126:21 127:4 128:14 129:21 132:4 135:4 137:21 178:12 179:22 180:15,21 182:15 236:10 248:21 280:21 287:8 334:11 377:8,14 377:15 evaluations 18:3 333:1 event 61:5 76:15 187:12 229:10 events 76:14 146:19 212:8 271:21 303:1 eventually 308:5 everybody 6:19 151:1 163:2 237:6 378:12 everyday 110:13 115:2 evidence 55:9 72:15 99:14 131:9 132:12 238:20	253:7,7 257:11 281:3 284:19,20 285:11,12,19 365:22 366:1 evidence-based 39:5 85:10 99:18 185:18 238:8 243:10 319:1,17 evolve 331:10 332:1 evolves 153:16 evolving 16:20 21:6 31:7 35:17 55:15 128:5 138:21 251:7 288:3 exact 42:11 48:17 262:13 exactly 30:15 32:2 33:19 38:7,20 39:16 41:18 42:5 43:14 47:6 49:14 53:14 155:18 181:12 185:15 187:11 226:7 229:8 266:7 359:3 exaggerated 257:20 examination 267:16 examine 267:7 299:18 examined 331:8 examining 329:7 example 42:8 43:8 43:18 44:11 51:20 60:18 61:3 69:13 71:1 73:19 76:1 77:3 79:15 86:8 87:21 88:18,20 90:7 96:1,15 100:9 111:7 123:22 125:1 126:10 135:15 143:14 149:11 158:8 166:12 172:20 176:1 182:7 193:22	195:14,19 200:8 203:6 210:5 213:11 214:11 215:6 217:13 218:1 220:11 224:18 226:4 227:7 246:17 255:16 259:11 276:10 284:14 294:2 296:10 302:14 309:12 314:5 315:2 320:5 336:22 340:11 347:17 348:11 351:6 352:3,17 357:16 373:18 examples 19:21 60:5 68:11 71:8 79:15 80:8 122:5 162:10 234:22 235:3 356:6 exceed 16:8 exceeding 242:15 excel 177:1 excellent 129:18 exception 355:10 375:3 exceptions 354:22 exciting 144:14 exclusively 273:3 exclusivity 205:8 205:13 210:3 excuse 357:4 execution 105:6 313:14 Executive 1:20 14:6 188:7 exerting 196:8 exhaustive 22:15 exist 40:7 134:9 153:20 212:13 243:12 269:15 307:12 313:18 325:16 347:2 348:1 existence 244:16 existing 16:20	21:10 31:7 40:4 41:15 73:17,20 76:7,16 77:22 79:17 80:6,12 87:17 88:3 103:7 107:11 108:2 116:10 134:22 135:8,15 150:12 152:9,10,17 153:3 165:5,17 175:3 178:9 183:6 215:2 267:21 288:3 294:8 298:15,17 306:17 308:14 313:13,19 327:15 328:17 333:6 343:16 356:1 375:6 expand 268:3 273:20 376:8,15 expanded 136:21 175:15 315:11 319:8 expanding 214:6 expect 9:5 106:3 expectation 224:17 expectations 7:9 82:9 198:19 199:7 209:9 expected 43:7 60:3 204:9 expensive 245:1 299:1 experience 10:14 19:6 21:3 36:19 75:17 81:13,14 86:19 95:8 108:10 133:13 171:1 175:9 189:9,21 193:11,12,14,15 194:5,16 211:21 239:18 244:4 246:6 293:10 308:7 309:16 360:17 373:20 experienced 255:7 334:4 360:14
--	--	---	---	--

experiences 109:20 110:3 194:15 242:5 300:13 324:1 377:9 experiencing 302:4 experiment 194:6 experimenting 128:1 255:18 expert 29:8 50:20 51:12 275:5 expertise 193:9 273:11 297:15 experts 40:17 54:18 185:7 244:1 263:1,3 295:9 312:12 339:3 365:7 expired 200:3 explain 59:21 97:10 204:17 217:16 229:22 332:2 356:5 explained 200:12 203:16 228:17 229:2 explaining 229:4 explanation 207:14 explicitly 190:18 351:7 exploration 87:16 explore 51:11 88:2 286:7 exploring 63:9 expose 285:7 exposed 270:20 exposure 101:5 218:3 219:17 Express 2:24 211:4 211:7,8,19 213:9 expressing 262:17 extend 242:4 extended 238:18 240:8 308:19 extended-release 284:21 extending 224:8 extensive 104:18	223:15 363:2 extensively 375:11 extent 108:16 109:10 134:22 135:9 147:6 152:12 157:12 186:2 235:13 298:17 369:3 external 40:16 193:14 extra 82:4 158:18 239:3 278:14 extreme 136:5 extremely 244:22 261:18 295:12 eyes 342:6 E2D 182:11 E2E 181:16 182:7 182:18 186:19 <hr/> F <hr/> fabric 253:3 face 15:13 20:2 22:14 23:10 81:11 365:13 faced 23:18 faces 71:12 facets 319:22 321:8 face-to-face 302:9 307:13 309:17 facilitate 19:22 48:20 66:4 78:8 92:19 107:10 125:19 174:5 290:18 291:15 292:18 facilitated 142:3 facilitating 172:1 247:2 facilities 269:5 345:21 372:10 facility 73:13 372:14 facing 107:5 177:11 254:11 fact 9:20 41:20 42:20 59:10 95:7	100:15 133:18 180:13 228:18 229:5 232:19 268:16 285:12 330:17 332:11 364:9 factor 114:13 154:15 178:6 214:9 factors 25:3,4 61:5 167:2 185:15 241:15 246:21 267:13 failing 130:3 204:18 fails 201:19 failure 51:7 112:8 114:5,15,18 115:8 116:5 210:21 failures 23:1 74:17 111:6 114:13 117:9,11 203:15 fall 51:12 200:9 202:18 241:18 false 261:12 familiar 111:6 351:2 373:6 familiarize 10:13 Families 2:17 129:1,5 131:2 family 3:2 235:18 235:22 236:1,5,5 239:11 240:14,15 241:12 242:8 243:3 277:22 279:22 far 142:9 179:9 224:7 257:16 263:20 276:5 277:7 344:9 359:3 375:14 faster 294:19 favor 215:4 favorable 120:7 269:21 favorite 37:4 fax 90:17 107:9	233:22 FDA 1:12,15 4:18 4:25 5:7,19 6:14 9:8 10:3,4,6 11:8 11:9,10,15 12:1,6 12:20,22 13:8 15:5,20 16:3,5 17:1,2,21 19:18 21:18 25:2,8,16 35:14 46:19 47:14 65:7,15 68:9 77:20 81:20 83:5 84:17 86:8,12 87:4,8,21 88:2,15 89:14 90:7,20 92:22 93:7 94:2,4 94:5,21 97:6 99:7 99:9,13,21 101:11 101:21 102:9,22 104:6 106:5 107:12 112:4,5 114:1 129:10,19 130:9,20 132:2,19 134:20 135:7,14 136:15 137:14 138:15 139:18 144:11 147:15 148:5 157:8 162:18,21,22 165:7 166:10 168:13 169:1,12 169:19 177:6,19 182:6,12,17 184:13 185:12 188:14,17 189:1 189:13 190:8 192:9,17 193:11 194:12 196:12,18 197:9,20,22 198:6 198:7 199:5,19 200:11,14 201:14 201:15 203:1,5,19 204:6,19 205:1,13 205:16 206:15 207:8,12,19 209:6 210:9,10 213:18 214:17 215:21	223:20 224:5 226:17,18 228:5 236:7,12,21 237:16 239:6 240:4,8,20 241:9 242:15 243:5 245:18 251:18 252:7 258:2,6,13 259:3,8 260:2,6 260:13,14,16,18 260:22 262:7,10 262:17 263:8 265:7,20 267:9 271:18 272:13 288:1,12,14 290:11,12 291:16 292:3 293:4,9,13 296:6 297:18 299:12,17 302:7 304:12,16,21 305:5 306:4 310:21 311:5 313:18 316:1,7 317:8,12,21 319:7 320:4,5 321:11,22 322:4,7,9 323:4 323:22 325:11 326:2,16 327:14 328:13,17 332:19 332:21 333:11 344:10 345:16 357:2,4 358:16 378:9,14 379:10 FDAAA 135:18 137:13 199:12 203:6,19 204:6 FDAs 257:21 FDASIA 136:18 FDA's 85:6,14 88:8 91:14 92:6 94:15 96:16 97:1 98:7 104:15 105:20 130:5 132:11 134:12 188:10,19 202:10 251:19 288:9 297:22 300:15 306:7
---	--	--	---	--

308:22 314:13 328:3 374:4 FDA-approved 308:13 FDA-mandated 171:2 FDA-provided 290:9 FDA-sponsored 94:9 feasibility 88:7 feasible 112:17 343:8 feature 52:10 71:14 features 22:4 75:20 141:9 154:4 February 105:9 257:22 federal 9:12 10:19 26:11 34:6 51:16 57:1 226:5 227:5 227:6 346:4 376:21 federally 119:9 federally-required 332:22 feedback 9:13 15:12 17:15 18:5 20:16,20 21:1 27:9 28:6,8 39:12 40:16 50:20 54:5 54:13 56:6 57:11 62:8 64:5 68:10 71:2 78:14 79:13 82:18 141:4 142:8 157:14 177:21 187:11,13 233:13 233:16,17 299:5 317:13 373:11 feeding 229:6 feel 29:12 162:10 183:21 295:10 364:5,14,17 fees 16:18 fentanyl 173:16 fetotoxicity 218:1 Fetterman 2:14	4:15 108:21,22 109:1 152:18 161:16 fetus 218:4 fewer 118:2 300:13 fibromyalgia 264:9 fidelity 101:2 field 263:5 fifth 196:4 figure 34:14 217:2 figuring 337:21 fill 43:22 119:16 170:14 176:4 287:19 349:4,18 filled 223:8 289:7 filling 18:16 177:3 313:11 347:12 fills 211:19 final 55:19 71:16 132:8 260:8 262:11,12 finalized 87:3 181:18 finalizing 20:6 finally 16:17 20:11 35:15 41:3 52:11 54:2 57:12 73:6 75:4 80:3,19 93:18 99:17 115:17 118:15 128:17 190:7 196:4 262:10 296:6 330:1 332:13 357:4,14 Finance 259:13 financial 110:1 249:18 331:7 find 8:21 10:10 17:4 32:4,22 43:6 43:14 59:2 63:1 74:19 195:7 232:8 324:6 325:5 357:1 357:7 finding 41:8 237:22 255:17 374:6 findings 26:18 31:11 41:8 50:16	54:9 215:1 fine 375:12 finish 265:17 finished 8:3 12:17 28:22 82:1 firm 198:12 firms 310:14 first 6:16 10:14 18:19 32:6 34:16 40:2 41:15 71:22 78:18 82:22 83:15 93:7,22 104:20 121:2,8 142:17 143:1,2 152:19 155:16 166:1 167:9 169:18 171:8 172:4 183:15 190:12 202:14 207:8 213:5 226:15 228:16,18 230:3 232:5 235:16 236:22 237:7 249:10 258:1 259:2 265:1 306:3 362:20 371:16 377:9 fit 19:16 28:12 176:1 179:10 186:15 222:21 223:16 377:1 fits 37:15 55:21 135:21 139:3 331:18 five 21:4 23:19 189:11,15,22 194:7 286:4 fix 27:22 fixing 115:17 flaws 130:16 flexibility 19:12 79:8 80:7 85:18 90:15 99:4 104:10 221:9 300:4 flexible 55:20 87:12 89:8 112:17 Florida 345:21	FMEA 112:1,4,6 113:6,12 114:4 116:8 117:4 118:1 118:11,16 focal 192:7 focus 17:21 34:4 53:1 66:1 70:17 97:21 98:5 116:12 130:12 136:8 139:2 145:20 146:12 171:7,16 172:11 176:11 193:8 197:1 216:6 217:22 219:13 253:6 267:18 268:7 288:6 327:5 336:12 337:1 338:5 focused 24:14 29:6 96:3 105:1 118:2 130:9 218:16 219:6 344:18 367:7 focuses 40:18,19 51:15 123:18 185:8 241:11 focusing 70:19 150:8 217:6 folded 302:18 folks 198:9 follow 54:12 68:4 124:7 219:10 242:22 313:1 364:17 followed 48:20 103:9 263:14 296:4 301:6 378:12 following 64:15 72:4 86:5 93:5 234:5 346:3 follows 53:22 284:7 follow-up 113:19 233:1,4 355:16 font 90:2 food 1:1 16:4 112:3 135:16 136:17	249:21 250:3 force 133:7 179:4 forced 338:19 forefront 318:16 foregoing 82:19 286:11 380:6 foremost 228:17 forgot 115:14 form 44:12,15 60:11 68:1,5 69:8 69:15 80:5,20 88:19 90:15,17 105:19 111:10 149:4 186:13 216:12 233:21 formal 109:19 243:10 244:2 formally 107:15 format 9:6 10:2 42:1 47:9 48:17 48:19 49:20 65:11 66:8,19 67:11 68:4 186:13 221:2 244:14 247:12 283:11 288:17 290:21 292:12 formats 243:22 289:7 formatted 69:12 former 178:21,21 263:4 forms 17:16 36:3 43:21 44:2,5,9 58:18 61:16,18,22 62:6,17,18 64:21 65:1,1 67:1,3,8,17 67:21 68:3 69:11 80:20 90:12 105:12,16 106:2 172:5 217:13 356:16 372:6 formulary 154:8 forth 223:8 240:20 forum 9:10 159:16 160:16,19 161:6 161:16 162:5 322:3
--	---	--	--	---

forward 20:22 26:9 63:17 70:3 81:5 95:3,9 99:12 102:8 108:13 144:14 161:13 169:2 178:10 188:13 197:9 253:1 255:1 298:8 305:4 333:11 334:10,16 337:16 377:11	Friday 324:8 380:7 Frieden 247:16 friendly 171:19 Frommer 2:23 197:16,19 front 146:5 148:8 177:10 244:7 front-end 315:18 front-line 299:5 324:2 fruition 370:8 frustrated 341:8 frustration 340:10 353:19 357:9 FTC 207:20 fulfill 84:17 339:18 fulfillment 108:9 full 286:3 fully 147:19 239:21 338:12 full-time 268:22 function 196:15 238:7 functions 44:8,10 fundamental 37:14 100:16 fundamentals 113:6 funding 238:20 379:7 funds 249:8 further 17:18 51:11 59:2 63:1 65:4 78:14 79:7 87:14 102:10 106:5 108:13 125:9 132:13 139:1 147:12 169:20 193:21 252:8 268:4 270:4 270:7 290:17 291:22 299:17 301:9 305:3 316:17 328:2 furthermore 87:10 312:9 368:1 future 13:7 49:4	105:4 107:10 153:1 174:15 178:13 208:6 241:22 267:17 281:6 323:9 326:2 331:20 334:17 futures 137:21 F.A.A.F.P 3:2 5:4 F.A.P.M 2:21 4:22 <hr/> G <hr/> gain 88:7 166:16 208:21 335:17 337:22 gained 170:22 189:21 193:11 gap 243:11 248:21 274:2,12,20 282:12 283:21 284:4 285:1,9 gaps 32:20 33:1,4,5 118:1 177:3 243:11 247:7,9 251:17,18,20 273:18,21 275:8 275:17 276:6,19 280:10,12,19 281:8 282:9 283:9 283:14 garner 244:13 garnered 276:13 Gary 2:6,19 4:21 13:11 25:20 29:15 140:4 164:17,19 169:15 272:15 371:5 377:8,10 gather 188:11 gathering 17:19 gauge 302:13 gears 34:11 general 2:11,19 4:12,19 46:13 47:20 72:1 83:2 83:20 86:13 89:5 129:17 149:11 164:10,12 183:22 191:8 215:5	256:12 277:11 294:1 316:15 332:21 generalizable 192:18 323:9 generally 360:14 generate 180:2 generated 118:1 generic 137:1,6,9 138:1 199:16 202:13,21 203:21 204:14 206:1,14 224:14 generics 138:16 207:4,10 208:16 209:10 224:21 225:13 genetic 283:2 genetics 283:2 genomics 283:1 gentleman 343:13 gentlemen 164:15 geographic 276:18 326:2 getting 40:16 149:10 158:20 187:11 202:7 217:5 272:22 285:5,16 338:2 358:20 gift 20:12 164:6 give 9:8 15:5 42:4 48:2 82:18 168:16 260:22 277:15,18 373:12 375:1,9 given 12:5 52:6,13 67:13 68:6 100:3 104:10 106:7 117:1 118:4 130:10 215:15 289:3 310:10 313:3 315:4,21 316:9 340:20 341:16 gives 137:13 141:4 giving 15:10 82:2 203:6	gleaned 241:18 Glen 236:14 global 146:18 181:8,14 globally 278:20 279:6 glorious 164:5 go 7:3,4,7 12:14,16 17:1 41:17 56:19 110:10 113:16 115:8,17 120:22 123:14 125:2 156:3 158:20 165:6 187:4 196:14 201:12 209:18 218:21 220:13 230:19 231:3 252:10 254:22 265:13 266:6 278:12 319:21 324:12,13 339:7 340:1,21 349:17 355:8 359:7,14 361:12 363:1,3 374:6 377:16 goal 31:10 53:5 98:9 104:1 121:8 125:21 126:20 127:6 130:11 146:10,11 148:6 170:6 173:7 188:15 189:16 190:13,14,18,20 191:2 193:2 209:8 216:14 217:15,21 218:3,16 267:7 271:18 288:4 goals 23:13 24:1 26:6 37:22 99:6 100:1 103:18 120:20 121:1 128:8 130:5 146:14 189:19 230:9 240:7,20 288:9 307:19 316:12 317:5
--	---	--	--	--

322:12,17 376:1 goes 46:18 49:9 123:20 125:9 162:2 201:11 203:7 209:5 221:5 232:11,12 234:9 236:19 244:6 251:13 379:4 going 6:13 7:6,16 8:12 11:7,16 18:4 25:15 29:10,16,21 30:13 32:10,18 34:10,20 37:16 41:14,17 42:22 46:4 50:6,7,19,22 51:11 53:13 54:6 55:21 56:18,19 57:7 64:1 70:8,10 70:13,16,18 71:1 71:22 72:8 74:18 74:21 81:11 82:7 83:1,3 93:21 108:10 123:10 124:2 144:20 155:6 156:14,15 164:12,17 165:6 178:19 185:9,10 186:20,21 187:2 187:20 198:16 204:3 208:8 209:17 216:2 220:14 221:8,17 224:22 225:12 228:22 230:1,9,21 253:1 254:8 262:18 265:17 266:3,10,21 267:4 274:9 277:18 286:14,16,19,22 321:7 322:17 332:2 378:3 Goldman 2:21,22 4:22 178:17,18 220:3 222:3,8 227:14 228:1,4 231:20 good 6:5,7 7:20	13:10,17,20 14:1 14:8,12,15,18,21 34:13 38:19 57:4 63:19 70:6 83:19 91:7 102:18 108:22 110:13 129:2 131:18 160:19 164:20 169:17 185:3 188:6 197:17 198:10 211:5 231:22 235:19 263:11 283:13 285:7 287:4 294:2 297:5 305:13 318:5 328:9 345:8 359:21 368:14 378:13 gotten 54:4,14 government 272:20 297:7 grade 105:18 130:4 granted 16:3 137:1 207:8 graph 257:7 graphics 66:9 grappling 22:17 grassroots 259:19 260:1 gratified 297:21 great 1:12 121:12 122:1 130:15 131:2 138:21 167:9 187:8 226:21 234:20 251:19 347:3 greater 32:21 49:7 87:16 134:4,7 148:5 166:6 186:5 186:16 194:22 213:7 267:20 307:14 310:1 greatest 109:9,10 186:2 254:19 298:17 greatly 303:12 308:16	green 12:9 256:18 257:10 264:22 266:6,9 Greenberger 2:17 4:17 131:16,18,20 150:5,20 151:5 grocery 269:6 group 23:6 24:11 24:13,15 25:1,19 25:21 29:16 30:5 30:10 39:18 117:17 119:12 160:17 161:20 172:12 193:8 195:13,17 207:7 225:13 229:15 242:21 251:3 252:6 326:20 339:6 366:22 368:12,14 grouped 172:17 groups 15:9,14 22:17 24:9,22 26:9 29:2 30:3 183:5 196:9 228:6 229:20 326:2 370:13 grow 364:21 growing 240:16 241:5 326:13 375:15 grows 101:12 guess 166:19 220:4 222:15 361:20 369:8,13,22 guidance 24:12 25:2,7 41:11 54:10 87:4 97:2 107:12 168:14 181:18 184:14 203:20 204:7 206:9 209:7 320:7 guidances 114:3 249:22 guide 61:9 65:19 75:2 190:10 200:17 301:12	328:18 guideline 155:16 277:15 guidelines 154:9 158:10 241:1 guides 60:6 61:14 64:16,17 65:4,22 289:5 308:10 320:8 guiding 118:12 gut 260:6 <hr/> H <hr/> Ha 3:12 5:12 305:11,13,19 332:3 habits 110:11 HACCP 112:3 113:2 half 82:2,3 130:1,1 144:6,8 198:4 268:17 286:9 hallmark 103:3 halls 7:12 Hampshire 1:13 handle 365:8 366:10 handled 233:14 366:11 handling 300:14 hands-on 243:15 hand-written 313:21 happen 8:3 34:4 155:21 156:16 happened 237:7 happening 237:9 375:8,10,11 happens 43:19 140:13 181:9,10 183:19 209:19 254:22 281:12 341:13 happy 152:4 296:21 344:20 368:18 hard 84:16 139:11	219:9 239:3 harm 130:15 135:22 136:4 263:11 harmed 261:7,16 harming 263:19 harmonization 106:11 harmonized 105:10 harmonizing 317:17 harnessing 190:7 hat 9:7 12:20 15:5 275:21 hats 276:4 Haug 2:23 197:16 197:19 hazard 112:16 117:9,11 hazards 117:6,13 head 102:19 164:22 374:15 headache 264:9 heads 44:22 health 2:2,3,8,18 3:20 13:18,21 14:2 46:16 47:4 48:3,5 50:5,5 57:5 63:20 76:17,19 77:6 85:4 100:12 109:22 119:6,7,7 119:10,11,15 121:14 123:22 124:3 126:8,12,16 127:1,2,8,21 128:2,13,18 129:6 131:4,17,21 133:7 134:4 136:6 140:15 149:17 159:10 161:12 183:13 190:13 194:6,22 196:13 211:11 213:8,10 223:1,2 237:15 238:3 239:8 243:18 244:12 247:18,19 263:6,6
---	--	--	--	--

267:10 271:8	128:4 152:15	272:19 275:10	241:5	home 239:1 309:19
288:7 289:17	154:5,14 169:9	279:3 323:7 356:5	heroin 256:10	312:17 340:16
297:4 298:19	177:22 183:7	358:22 361:6	hesitation 208:19	349:21 351:18
303:9 305:3	184:22 186:6	362:11 365:10	heterogeneous	354:15 355:12
316:14 318:13	187:3,19 188:1,22	368:21	275:9	homogeneous
323:1 326:6,14,18	189:19 191:17	hearing 7:22 26:10	HFMEA 113:8	251:3 252:5
326:20 327:13	192:2,11 194:11	63:17 81:5 104:6	114:10	honest 187:1
330:5 332:6	195:1,14 196:20	161:13 188:11	HHS 129:17,19	honestly 273:13
333:15 334:1,8,14	197:3,12 227:3,8	369:8 377:4,15	Hi 13:14 83:19	honor 245:9
335:7,14 337:15	228:6,14 229:19	held 19:17 138:11	142:12 225:20	honored 179:4
338:7,14 339:19	230:2,3 246:15	378:11,22	235:19 276:22	hooked 255:19
341:18 342:20,21	247:22 267:8,21	Hello 14:5 197:17	high 88:8 117:9,11	hope 28:22 82:15
343:19 344:19	268:4 269:7,15	266:16 333:17	117:12 180:2	85:3 90:21 118:9
345:1,11,19 347:1	271:12,15,16	help 9:16 19:22	258:3 335:1	132:7 133:4 135:1
347:2,14,18,22	272:21 288:4,6	22:5 28:16,17	376:13	hoped 182:17
348:12 358:9	294:3 299:9 304:8	31:13 32:14 33:5	higher 131:6 173:2	308:11
359:10 366:16	315:2,3 323:15	33:7 40:11 41:1	361:13 365:12	hopeful 258:12
367:9,12,20 369:2	330:2,8 342:5	46:1,21 48:16	highlight 10:8	hopefully 29:11
370:3,14,20	346:8,19 358:4	50:11 53:3,8,9	78:15 81:10 193:1	81:15 82:4 164:4
healthcare 9:17	361:20 363:8,9,16	56:21 64:12 70:4	289:22	164:7 235:10,14
16:12,15,20 17:20	369:14 376:2	87:14 91:16 92:19	highlighted 17:18	243:5 271:21
18:8,10,13,15	healthier 84:5	98:13 105:14	19:11 21:14 81:16	hopes 258:4
21:10 22:5 23:3	HealthSystem	157:3 160:19	143:16	hoping 322:10
24:4 31:8 32:20	344:16 366:21	169:3 197:1 208:4	highlights 26:2	horizon 271:13
33:20 35:6 43:7	health-base 246:7	214:16 264:13	106:19	hospital 72:12 77:5
47:13,19 48:2,9	Health-System	271:17 281:11	highly 285:3,6	77:6,11,12 119:9
48:11 49:15 51:22	3:16 318:8	296:17 324:13	301:20 303:2	161:8 227:2
54:21 55:12 57:15	hear 12:2 20:14,19	325:7 332:8 333:3	309:2 336:5	324:16 326:18
57:16 58:1,8,21	21:18 28:6,20	365:20,21 366:2	343:19 361:9,10	341:14 350:5,17
59:4,8 60:2 62:2	81:5 91:5 102:16	368:18 370:4	high-priority 117:5	352:13 355:9
63:11,13 64:19	108:20 118:22	373:12	high-risk 121:4	367:20 369:21
65:14,18 66:10,14	178:16 188:5	helped 157:6 261:5	126:1 136:21	374:17
66:22 67:14 68:6	231:16 245:6	261:15	155:9,15 319:19	hospitals 71:6
68:13 72:11 76:5	266:14 297:2	helpful 18:11,12	hinders 308:5	121:16 192:11
77:15,17 80:6	314:6 328:7	62:13 63:2,11	hired 370:4	195:6,15 269:4,6
84:20 85:21 87:18	344:13 379:20	108:15 157:15	Hispanic 120:3	318:13 326:6
87:20 88:3,12	heard 8:8 17:22	216:16 232:16	history 118:12	334:1,14 342:20
89:22 91:17 95:2	18:7 19:13,20	301:10 325:5	174:20	346:2,9 354:7,21
97:20 98:11 101:9	27:4 28:10 36:15	350:17 351:21	hit 279:12	369:1 370:5
101:14,20 102:3	37:1,9 38:10,11	352:7 356:13	HL7 46:16	hosting 328:14
102:12 109:2	52:20 56:11 62:9	357:14 368:12	HMOs 192:12	hour 82:2,3 286:9
111:3 112:21	62:10,16,19 68:8	373:5,9	hoax 264:7	302:4
115:9,14,20,22	78:13,18 79:3	helping 26:6 49:12	hoc 109:13 117:2	hours 246:1 278:20
118:14 119:8	121:10,20 143:3	68:14 142:8 159:6	holder 202:1	337:18,20
120:8,11,15,22	150:9 185:1	263:21 319:5	holding 31:8 51:12	House 239:6
121:7,13 123:13	187:10,12 226:22	helps 48:14 124:17	236:7	housekeeping 6:16
125:17 127:7	234:20 235:11	124:17 155:17	holistic 92:3 100:22	hubs 214:16

huge 35:3	39:7 76:12 224:10	75:20 79:9 95:17	impractical 171:12	incidence 274:13
human 114:13,14	342:4	117:17 142:1	improve 16:13	274:16
302:11	immediate 153:10	158:10 296:3	38:10 46:4 52:8	include 10:3 17:11
hundred 211:10	173:16 350:3	331:3 343:8	56:14,17 70:4	46:22 59:1 60:5
hundreds 212:21	immediately 153:8	344:15	85:2,16 87:14	61:19 64:15,17
Hunt 1:19 14:5,6	impact 19:14 35:3	implementing 21:4	88:19,22 103:5	65:21 66:16 69:8
378:18	75:18 78:7 120:17	23:19 35:11 97:11	121:2,5,8 125:19	74:2,10 89:13,15
hyperlink 239:2	132:15 133:3	98:9 106:9 108:11	126:13,16,20	90:8 93:14 95:19
hypothesis 282:5	134:15 135:21	138:11 171:1	127:4 129:21	99:6 101:1 103:12
<hr/>				
I	136:11 137:4	177:10,17 226:6	144:15 196:20	128:15 130:2
idea 113:2 150:14	212:19 242:5,13	329:22	197:12 199:4	175:14 176:13
159:3 185:2 210:7	266:10 278:8	implications 77:8	212:16 242:5	185:5 189:16
231:17 264:2	303:3 306:8	77:16 343:6	288:13,20 291:1	195:12 267:1
280:9 284:22	307:14 321:5	imply 277:2	291:22 293:5	272:2 293:14,17
367:11	329:11 330:6	importance 17:18	300:16 303:8	318:11 322:13,16
Ideally 307:8	334:11 337:1	64:7 84:16 105:5	304:7 305:3	325:19 347:4
ideas 81:6 107:15	340:9 342:9,10	137:8 138:22	318:16 322:15	371:21
367:10	impacting 337:10	343:15	328:15 329:18	included 10:9
identifiable 89:17	impacts 20:6	important 15:17	365:21 366:2	45:17 46:18 47:21
identification	296:15	26:7 27:9 32:1	improved 127:17	48:7 53:22 55:2
26:19 276:6	impairment 291:11	34:21 40:22 54:12	147:12 165:13	59:8 60:21 71:8
identified 41:4	impede 171:15	78:1 92:15 97:4	202:1 296:16	86:21 96:2 107:15
53:13 54:3 100:4	178:4 310:22	100:7 101:7	300:12 355:22	264:19 268:14
117:5,8 190:15	impediments	114:12 120:12	374:5	includes 15:2 31:8
237:12 240:8	171:12	133:16 147:7,15	improvement	33:16,17 38:21
340:15 347:10	imperative 179:21	152:7,16 155:2	105:3 113:10	40:6 44:12 54:7
identifier 173:22	344:8	158:6 169:4	152:21 238:6	78:2 172:12
176:18 303:19	implement 28:3	188:21 191:9	244:15 297:20	239:14 244:14
identifiers 172:7,15	36:22 49:11 88:11	196:13 214:4	299:6 328:2 330:7	262:22 263:2,5
identify 8:15 31:11	91:2 93:4 142:3,9	217:20 218:20	improvements 69:6	322:21 356:7
32:14 40:22 50:11	193:5 206:17	241:15 242:8	69:19 215:1 320:3	357:2,17,22
53:9 54:18 88:8	238:13 373:20	243:16,21 244:20	improves 302:12	including 24:18
91:15 113:17	implementation	248:1,15 250:3	improving 24:5	45:9 57:17 58:22
193:16 216:20	78:16 80:7 84:15	255:13 257:8	97:4 112:10	62:11,18 63:10
264:13 270:19	85:3 93:11,16	267:13,13 271:10	318:21	68:18 69:13 92:19
304:14 305:7	97:19 98:22 101:2	289:13 290:2	inability 319:12	94:10 101:10
identifying 40:14	103:13 106:8	307:20 313:10	340:6	135:16 174:1
53:8 193:19	107:8,11 120:16	317:22 319:4	inaccuracy 283:15	175:13 178:9
iffy 206:12	124:17 127:11,16	321:13 328:21	inaccurate 117:22	184:17 204:4
ignored 115:16	142:18 170:20	329:8 330:4,22	inadequate 260:17	211:18 221:2
II 1:25	171:13 178:12	333:8 334:14,15	inappropriate	222:6 238:6
Illinois 2:15 119:1	190:11 195:5	334:16	316:20	243:17 244:11
119:6 227:1	250:2 297:17	importantly 8:11	inappropriately	263:4,6 268:21
illness 335:1	304:20 305:9,18	9:18 87:7 325:22	320:14	269:3 287:18
illustration 332:5	345:12	333:4 337:12	incentive 127:22	289:4 298:18
imagine 21:2 38:22	implemented 21:9	impose 16:10	205:3	305:22 326:18
	33:20 37:19 75:13	imposed 136:21	inception 189:10	336:6

income 259:17	indicated 172:21	industry-paid-for	283:6 288:16,20	innovation 87:13
inconsistent 43:20	219:20 256:8	264:21	289:1,6,11,13,16	107:10 136:18
incorporate 25:7	indicates 269:18	industry-wide	289:19 290:1,5,8	innovations 301:15
56:9 90:1 150:15	indicating 219:3	317:15	290:22 291:2,6,13	innovative 56:2
155:8 191:12	indication 122:19	infeasible 300:22	292:2,13,15 293:8	87:22 136:22
incorporated 41:10	122:21 123:3,8	influence 259:15	298:22 299:2,12	243:13 343:9
50:4 71:21 122:20	165:4,14 166:8,11	influenced 259:8	299:13,15 301:3,7	374:21
152:22 168:19	167:2 168:19	inform 61:7,12	301:8,13,20 302:2	innovator 137:7
298:15	indications 166:21	146:11,12 155:18	303:12 306:20	201:7,10 202:22
incorporates	363:12	325:20 362:16	307:2 308:14	204:22 205:3
123:19 294:5	indicator 191:21	informal 110:2	314:12 315:6	206:1 207:22
incorporating 46:6	indicators 22:6,9	information 10:8	316:8 320:17	208:12 209:10
48:5 123:21	191:11 361:18	25:2,12 40:12	322:15,16 324:14	224:21
189:20 193:11	362:15	42:16 43:6,11	327:10 332:12	innovators 210:11
302:10	individual 17:10	45:11,13 46:5,7	345:10 356:14,18	224:14 225:13
incorporation	30:9 121:19 125:6	46:11,14,21 47:3	356:21 357:2,8	innovator's 207:3
238:22 322:22	147:10 150:17	47:9,12,14,21,22	361:15 362:15	inpatient 76:11,12
increase 16:11	251:11 273:19	48:1,2,3,4,7 49:18	363:6 364:19	78:6 79:18 80:11
103:20 105:14	296:1 309:21	49:19 50:1,3,5,9	368:16 373:14,14	120:13,18 123:18
121:3 125:22	311:19 315:22	50:10 51:1 52:7	374:11	155:3,4 156:1
169:11 176:13	339:4,8 346:22	53:3,17 59:2,11	informative 139:17	341:15 345:13
238:19 246:22	356:15 361:7,11	59:12 61:4,19	informed 39:11	349:7,14 350:15
255:4,8,11 256:7	369:1	63:1 64:11 65:7	67:4 96:11 153:13	350:19 351:7,8,12
256:20,22 271:9	individually 44:18	66:2 67:9 68:14	265:15 269:13	352:7,9 353:1,15
321:4 347:7,15	121:1 351:14	70:5 78:21 86:20	352:21	357:22 369:5,16
increased 177:6	individuals 114:21	87:1 88:3,5 90:6	informing 174:12	370:17 371:3
195:5 355:18	250:22 252:11	90:13 96:9,17,22	infrastructure	input 9:11 10:18
358:6	253:5 274:4	100:10 107:20	47:11	17:19 26:5 27:7
increases 257:3	individual's 250:12	115:21 124:13,22	infrastructures	27:14 28:20 38:7
299:12 369:10	induced 122:20	125:13 130:2,8,19	298:18	46:17 54:20 55:2
increasing 284:20	industries 19:10	134:11,18 141:21	infusion 59:5	168:16 188:11
285:12 358:10	110:16,22 111:3	142:1,14 143:19	ingrained 110:17	238:11 259:6
increasingly	111:15,22 112:19	144:1,13 147:3	inherent 36:1	296:20 298:1
155:10 194:20	118:14	161:21,22 169:20	initial 104:21 217:6	327:14,17
197:4	industry 2:13	172:1,6,8 174:16	269:10	ins 373:22
incredible 340:8	19:10,15 54:17	174:21 180:4	initially 19:5 62:12	insert 186:12
IND 180:6 181:3	91:8 104:18	184:15 186:12,14	260:7	200:18
182:10	107:19 110:20	190:3 194:12,19	initiate 94:2 327:1	inserts 96:22 289:5
indefinitely 8:13	112:2 130:5	195:2 197:5	initiation 352:1	inside 194:10
26:16 379:20	178:21 214:2	205:20 219:13	358:1	insights 88:7
independence	228:5 229:19	220:21 221:5	initiative 30:2,8	108:12 162:1
248:8 249:12	242:20 250:1	223:7 227:4 231:9	96:16 98:5 106:12	Inspector 129:17
independent 77:2,4	262:20 264:4	231:14 232:20	107:14 144:13	332:21
77:5 80:21 95:4	266:7 274:7 329:3	241:8,17 244:13	196:10,12	instance 45:12 51:6
179:1 225:9 310:3	industry's 92:4	251:15,17 252:9	initiatives 1:19	138:4 301:4
310:8 317:22	industry-funded	266:1 276:12	14:17 91:15 237:8	359:21
indicate 69:11	257:13	277:11 282:19,20	246:5 376:7	instances 151:13

301:9,21 311:2 315:6,10 339:14 342:14 359:22 Institute 113:11 institution 154:10 institutions 91:21 instruction 246:1 instructions 80:4 267:3 insufficient 22:7 insurance 209:21 214:9 224:2 insurers 128:2 integral 197:11 integrate 9:16 16:19 17:20 36:19 53:10 87:17 91:17 108:1 128:12 175:2 183:6 222:13 250:11 288:3 292:6 327:12 integrated 21:9 24:4 33:20 50:21 77:15 79:2,16 80:15 106:21 121:14 128:5,7,8 128:9 160:12 170:9 171:10 190:4 193:13 195:11 197:3 222:17 234:8 237:2 238:4 242:1 243:7 313:13 332:6 346:7 350:2 integrates 171:20 integrating 31:7 120:10,21 125:15 159:14 292:11 294:3 300:9 integration 21:16 24:8 26:9 27:12 30:2,6,7 88:2 98:5 120:7 121:3,9,18 122:2,6,9 123:13 125:8,16,21 142:15 156:1	160:8 244:11 247:21 250:6 253:2 292:19 299:3 304:15 330:2 intended 11:4 15:18 92:14 147:18,22 265:8 intent 10:20 15:9 242:3 interact 330:13 332:9 interacted 378:18 interacting 269:5 interaction 89:9 302:11 330:15 interactions 268:12 307:14 347:9 interacts 346:9 interest 132:21 142:16 162:12 248:9 249:13 284:2 285:20 320:9 350:10 interested 6:21 9:10 27:20 46:6 49:2 107:17 160:2 258:6 281:2,7 290:7 interesting 20:16 182:4 interests 259:20 interfaces 327:5 interfacing 355:22 interfere 306:15 309:8 internal 40:16 227:3 325:7 internally 374:20 international 179:17 180:20 internationally 179:1 345:22 internet 90:5 interoperability 298:21 interoperable	314:4 interpret 159:12 interpretation 350:16 interrupt 18:12 78:9 interrupted 6:18 interruptions 79:5 intervene 219:15 intervention 175:22 244:17 300:20 303:7 362:13,18 interventions 22:22 23:15 51:3 99:11 113:18 175:17 362:2 intricate 177:2 introduce 10:7 12:21 13:7 110:7 introduced 10:15 103:8,14,16 105:10,14,20 106:12 109:12 329:2 introduces 326:12 introducing 30:14 258:13 326:9 introduction 30:18 237:7 intuition 116:22 intuitive 109:13 110:12 117:3,20 118:9 invested 84:8 305:2 investigation 207:21 259:14 investment 29:10 84:11 297:19 invitation 109:4 involve 192:16 279:9 300:19 involved 13:1 27:14 100:16 120:21 138:4 151:17 183:19 185:11 188:2	209:21 214:6 223:21 230:6 240:3 266:20 312:4 324:22 367:6 involvement 160:21 213:7 317:22 involves 74:12 involving 270:11 in-depth 290:15 in-person 60:19 62:11 IP 198:6,7 iPLEDGE 205:11 294:14 351:3,5 ironic 249:20 ISMP 113:13 isotretinoin 138:5 202:14 issue 37:14 92:21 94:18 136:14 188:21 202:18,20 202:21 234:11,12 242:9 244:8 246:14 252:18 317:20 330:10 332:17 issued 262:11 312:20 issues 19:15 27:3 34:3 58:22 60:22 83:2 91:10 137:22 157:17 164:13 196:13 232:1 236:8 237:5,10,11 243:19 246:14,19 247:18,19 249:7 282:21 287:6 295:17 296:17 305:16 310:14 340:2 344:18 360:13,18 issuing 24:11 31:10 iterative 39:22 272:6 iteratively 55:11	IV 113:14 IWG 242:20 <hr/> J <hr/> j 2:23 4:23 202:5 January 134:3 Japan 181:11 182:2 Jeff 2:14 4:15 108:20 109:1 118:21 161:3 jeopardize 266:5 Jim 2:21 4:21 169:16,22 178:15 222:12 223:17 233:5 Jo 3:17 5:15 328:7 328:10 333:13 JoAnn 2:15 4:15 118:22 119:4 128:20 140:6 148:16 154:1 161:4 335:10 359:13 job 7:20 18:14 21:11 27:10 129:18 130:7 341:9 342:6 jobs 379:7 joined 6:22 joining 6:9 Joint 113:9 journal 59:11,12 113:9 246:12 journals 59:15 judge 102:2 218:17 judging 219:4 judgment 239:18 juggled 7:8 July 1:9 96:1 164:7 259:4 260:9 320:4 380:7 jump 362:19 J.D 1:24 3:8,10,17 5:10,11,15 <hr/> K <hr/> Karty 3:2 5:4 235:8
---	--	---	--	---

235:17,19,20 275:20 277:18 Kashoki 1:21 14:8 14:9 142:12 146:1 216:1 219:10 276:22 361:4 Kate 2:3 4:7 13:17 57:4 273:14 Katie 3:21 5:17 345:6,9 358:14 359:8 366:15 370:1 371:9 373:10 keep 93:5 159:2 225:15 323:20 378:21 keeping 81:21 162:12 230:11 338:10,20 Kelley 3:19 333:15 333:17,21 359:7 366:18 368:17 Kelly 5:16 kept 47:17 Kevin 2:4 3:8 5:10 14:22 287:1,10 297:1 362:20 key 33:22 62:6 94:10 108:14 112:12 118:6 171:7 175:1 177:5 178:6 189:11 190:12 192:3 196:21 238:5 268:7 271:17 290:4 302:10 keys 171:22 killer 254:16,20 255:5,9 256:8,10 killers 255:15 257:6 kind 12:15 29:4,7 32:4 33:7 39:15 40:6,8 43:2 46:2 47:5,12 56:8 122:22 141:4,18 144:3 149:4 154:4	154:18 155:22 157:19 159:19 164:6 219:3 227:11 229:8 247:19 275:5 277:13 281:3 330:9 339:5 359:6 370:17,20 371:11 373:21 kinds 35:3 156:15 205:12 216:9 224:6,9 227:7,8 knock 208:16 know 7:18 13:8 18:20 19:2 20:3 27:15,21 28:9 31:17 32:10,12 33:3,15 41:22 43:8 54:19 55:12 55:13,21,22 56:10 56:10 83:7 133:4 134:1,8 141:22 151:2 152:4 155:12 162:7 194:8 199:13 209:4 226:10 228:2 232:4,20 253:10,11 261:13 261:17,19 264:18 267:9 274:21 275:4 277:1,6 281:5,19 283:6 295:9 309:16 358:17 362:13 371:22 376:3 378:1 knowing 232:8,12 244:7 251:5 252:3 knowledge 100:13 165:22 168:9 184:21 191:5,20 196:19 243:11 250:12 269:19 273:10,18,21 274:11 275:17 280:10 281:15 282:3 316:19	322:14 337:11 364:5 known 92:11,21 129:10,14 130:14 211:17 292:7 365:21 knows 130:22 Kolodny 3:4 5:5 235:9 253:21 254:1,3 283:14 284:8,10 Kopelow 3:3 5:5 235:8 245:6,8 274:1 280:17 281:19,22 284:11 Kroetsch 1:22 4:5 13:14,15 25:18 29:14,18,20 121:21 150:3,22 158:22 160:18 162:6 225:20 231:11 280:8,22 358:19 360:12 373:1 <hr/> L <hr/> lab 72:16 74:10,20 156:7 158:12 174:20 175:17 LABA 168:1 LABAS 167:22 label 15:22 47:1 157:2,9 190:20 231:7 232:12 labeled 176:17 labeling 22:7 46:8 46:10,12 58:9 121:22 157:4 172:16 179:18 185:14 186:7 231:21 232:2,6,7 232:13,13 292:7 292:15 labels 46:15 laboratory 43:9 190:22 348:18 labs 158:13	lack 41:21 42:7 54:20 136:12 308:8 319:11 321:13 323:13,15 lacks 129:19 260:14 laid 154:1 landscape 46:1 language 45:6,18 69:18 173:9 308:13 large 44:2 185:19 213:12 323:14 346:6 largely 53:1 larger 77:2,5 149:11 367:2 largest 170:12 211:9,11 lastly 63:14 379:16 379:18 late 6:4 94:12 254:14,16 257:1 latest 39:11 99:15 232:12,20 239:9 364:12 Laughter 228:3 281:21 358:18 371:7 law 198:6 Lawrence 2:23 197:16,19 Lawyers 197:20 lead 32:21 79:4 215:1 289:15 295:16 310:1 leader 27:12 133:5 leaders 263:5 leadership 188:10 190:8 196:8 leading 84:2 257:2 263:3 300:12 leads 29:15 180:5 learn 21:8 28:6 38:7 55:15 111:15 114:21 159:18 173:20 373:21	learned 21:14 27:18 28:4 29:5 39:13 41:10 56:13 109:20 117:19 152:10 290:5 learners 249:18 253:8 learning 27:20 35:15 49:2 52:7 60:16 62:15 111:12 114:20 160:2,22 250:8 253:9 277:13 301:11 learnings 191:12 leave 350:15 leaves 81:22 led 258:5 306:4 left 12:11 83:10 140:2 251:16 354:15 leftover 255:17 left-hand 124:14 legislation 238:12 legislatively 188:18 376:7 legitimate 217:20 259:10 262:6 309:10 Lehigh 109:3 lenalidomide 122:8 124:11 lend 135:18 136:7 length 62:18 66:5 68:4 161:10 lengths 355:18 lengthy 289:15 lens 212:12 lessons 21:13 39:13 41:10 56:12 117:19 152:9,22 lethality 184:18 letter 201:5,10 207:18 262:17 263:7 letters 59:8,9 89:22 let's 43:9 111:1,7
--	---	--	--	--

187:1 267:19 323:2 341:10 371:8 level 69:2 77:9 105:18 159:22 172:6,15,20 173:1 173:22 176:18 214:19 215:7 227:5,6 244:21 281:15 299:22 300:2 310:5 311:21 361:13 363:10 levels 176:20 252:3 299:20 leverage 196:18 222:22 317:9 367:22 375:6 leveraged 76:20 174:15 leveraging 172:8 271:8 298:17 liability 203:15 209:20 224:2 library 47:17 license 200:4,5 licensed 295:8 309:6 licenses 279:1,11,11 279:14 licensing 278:13,17 278:22 licensure 238:16 242:14 244:19 251:9 life 109:20 110:13 243:19 lifecycle 92:5 lifesaving 306:22 310:22 lifespan 104:22 life-enabling 211:14 life-sustaining 211:13 light 12:9 83:9 100:19	liked 18:17 113:2 likelihood 61:6 219:17,17 likewise 113:11 118:14 limit 143:4 302:2 309:10 348:7 limitation 100:17 limitations 60:17 277:7 limited 23:16 71:7 97:21 101:21 126:2,6 128:11 140:7,12,12 145:10 148:18 173:17 195:21 205:20 275:10 296:11 301:19 320:20 334:13 342:22 359:1 360:2 limiting 62:18 84:21 97:9 143:5 339:9 limits 108:15 223:11 311:9 Lindsey 3:19 5:16 333:14,21 345:3 366:15 line 177:10 219:2,4 230:11 235:6 256:19 257:4,6,10 264:22 266:6,9 292:16 378:22 lines 120:12 219:8 370:21 link 126:2 128:11 140:7 148:18 236:19 324:18 linked 116:5 127:16 189:17 191:5 links 33:22 42:3 90:9 121:20 124:20,21 125:4 125:12 160:10 Lippmann 1:24	14:18,19 223:18 225:17 list 43:18,21 44:4 71:8 202:9 262:21 262:22 280:12 356:8 listed 10:19 21:17 23:9 24:2 168:20 200:1 201:7 204:8 205:17 listen 54:15 260:18 listened 19:9 listeners 378:13 listening 11:9 17:17 19:17 27:16 368:13,15 378:10 listing 90:7 lists 19:20 literacy 291:11 323:1 literally 212:21 litigation 204:2,3 litmus 324:7 little 6:4 15:11,14 18:5 20:10,19 30:10,22 34:10,11 39:17 41:17 46:10 50:6,9 70:13,16 120:5 131:9 140:1 140:9,20 141:7 143:3 178:19 199:8 201:21 206:8 273:20 284:11 285:21 323:2 339:3 340:7 366:17 369:9 370:21 376:18 live 6:9 84:5 240:18 lives 84:6 103:5 110:7 115:2 211:10 living 250:7 lobby 7:19 local 312:11 located 345:20 location 90:5 276:18 356:15	locations 295:18 296:1 360:21 lock 183:10 locus 227:11 logged 352:18 logic 33:7 44:17,17 logical 43:12 109:15 177:12 login 314:15 logistical 223:22 336:14 338:9 340:8 logo 89:17 logotype 89:15 long 7:6 65:10 66:19 67:11 92:2 132:10 141:22 246:6 258:16 311:21 longer 22:9 84:5 184:2 341:15 long-acting 238:18 240:9 246:19 308:19 long-run 151:16 long-term 261:20 263:19 269:4 284:22 285:7,11 285:13 look 13:5,5 26:9 41:13 42:2 43:10 43:12 45:20 51:6 53:15 63:17 81:4 95:9 101:17 102:8 108:13 111:7 112:5,20 140:2 145:5 146:16,22 147:7 152:7 178:10 185:21 189:13 197:9 202:16 213:20 219:1,9 221:10 225:21 230:5 246:21 257:7 260:1 265:16 275:18 279:19 283:1 305:4	321:22 322:4 329:4,5,5 333:7 334:9 337:4 338:5 356:10 367:22 375:5 379:12 looked 54:3 112:22 113:1,3 220:21 337:9,10,11,11,12 looking 9:13,14 20:21 24:15 43:14 51:1 53:7 70:3 95:3 145:7 154:2 156:19 157:1 161:13 165:2 166:22 167:4,7 168:12 185:13,14 194:14 216:1 221:10,11 232:14 288:1 314:10 324:3 334:16 368:13 375:18 376:19 377:11 looks 28:21 38:20 99:12 112:13 115:5,7 188:13 333:11 377:17 loop 56:6 lot 13:4 19:3 21:7 27:10 31:19 33:10 34:5 36:9,18,19 37:8,12 41:16,19 44:5 45:8,15 46:12 49:5,21 50:4,12 52:10,20 54:13 79:3,5 127:13 152:9 154:22 155:5,13 158:16 161:1 183:14 208:13,14 221:22 229:13,16 231:1 232:6 235:11 267:6 377:4,22 378:20 379:4 lots 218:20 lovely 380:4 low 258:15 264:9
---	--	---	---	---

291:10 lower 134:16 172:22 257:16 258:21 lowest 107:7 lunch 7:15 82:6 158:20 163:4 lunchtime 164:8 L.L.C 2:22 L.L.P 2:23	299:14 306:4 362:5 364:22 371:22 375:17 Malkin 2:23 4:23 197:15,17,18 224:10 manage 22:5 52:13 106:14 109:20,21 135:18 170:14 188:20 189:14 195:16 211:9 214:16 227:2,9 251:22 267:22 311:10 323:20 324:9 327:3 332:8 332:8 362:8 370:4 managed 3:18 105:7 227:6 328:8 328:12 329:12 331:3 332:14 333:2,4 346:19 management 2:1,2 2:4,7,9 13:13,19 13:22 14:4,14 19:19 21:5 57:6 63:22 70:8 76:18 79:21 92:7,18 93:8 94:2,20 95:7 95:21 98:4 99:16 103:9 104:7 107:22 109:14 110:2,14 111:4 113:22 114:8 116:13,21 124:4 127:11 134:7 138:6,16 141:18 145:13 148:1 155:8 161:17 165:1 170:21 171:2 175:11,16 179:5,7,21 188:14 189:18 190:17 192:6,7 193:5 195:10 196:16 197:10 198:22 218:5 237:14 238:1,2,12,21	239:13 242:10 249:7,14 266:18 266:20 270:22 277:22 289:2 292:22 298:20 300:6 302:15 307:18 314:1 318:22 325:8 330:18 345:13 350:16 366:3 manager 211:9 managers 109:17 109:18 manages 170:8 171:4 managing 98:17 155:1 171:2 177:2 190:6 192:18 329:9 331:16 347:4 mandates 241:2 mandatory 238:14 242:12 258:13,17 277:21 278:7 280:4 manifest 246:14 manifestations 250:1 manner 7:21 86:8 145:1,17 214:22 283:22 289:10 343:8 manual 74:15 79:4 173:11 175:21 223:5 233:20 manually 176:4 manufacturer 124:13 202:13 204:8 205:2 310:13 335:20 357:18 360:11 manufacturers 2:12 137:1,15 138:1,10 177:20 199:16 204:14 205:19 206:2 224:14 248:2,6	249:8 259:18 290:13 300:3 305:5 313:18 316:5 367:15 manufacturer-pr... 290:10 Manzo 2:1 14:12 14:13 140:5 222:11 368:21 map 113:15 254:22 255:2 mapped 39:20 March 137:20 mark 184:4 marked 46:22 122:22 markers 185:20 market 130:12 134:2 149:19 220:17 230:13 258:12 329:2 marketed 192:8 marketplace 319:10 333:9 maroon 254:19 Martin 2:24 4:24 211:3,5,6 Mary 3:17 5:15 328:7,10 333:13 377:9 Maryland 1:13 mass 287:14 massive 245:19 master 348:5 matched 315:20 material 66:14 90:14 106:16 299:14 materials 20:7,13 33:12 42:1,3,4 45:9,11,12,17,21 46:19 58:11,17,17 59:17 60:3,17,22 64:7,16,20 65:6 65:21 68:18 69:1 69:5,6,11,15,17 69:20,22 70:4	86:16 106:2 265:7 289:4 293:7 301:1 matrix 113:5 matter 92:10 118:8 133:12 187:1 244:1 matters 230:7 maximize 25:10 92:16 300:11 McGlinnis 246:11 McKesson 149:12 149:12,13,14 mean 30:14 32:2,8 33:2 39:1,16 47:6 74:18 76:8 151:1 153:7 154:19 203:8 205:4 206:6 225:11 278:11 348:4 359:3,11,12 359:22 meaning 44:3 203:5 207:9 meaningful 96:12 343:1,21 means 34:13 40:15 41:6 72:7 112:16 200:17 213:13 217:2 218:13 325:12 327:12 329:5 331:2 336:16 368:5 meant 146:14 203:8 259:22 277:2 measurable 55:5 189:16 190:22 219:21 measure 85:15 93:4 100:3,20 113:18 247:12 249:2 276:9 316:13 317:2 measured 101:15 104:20 216:11 252:14,22 253:5 measurements 101:16
---	---	--	--	--

measures 15:21 23:12 25:13 101:1 126:9 322:6	347:7,14 349:1 366:22 367:3,19 367:21 372:3,6	301:15 302:17 305:4 306:22 307:3 308:1 311:1	323:7 328:14 368:5 378:2,21 379:14	332:3,20 358:20 360:13 366:15 368:2 371:10 374:19
measuring 21:11 99:19 217:4 244:16 322:9	Medicare 128:2 medication 2:6 13:12 64:16 65:4 65:5,19 75:2 96:17,22 109:11 115:6 123:3 124:4 124:10 140:17 144:13 149:6,10 155:15 172:5 174:11,20 192:21 200:17 219:18 271:4,6 288:15 289:5,6,19 290:6 291:5,17 293:3 295:6,9 297:15 300:2 301:4,12,21 302:15 303:4 304:10 307:18 308:10 317:7 318:17,21 319:2,3 319:13,17,18,20 320:8,11 324:22 326:4,15 327:1 328:18 330:12 339:2,15 340:12 340:17,18 341:1 348:8,20 349:7,11 349:18 350:4 351:9 352:9 353:7 353:17 355:2,6,17 359:12 365:1,2,6 365:18 366:10 370:22 371:4	317:10 319:6 320:13 326:8,11 326:12 328:22 329:1,4 330:20 335:3,3,5,8,10,22 340:6 344:2,5 346:16 347:8 354:20 358:6,21 360:20 364:9,10 368:4 medicine 47:17 195:20 242:14 243:3,3 245:13 247:10 255:18 277:22 medicines 84:4,9 188:16 MedSun 187:7 MedWatch 232:5 meet 9:19 26:6 72:8 126:12 176:16 244:4 248:6 261:20 271:5 291:2 294:19 296:9 307:19 310:3,10 317:4 338:19,19 367:15 meeting 1:6,12 6:6 6:15,20,22 7:6 8:6 8:20 9:6,9,18 10:2 10:10,16 11:2 13:2 26:7,13 29:1 29:3,7 31:3,9 34:5 34:7 40:20 50:15 51:15 54:1 90:21 94:11,12 124:6 132:3,8 137:19 146:13 157:16 161:18 163:1 196:22 199:6 236:7,13,18 242:15 260:12 267:16 278:15 288:8 306:5 320:5	meetings 17:16 29:6,8 161:6,18 161:19 168:17 207:15,16 208:7 241:19 259:5 Megan 2:2 4:11 14:2 70:7 148:14 227:12 232:22 371:5 melded 113:6 member 84:13 85:13 322:3 366:20 377:21 members 11:10 12:7,21 13:9 20:21 84:7 87:15 131:3 139:19 140:1 215:19 225:2 234:18 287:16 288:11 296:20 310:6 318:10 319:3 320:12 323:18 324:5 325:6 329:9 367:19 378:9 men 133:11,19 134:5 mention 31:14 46:8 206:7 226:10 265:20 mentioned 11:18 15:22 24:22 26:14 30:1 36:8 48:12 50:3,12 51:14 54:10 74:9 148:20 179:18 183:3 184:6 187:14 204:12 206:20 214:2 221:21 222:12 224:2 225:21 226:12 227:15 233:5 292:8 309:1 314:5 318:6 331:17	mentions 207:19 merchants 287:14 message 67:16 234:12 344:1 messages 18:18 58:20 62:6 240:10 271:2 281:9 messaging 168:3 271:1 met 23:14 61:20 130:4 207:14 294:10 295:6 349:3 352:11 356:4 metabolism 133:13 134:9 method 32:8 111:5 159:17 309:18 338:12 methodologies 24:16 51:8 methodology 113:8 113:15 114:7 methods 32:13 51:1 60:9 87:13 99:9 109:5 110:17 111:1,19,21 113:1 114:2,5 116:17 118:17 138:15 153:18 307:16 315:7,10 322:19 323:16 metric 190:22 218:17 metrics 56:12 244:7 315:15 317:4 Michie 1:19 14:5 378:18 379:3 Michigan 3:20 333:15 334:1,3 336:18 339:12 microphone 12:13

12:18	135:3 148:3	Moncur 2:2 4:11	333:19 334:10	292:3 362:20
mid-cycle 94:11	184:20 190:16	14:1,2 70:6,7	350:10	376:6
military 111:2	191:7 193:1 194:1	148:15 227:13	movement 308:17	name 14:9,12,22
million 120:1	216:8 217:7	233:3 234:14	moving 7:20 72:19	42:11 44:17 57:4
211:10,20 245:20	mitigating 100:4	371:8 373:10	88:18 298:8 339:5	63:20 102:19
246:1 268:21	147:8 316:3 322:2	money 208:13	376:1	119:4 131:20
271:14 287:18	mitigation 1:4	225:1 249:19	MSW 2:17	135:12 169:22
millions 261:3	35:18 91:12	monitor 62:4 76:13	MTM 290:15,17	188:7 197:18
mind 93:5 98:2	129:21 132:4	264:16 284:16	302:15,18,20,22	199:15 203:21
139:22 226:16	136:9 137:22	344:4	374:19 375:14,21	254:2 266:16
mine 53:1 193:15	138:20 145:11,21	monitored 190:21	375:22 376:4,8,15	318:6 328:10
minimal 59:15	172:18 196:2	258:9 314:21	multiple 11:4 16:11	333:21 345:9
minimization	218:4 232:11	320:15 369:7	26:5 111:8,9	348:13 368:11
86:12 97:22 118:7	236:10 287:8	monitoring 57:18	114:3 183:20	names 42:10 44:7
118:13,17 197:10	334:12	138:17 190:6	195:8 201:2	106:1 262:21
minimize 22:3 38:1	mix 232:21	191:3 195:21	233:19 237:5	naming 185:13
95:2 96:19 100:16	mobile 88:1 90:17	214:18,20,22	259:5,6 279:1,15	Natalie 3:5 5:6
102:11 110:8	291:4,8	238:14 270:17	286:18 291:16	235:9 266:14,17
114:17 173:7	mobilizing 252:17	302:22 323:8	303:16 311:11	272:11,17
189:5 293:21	mode 112:8 115:9	324:22 348:19	326:11 340:13	nation 170:14
369:4	model 103:7 128:5	352:4 365:16	municipalities	284:2 334:8
minimized 129:15	128:7 193:5 239:1	month 17:9 221:3	278:16 279:7	367:12
minimizing 92:16	269:17 270:15	monthly 352:4	Murray 3:3 5:5	national 2:16 3:8
139:5 268:2	307:18 322:8	months 13:2 26:3	235:8 245:6	3:12 47:17 112:22
minimum 363:4	models 127:14,19	27:18 50:18 68:9	253:20 273:16	128:22 129:4
minor 88:17,22	128:1 192:18	104:20 106:4	mutually 38:5	131:1 161:19
minus 8:19	290:19	182:13 183:15	Mwango 1:21 14:9	179:17 180:20
minutes 11:14	moderate 165:22	234:6	140:4 215:22	238:19 239:6
12:11,14 15:10	166:16	morbidity 254:6	276:21 361:3	240:2 245:13
82:3 83:5,8,9,10	moderator 6:13 9:2	morning 6:5,7 7:14	myeloma 340:13	287:1,12,16 292:4
83:11 272:13	9:4	8:4 13:10,17,20	myriad 200:8	303:18 305:12,20
315:3 358:15	modes 51:7 114:6	14:1,8,12,15,18	289:7	312:10 314:8
misleading 273:12	modification 93:17	14:21 57:4,8	M.A 2:3,8 4:7,9	318:9 322:3
misled 257:14,17	99:1 176:11 177:7	63:19 70:6 83:19	M.B.A 1:16,19 2:19	338:18
misnomer 46:10	177:14	91:7 102:18	3:15 4:4,21 5:13	nationally 336:18
missed 355:6	modifications 69:3	108:22 110:9,10	5:22	nations 92:1
missing 179:8	114:11 115:3	121:10,21 129:2	M.D 1:21 2:6,21	nationwide 313:19
265:18 357:8	modified 75:11	131:19 132:6	3:2,3,4 4:22 5:4,5	nation's 211:8
371:20	210:19 322:20	179:19 184:6	5:5	natural 270:12
mission 254:5	modify 73:16,20	227:1 314:6 373:3	M.H.C.A 2:15 4:16	naturally 68:22
267:9	74:1 102:4 135:8	376:20	M.P.H 1:21 2:4	nature 119:18
misuse 241:6 275:1	165:17	morning's 85:5	M.S 1:18,22 2:2	175:20 193:5
mitigate 23:1 32:12	modules 60:6 181:7	mortality 254:6	3:19 4:5,11 5:16	204:16 233:16
34:20 59:20 86:1	301:11	move 31:13,20	M.S.W 4:17	navigate 336:2
94:17 99:5 114:18	molecular 153:4	39:19 41:1 59:14		367:8
117:12 189:5	moment 320:1	159:13 192:15	N	NCCN 343:4
mitigated 117:13	373:2	250:18 267:19	NACDS 287:13	NCPA 305:21

308:12 309:12 310:2,17,20 311:4 311:16 313:6 315:19 317:2,12 317:19 338:16 343:15 NCPA's 309:5 NCPDP 174:16 292:5 332:5 NDA 200:16 NDAs 17:12 nearly 129:22 130:1 189:22 221:13 necessarily 37:6,16 38:12 42:15 100:5 165:10 200:13 208:15 necessary 22:10,21 25:5 32:15 36:1 65:8 85:18 99:4 105:15 106:18 140:13 154:17 157:4 165:15 166:11 168:10 176:22 177:1 186:18 196:6 217:14 237:12 293:11 294:16 309:22 311:20 313:4 314:18 324:8 361:11 necessity 184:10 299:1 364:4 need 8:17 18:14 19:11,13 25:11 26:16 27:15,21,22 28:9,16,19 29:5 29:12 32:15,19 33:1,3,15 36:21 37:17 38:9,13 41:19 45:5,14 49:7 54:16 55:7 55:11,13,14,19 56:1 73:7 74:5 75:11,12 77:20 78:9,19 81:18	86:1 88:16 96:8 110:19 111:18 115:1 133:22 134:15 141:5 147:10 149:20 150:14 156:16 168:10,18 180:11 184:20 186:5,14 186:20,21 187:5 187:21 193:21 194:3 196:1 200:13 201:6 204:21 207:5 219:15 225:6 239:19 247:8,9,11 247:12 253:12 261:4 267:7 268:10 274:10,11 274:11,12,19 276:6 283:18,21 284:4,4 289:9 313:16 322:12 325:16 327:3,18 331:15 340:21 342:1 352:16 354:2 358:6 362:12 371:22 372:2,4 374:16 379:5,20 needed 16:1,13 33:8 34:19 40:3 82:10 84:22 94:17 130:19 157:8 340:18 344:4 350:4 361:19 362:3,4,17,18 370:11,13 379:2 needs 52:7 71:11 72:22 77:9 78:21 116:3 141:15,17 148:4,7 152:21 153:2 155:18 192:8 243:10 246:8 247:6,8 248:20 250:22 251:1,18 252:11 253:5 273:19	275:7 280:15 281:17 282:12 283:9,9,16,17 289:11 296:10 320:11 324:3 327:11 354:22 356:21 367:15 negative 120:19 173:4 212:18 218:10 negatively 320:19 negotiate 201:16 206:10 209:11 negotiated 35:14 negotiation 203:20 negotiations 208:2 negotiators 201:17 net 271:19 nets 269:14 networking 82:5 neurotransmitters 133:15 Nevada 345:21 never 7:11 114:14 137:13 268:5 343:12 new 1:13,21 14:10 21:6 35:18,19 36:14,20 41:10 53:10 55:13 56:2 73:22 75:8,11 84:9 87:13 88:11 94:15 113:21 117:11 125:2,11 127:12 136:14 139:2,21 150:8 152:8,11,11 153:4 162:1 165:4,18 166:2,8,11,21 167:1 168:7,19 177:17 181:22 182:14 186:12,13 205:11 241:21 243:13 246:11 257:11 264:5,6 299:2,3 328:22 331:22 333:9	343:5 354:9 370:7 News 260:13 nice 46:20 nicely 173:19 Nicholson 3:8 5:10 287:1,3,10 360:16 362:19 375:14 NIH 283:1 nine 161:18 346:9 NME 94:8 95:5 NMEs 150:9 non 97:12 143:20 175:16 284:21 noncompliant 348:4,6,10 nonmalignant 241:13 nonprofit 131:22 non-cancer 257:20 263:18 264:11 non-certified 352:8 355:14 non-chemotherapy 123:5 non-dispensing 175:11 non-medical 255:16 316:20 non-profit 83:22 normal 87:19 223:6 normally 144:10 Northeast 345:20 notably 292:16 295:12 note 57:19 59:12 165:10 241:15 307:20 noted 65:16 98:14 144:6 315:17 321:11 332:21 notes 201:18,22 216:2 notice 9:12 10:20 26:12 34:6 44:6 51:16 57:1 202:11 224:11 226:5	236:12 noticed 37:5 notification 220:12 notifications 220:20 221:1,22 notifies 204:19,20 notion 276:17 279:21 Novartis 2:19 164:18 165:1,10 November 97:1 novo 116:9 180:11 NPIs 303:19 NQF 322:5 NRC 112:2 nuclear 111:2 112:2 number 44:2 57:14 58:7 64:9 88:21 118:6 151:7 172:3 214:6 226:14 278:20,21 279:13 285:8 288:12 315:3 320:3 326:13 346:7 358:10 360:2 362:22 numbers 176:6 291:12 numeric 279:5 numerous 289:4 300:6 nurse 116:1 268:18 270:2,2 273:9 nurses 58:4 185:11 192:12 213:8 268:6,11,13,18,21 268:22 269:2 272:2,8 336:7 nursing 230:20
O				
Oak 1:12				
objectives 57:9 64:3 105:2 183:8				
observation 109:7				
observational				

180:10	330:11	90:6 106:13 160:9	258:15 259:1	options 60:15
observations	Ohio 345:20	240:18 294:18	260:16 261:4,7,20	62:10,14 226:15
227:14	OIG's 205:17	301:11 315:7	262:2,5 263:13,18	299:3 305:8
observing 274:8	okay 6:3 15:3 29:18	356:17	263:19 264:1,8	oral 336:22
obtain 68:2 106:16	72:19 73:10 81:8	on-call 310:4	265:10,19 276:8	orally 291:13
177:21 200:5	83:18 140:3	on-site 355:13	277:8 278:6	order 33:3 40:3
204:14 238:11	156:17 158:22	open 7:1,2,5,22 8:4	284:14,21 286:8	67:20 75:6 79:18
296:9 326:8 327:3	160:17 162:11	8:9,13 10:4 11:19	308:20	112:11 122:21
353:3 359:5	164:3 206:15	26:16 27:2,6	opportunities	123:3 128:15
obtainable 290:9	210:6 233:3	326:17 350:16	21:15 26:4 28:14	141:6 155:20
obtained 327:20	234:14 235:14,16	374:8 377:3	28:18 36:6 94:9	170:18 205:10
obtaining 176:5	281:19 286:14	379:20	151:14 241:8	217:1,14 222:18
233:21 354:5	376:17	opening 4:3 117:1	259:6 299:10	225:7 277:15
obviously 151:15	old 282:1	openly 242:17	304:14 375:19	309:15 316:13
185:3 229:13	older 136:8	operate 287:17	376:8,14	323:8 324:22
232:3	onboard 75:9	339:17	opportunity 11:11	349:15 350:6
occur 76:15 115:12	145:3 166:21	operates 59:21	12:6 23:22 46:17	352:8,14 354:22
117:6 312:3 327:2	329:3	operating 282:14	55:1 85:1 88:10	364:20 374:1
369:20	once 28:2 32:12	operation 198:19	91:9 102:7,22	orders 149:6,8
occurred 80:2	41:3 47:15 48:6	operational 195:5	113:21 114:5	351:13
208:9	54:2 74:4 87:3	363:21	129:3 131:12,19	organization 2:13
occurs 114:19	204:18 335:7	operationalize	132:5 139:13	91:9 116:20
173:6 199:19	355:19 374:11	319:12 325:8	145:3,8 160:8	131:22 226:16,17
269:11	oncology 124:19	operationalized	166:7,19 169:19	254:5 259:12,16
offer 60:14 62:9	213:11,13,14	181:18	178:14 188:9	259:18,19,22
88:9 107:4 208:5	ONDCP 274:15	operationally	189:8 196:18	262:16 273:10
240:17 299:5	onerous 296:13	295:4 363:22	197:7 210:3	314:10 368:7
300:3 310:6	ones 151:17 152:4	operations 1:17,22	265:11 270:3,7,12	organizational
317:10	153:9,11,19	6:11 170:2 199:8	286:1 287:5	76:22 77:13
offered 68:17 160:7	183:20 202:14	300:10	296:19 297:18	organizations
312:22	228:9	opioid 3:5 237:14	302:20 305:15	86:22 87:2 91:22
Offering 63:8	one-document	237:19 238:1,3	306:6 317:20	139:11 195:1
offerings 240:11,21	288:18,19 290:22	239:14 240:9	318:18 321:7	238:9 240:6
offers 106:21	292:17	242:11 246:20	328:1 379:19	245:13 259:9
196:18 241:7	one-pager 301:5	253:22 254:4,6,9	opposed 82:3	260:5,20 261:2
office 1:18,20,21,23	302:5	254:12,12 255:21	100:20 232:2	272:21 273:7
2:6 13:11,15 14:6	one-part 281:20	256:19,22 257:15	264:20 296:1	331:3 332:14
14:10,17,19 60:20	one-stop 62:22	257:21,22 258:14	347:11 356:15	333:2,4 334:17
63:4,22 94:15,15	ongoing 61:2,15	259:3,15,17	opposition 238:14	373:7
197:22 213:21	91:14 96:16	260:13,15 261:21	optimal 137:21	organization's
239:6 332:20	177:21 180:20	262:2,7,12 263:2	180:15 234:22	254:9
348:20,22	181:4 186:15	264:19 265:13	235:1 238:21	organize 23:22
Officer 2:5	187:14 232:8	266:5 277:8 279:9	optimized 95:1	organized 10:22
officers 155:4	239:8 300:15	opioids 238:19	option 62:11 63:2,9	72:21 82:13
offices 269:4	364:10	240:12 241:11	106:12 210:5	213:10 291:22
off-label 221:15	online 49:20 60:12	254:8 256:21	248:15 291:5,12	organizing 90:20
oftentimes 311:6	60:19 62:12,14	257:11,19 258:8	optional 142:6	299:19

220:11 324:14 Oswell 2:3 4:7 13:17,18 57:3,5 273:15 outcome 112:12 135:13 148:9 219:18,21 244:9 249:1 269:20 282:4 365:9 outcomes 23:15 99:22 100:18 127:2,17 146:18 147:18,20 242:6 244:5,13 256:3 278:9 315:21 316:7,14,21 317:2 317:5 322:15 329:18 330:5 333:8 368:3 outcomes-based 241:20 outlined 353:20 outlines 11:1 outpatient 71:6,10 76:10 78:6 79:20 80:11 119:11,15 119:19 120:14 155:1,9,10 156:2 160:12,13 236:3 341:17 345:14,15 346:10,10 348:21 350:15,19 352:6 352:22 353:5 358:1 369:15 370:5,18 371:2 372:15 outreach 300:17 outreached 268:18 outs 373:22 outside 7:12 54:17 96:15 97:3,13 143:22 164:8 171:14 223:16 248:3 347:12 outweigh 22:11 25:6 100:6 103:18 129:11 137:16	180:14 267:12 362:5 outweighs 16:2 199:21 overall 29:7 101:13 107:3 140:16 146:17 250:14 279:18 315:1 330:7 333:8 356:21 overburdens 102:3 overdose 256:4,8 256:11,13 257:3 261:22 overdoses 256:10 262:2 overly 328:20 oversee 24:9 345:12 oversight 15:2 289:16 overview 25:22 28:22 39:16 57:10 64:4 70:12 115:4 198:17 overviews 60:5 64:18 65:22 overwhelming 301:3 over-educating 269:16 over-saturating 289:14 owners 306:1 o'clock 286:4 O'Donnell 3:5 5:6 235:9 266:14,16 266:17 273:8	379:14 pages 65:10 66:6 66:19 67:11 paid 366:18 pain 133:13 237:14 237:18,22 238:2 238:11,21 239:13 239:20 241:10,13 242:9,10 254:15 254:20 255:5,8,15 256:8,9 257:6,20 258:7,16 259:11 259:20 260:1,4,5 260:19 261:2,3,9 261:15,18 262:4,6 262:22 263:14,18 263:20 264:1,9,11 277:22 284:14,22 panel 1:14,15,17 6:14 9:7 10:4,7 11:8,10,12 12:7 12:19,20 13:8 15:4 20:21 29:8 81:9 82:8,8,9,11 83:1 85:5 131:15 139:16,19 140:1 162:13 164:11,16 188:10 198:9 211:3 215:18,21 234:18 235:6,17 260:16 272:12,14 280:7 286:1,6,15 314:6 358:16 377:21,21 378:9 378:14 panels 10:3,18,21 10:22 11:5,15 12:3 26:10 27:3 377:1 paper 88:18 191:13 220:3 238:2,5,10 239:3 291:19 325:17 343:4 paperwork 18:16 300:14 paradigm 264:5,6 343:5	paradoxical 109:8 ParagonRx 2:14 108:21 109:2 parallel 237:9 257:3 parameter 252:20 parameters 249:3 249:20 paramount 341:5 part 9:4 34:2 58:10 58:11,14 63:9 64:19 77:2,5,15 101:19 106:11 110:6 114:7 128:6 132:18 146:8 148:7 155:2 160:11 179:13 197:1,11 223:6 232:21 270:14 327:11 335:16 362:12 364:11 partial 175:21 351:10 participants 6:8 173:10 316:8,11 378:7 participate 75:10 80:17 209:6 310:9 328:1 participating 187:19 188:14 participation 24:10 187:4 239:22 277:4,16 278:11 particular 9:22 23:14,15 25:14 80:5 81:15 85:20 100:6 102:2 103:17 115:18,19 116:19 126:5 132:13,17 135:20 136:11 141:15 151:10 157:16 184:16,18 185:8 186:8 195:7 217:15 224:19 227:16 230:5,12	233:7 240:1 241:16 257:17 270:10 293:3,16 294:17,20 296:14 298:6 321:3 322:11 327:4 342:20 363:19 365:1,2 particularly 116:22 133:2,22 134:14 178:1 181:5 186:10,11 190:1 197:4 205:21 226:18 257:19 272:19 328:16,18 328:20 329:1,10 332:17 parties 204:19,20 206:9 209:6 partner 2:23 88:4 90:22 178:10 197:16,19 293:10 partners 187:20 parts 9:3,4 191:9 party 73:12 105:8 passage 136:16 passed 265:4 Passengers 111:12 patent 200:2 202:18,20 204:2 patented 204:4 205:10 patents 200:8 202:15 Path 196:10 patient 3:1 5:3 19:14 23:12 35:7 38:17 44:11,12,13 44:14 52:3,8 58:4 61:2,9,12 63:3,5 64:14,16,17,20,22 65:1,5,15,20 66:16,17 67:3,6,8 67:13,15,17,21 68:3,6,16 69:8 71:17,20 72:18 75:2 76:4,6,13,14
---	--	--	---	--

81:17 84:14 85:4 85:21 92:20 96:4 96:17,18,21 100:11,13 101:10 103:21 105:12,16 105:22 112:22 115:10 116:1 124:2 125:12,19 126:14 129:6 131:4 135:12 140:16 141:15 144:13 147:22 152:13 165:19 167:7,9 170:1,21 171:16,17 173:5 174:11 178:4 183:5 184:18 186:1 191:18 192:19 196:20 197:12 200:18 212:3,8,13,19 213:5,21 214:4,5 214:7,9,16 215:8 218:5 223:9 226:20 235:7 240:15 242:5 243:16 244:12 249:1 255:20 260:2 265:5,14 267:1,5,18,22 269:3,10,12 270:1 270:5,13 271:3,17 272:5,7 278:8 282:4 288:8,15 289:5,16,19 290:7 290:18 293:18 294:13 295:16 296:12,16 300:12 300:16 302:1,12 302:13,18,20,22 303:1,4,9 307:9 307:13,15,17 308:5 309:9,22 310:1,22 311:8 314:2 315:13 316:18,22 317:6 318:12,17,21	319:4 320:17 321:10,15,16 322:14,19,21 324:9,18 325:14 325:18 327:4 329:18,19 330:5,7 330:13 331:4 332:15 334:6,21 336:16 337:3,11 337:22 339:9,10 339:12,22 340:1 340:13,16,18,20 340:20 341:4,5,12 341:14,21,22 342:4 343:14 346:18 347:5,7,11 348:11,16,19 349:10,15 350:3 350:13 351:19 352:14 353:18 354:12,14,16 355:5,7,11 356:16 357:13 358:3 359:20 360:4,8,17 374:17 patients 16:6 18:9 18:16 43:7,22 47:19 49:15 52:6 52:8 53:17 54:16 54:22 57:18 64:10 64:11,12 65:13,20 65:22 66:4,10,15 66:21 67:10,19,22 68:10,11,12,17,21 69:11,21 70:18 84:4 96:7 97:11 97:17 98:10 103:5 121:4 126:19 130:13 131:8,11 134:11,17 135:14 137:10 138:8 139:1,9,10 141:10 142:2 143:10 145:11 146:12 158:13 167:13 170:5 174:5 185:10 187:22	195:14 212:1 213:15 218:22 219:16 221:20 223:15 228:15 229:20 230:13 236:3 237:13,17 238:7 239:19 241:14 242:10 252:12 253:15 258:7,8 259:20 260:3,4 261:4,9 261:15,18,20 263:20 265:9 266:2 267:18 268:12 269:6,17 269:18,21 270:17 270:19 271:11,20 274:7,17 283:19 285:13 289:3,9,14 289:21 290:3,14 291:2,3,4,10 293:22 294:6 296:10 298:10 300:11 301:2,12 301:18 306:9,21 306:22 307:6 308:2 310:6 314:16 315:8 316:4 320:11,16 320:22 321:12,19 325:8 326:8,10,22 327:21 329:4 330:15,19 332:10 332:12,16 334:15 334:20,22 335:1 336:2,9,20 337:13 337:15,20 338:7 340:2,9 342:10 343:2,9,22 344:2 344:5 346:1,7 350:6 351:15,17 353:4 354:21 355:1 366:12 367:17 369:6 374:22 patient's 61:4 65:8 174:19 270:9	284:16 311:10 335:14 346:12 347:6,14 349:1,21 patient-accepted 185:18 patient-center 238:22 patient-controlled 113:14 patient-directed 4:8 64:2,4,6 266:22 patient-friendly 69:1 patient-owned 342:2 patient-physician 372:5 Patient-Prescriber 67:1,7 68:5 patient/prescriber 324:20 patterns 311:5 Paul 2:14,16,22 4:14,17,23 102:16 102:19 108:19 128:21 129:3 131:14 140:20 188:5,7 197:14 221:6 226:10 227:12 231:21 pay 127:13,15 128:15 209:17 224:22 261:9 338:1 payer 335:21 payers 128:1 376:2 376:3 payment 376:5 payments 127:22 PDUFA 9:19 10:1 16:18 17:18 23:20 31:1,4 40:18 50:14 53:6,12,15 53:19 84:18 91:14 92:4 94:7 267:7 271:18 379:7	peer 187:18 276:17 people 6:7 7:20 13:4 20:17,18 49:1 81:9 109:16 117:2 120:1 134:10 157:18 161:12 184:3 186:14 220:20 226:11 230:16 232:3 252:4 253:10,11,12 254:15,20 255:4,8 255:14 256:3,7,9 256:12 257:5 262:1 264:10 274:3 285:7,8 301:18 361:6 373:6 377:5 378:15 379:3,5 peoples 232:18 people's 253:5 perceive 155:14 perceived 127:7 128:16 180:11 184:10,19,20 227:15 percent 96:3 105:19 120:2,3 259:17 261:19 262:1 264:10 282:15 283:19 287:21 percentage 131:11 285:4 percentages 146:20 perception 126:4 140:11 perceptions 37:10 perfect 28:2 300:18 perfectly 250:18 perform 69:1 240:14 performance 127:13,15 128:15 218:9 244:15 249:1 250:13 274:12 276:9,20
---	--	---	--	--

period 17:13 106:3 189:3 255:12 256:5 Periodic 182:14,16 periodically 73:8 75:6 permanently 192:9 permits 11:13 permitted 203:1 354:7 person 60:10 141:1 255:17 369:17 personal 249:13 personally 362:21 perspective 170:7 178:20 254:9 287:5 288:11 305:16 336:16 339:20 341:6 342:5,5 362:1 perspectives 103:1 164:12 pertains 367:6 petition 207:19 petitions 204:13 Pharm 5:11 pharmaceutical 2:12 19:10 21:5 35:17 84:2 99:16 111:16 113:22 114:8,10 128:3 186:16 187:6 192:6 211:22 213:19 214:12 297:11 pharmaceuticals 2:20 116:8 164:18 pharmaceutical-... 162:3 pharmacies 71:6,9 80:11,21,22,22 119:14,15 170:11 170:19,22 174:5 175:4,13 176:22 177:15 195:7,15 214:7 222:18,18 269:6 270:18	287:15,17 289:8 289:20 290:16 292:22 294:21 295:2 296:14 304:19 305:15 306:2 308:6,15 309:2,3 310:3,16 311:13 314:17 329:13,13 331:8 332:18 339:7,11 339:13,17 341:1 345:14 346:11,22 347:21 348:9 350:1 351:8 353:5 353:10,22 354:9 356:20 361:2 363:20,21 370:6 370:10,17,18 pharmacist 65:13 77:10 123:8,9 124:15 125:6 213:14,15 233:18 271:1 273:9 290:6 290:19 295:14 297:12 307:7 309:22 311:9 313:2 316:19 324:6 330:11 333:22 337:21 339:4 345:10 349:2,4,12 354:11 361:7,11,16 362:21,22 364:6 370:2 372:13 pharmacists 3:11 3:13,16 58:5 127:8 170:16 171:21 172:13 177:8,15 178:1 183:4,13,13,15 185:11 187:10 192:13 213:9 214:14 228:9 229:3 234:3 268:6 268:11,14 269:1,5 270:6,12 272:3,8 287:19 288:21	294:21 295:1,5,8 295:11,18 297:3,8 297:11,14 303:8 303:13,14,18 304:6,19 305:2,6 305:12,21,22 306:9,19,21 307:9 307:13,21 310:9 311:13,14,19,22 312:1,15 316:5 317:9 318:1,8,11 320:21 326:19 332:9 336:7 339:1 339:8,18 343:17 343:19 356:9 361:9 363:1,3,12 363:18 364:7,18 365:6,15 367:2 370:12 371:12 375:20 pharmacokinetics 363:11 pharmacovigilance 179:2,12 181:6,21 182:19 186:22 228:21 pharmacy 3:18 48:6 53:17 59:5 76:18 77:3,4,11 79:21 107:19,22 108:9 119:5,18 121:15,17 122:2 128:10 152:13 170:2,8,12,13,17 170:18 171:13 173:19 174:9,18 175:3 176:19 177:4 211:9,11,12 212:14,20 214:3 222:14,20 223:16 230:20 270:11,15 270:16,22,22 272:22 273:2,6 286:19 287:6 289:2 292:21 294:8,22 295:13 295:22 296:1	297:7 298:20 304:22 306:2,12 306:13 309:6,15 311:20 312:2,3,6 312:8,11,12 313:9 313:13 314:1 318:7,11,12 324:16 328:8,12 330:10,11,14 331:16 332:7 339:22 340:19 341:10,17 347:13 348:3,5,9,21 349:6,8,14,17 351:9 352:19 353:1,1,6,15,20 354:18 360:21 361:12 363:21 371:2,3 372:15 375:16 pharmacy-specific 312:13 Pharm.D 1:18 2:1 2:19 3:12,19,21 4:21 5:12,16,17 phase 94:4 phases 39:21 philosophical 181:16 philosophy 182:7 182:11 phone 60:11 88:21 88:21 309:20 phones 6:17 68:19 PhRMA 2:12 83:15 83:21,22 84:7,13 84:16,18 85:5,13 85:17 86:4,6,12 86:18 87:15,21 88:1,8,13 89:3,9 90:19 104:5 Phyllis 2:17 4:17 131:16,20 139:15 150:4 physician 44:15 63:4 103:21 178:21,22 215:8	228:8 236:1 238:8 238:11 242:8 243:8 244:16 251:2,2 270:1 275:9 276:7 278:17 348:19,22 353:7 physicians 3:2,4 58:3,4 96:8 167:13 187:10 192:12 214:14 223:1 228:9 235:18 236:1,5,6 239:11,12,17 240:14,16 241:3 241:12,13 248:4,4 251:4 252:5,16 253:17,22 254:3 268:8 274:16,17 274:21 276:14 278:3,4,22 279:22 physician's 213:20 physiological 133:11 Ph.D 1:19 pick 44:3 PICME 244:21 picture 38:19 piece 51:4 278:18 279:9 pieces 32:5 55:8 59:11,13 276:12 277:19 366:7 pills 255:17,22 258:11 pilot 107:14 299:4 piloting 193:22 pilots 111:8 pinpoint 113:18 pinpointing 193:20 place 28:5 34:16 35:4 43:12 47:12 49:18,20 63:1 67:5 95:8 101:4,9 114:16 137:7 138:9 141:22 154:2,5 156:20
---	---	---	--	--

157:1,7 182:9,15 227:10 231:8 265:1 267:11 272:4 295:4 296:11 350:1 351:17 352:4 370:9 371:21 placed 311:3 places 356:5 placing 311:1 plain 69:18 plan 53:20,21 102:12 103:9 129:12 144:10 145:8 181:21 182:19 200:14,16 203:1 228:22 229:7 257:21 259:3 260:6,15,17 262:7,12,13 planning 7:13 13:1 94:3 116:13 258:2 377:18 379:5 plans 42:15 96:5 97:9,10 128:2 130:21 144:9 145:16 242:3 plan-only 145:6 platform 190:5 195:12 308:9 313:8 platforms 87:22 303:17 375:6 play 71:19 92:15 192:4 239:12 268:11 297:15 329:9 played 190:9 playing 377:6 plays 76:2 please 8:8 57:19 162:9 212:11 222:6 235:15 379:16 pleased 239:5 240:6 319:7 pleasure 254:2	plus 8:19 212:2 345:22 366:4 PMI 96:17 143:16 144:21 145:12 point 12:16 15:17 29:4 35:21 48:10 49:1 54:6,14 55:19 83:12 122:8 122:12 123:7 124:18 126:18,22 129:8 140:9 147:14 148:9 153:15 155:21 156:4 166:15,18 174:13 175:1 177:5 179:3 186:3 186:4 192:7 201:19 204:10 207:7,13 208:15 212:9 216:22 217:6 220:10 221:6 231:20,22 301:22 314:2 341:20 374:15 pointed 154:10 313:9 373:22 points 94:10 118:6 120:12 125:3,5 139:20 147:6 152:19 171:7 194:15 216:5 295:3 350:9 355:20 policies 122:11,13 123:21 138:9 159:4,9,19 239:15 296:2 343:6 policy 1:18,25 2:2 14:3,17,20 21:15 21:20 24:2,11 25:1 103:22 122:11,17 123:16 123:17 124:8 138:18 155:17 156:10 188:8 239:7 287:11 Pomalyst 103:15	105:11 353:9 pool 339:17 poor 264:8 poorly 285:13 population 92:14 119:22 120:3 165:19 166:3 167:4,8,9 168:7 184:19 185:8 246:7 274:14 275:9 285:5 populations 35:7 85:21 104:2 192:20 261:14 274:5 322:19 334:22 portal 63:15 68:20 90:7 121:12 174:3 195:18 293:6 314:15 374:9 portals 50:1 121:11 195:13 225:22 226:1 231:16 portions 213:6 pose 137:12 175:12 posed 26:11 85:19 345:17 346:4,21 poses 230:12 position 82:1 198:14,17 238:2,4 238:10 239:3 309:5 370:1 371:16 373:13 positioned 336:5 positive 56:6 120:19 142:8 330:7 possibilities 13:6 possibility 298:21 299:18 348:8 356:19 possible 48:8 86:11 86:21 93:9 108:16 116:21 129:9 149:1 153:17 160:4 185:14 186:2 190:5	227:19 240:15 298:17 302:17 327:7 333:20 342:14 355:16 369:9 374:21 possibly 229:7 256:17 posting 167:21 232:7 379:13 postmarket 189:2 postmarketing 179:6,12 180:7 181:1 182:22 367:16 368:1 post-assessment 244:17 post-market 92:6 post-marketing 229:9 post-test 312:19 pot 225:1 potential 9:15 91:15 92:17 94:7 94:17,20 121:5 122:1 125:15 126:21 129:11,14 130:15 143:17 152:2 165:20 167:12,19 168:4 184:18 198:13 201:20 231:8 258:22 278:3,8 306:15 320:13 321:4 353:3 365:8 potentially 41:7 74:22 127:3 137:12 139:6 210:1 263:11 348:10 350:5 355:17 PPAFs 64:22 67:2 67:13 practicable 190:5 practical 99:14 343:6 practice 37:5 53:18 87:19 93:15 98:21	113:12 119:13,19 127:9 136:2 160:1 162:1 191:13 198:2 213:2 236:2 242:13 243:12 247:4,7 248:3,20 251:17 268:22 274:2,20 276:7,20 278:2,4 280:11 282:9 283:9,14,19 283:21 284:3 285:17 286:19 297:7,12 304:21 305:1 306:13 318:7 327:19 361:17 364:20 375:3,10 practiced 362:22 practices 35:16,20 37:7 38:11,15 39:13 40:14 41:5 41:8 50:11 54:3 54:18 55:16 56:10 57:13 63:7 71:3 79:11 81:2 98:17 99:13 106:10 110:18 112:7 150:16 159:10,18 160:20,21 161:11 162:9 193:17 233:12 257:9,13 274:17 276:19 278:5 319:17 365:17 practice-based 250:7 practicing 243:15 268:21 269:1 361:14 practitioner 270:2 293:19 326:3 practitioners 54:17 72:4 88:6 98:10 108:7 177:22 192:20 268:19 292:14 293:2,22 325:20
--	--	---	--	---

pre 95:13 168:16 179:6 180:6 244:16 precision 284:5 predate 135:16 predict 246:22 predictable 38:2 85:15 93:3 predicted 92:11 predictors 193:18 predisposing 247:3 preemptive 112:13 prefaced 143:12 prefer 69:11 265:21 preferable 151:15 preferences 62:15 preferred 242:12 278:12 pregnancies 138:8 pregnancy 173:4 218:11,14 pregnant 218:6,7 premarketing 179:11 182:21 preparation 378:21 prepare 299:7 preparing 13:1 244:2 377:22 preprints 222:4 prerequisite 238:15 prescribe 192:20 prescribed 58:3 218:7 255:22 262:3,5 309:9 320:14 337:3 prescriber 3:1 5:3 44:12 57:7 59:22 60:6 61:17,18 63:5,16 64:19,21 66:18 67:14,15 72:17 74:11,20 81:17 89:4,9,11 90:11,13,16 101:10 105:12 123:2 125:5	141:10,11,13,17 166:3 167:4 168:7 169:4 173:5 174:9 174:18,22 226:20 235:7 245:10,19 246:5 248:5,13 250:10,21 251:14 251:21 252:13 265:12 269:11 270:14 272:5,7 278:6,17 280:15 298:16 316:18 324:19 352:5,8,13 355:12,14,16 356:11,17 370:13 prescribers 18:21 43:22 48:10 51:22 53:16 65:18 66:3 67:9 70:18 89:16 89:18 90:5 106:13 106:22 142:2,5 158:12 171:21 172:9,13 174:4 177:8,16 183:4 218:21 219:16 221:20 240:11 250:6 253:16 258:14,18 263:12 263:22 265:10 268:8 281:18 285:2 292:21 294:6,16 300:8,10 305:6 314:17 316:5 356:9,20 371:22 372:4 prescriber's 18:22 prescriber-direct... 4:6 51:20 57:10 57:20 prescribing 3:5 60:4 61:7 108:5,7 172:9 191:3 194:21 218:12 239:14,16 243:7 253:17,22 254:4,7 256:22 257:9,13 258:15 259:15	269:22 292:19 311:5 316:20 352:7 prescription 122:22 123:4,9 133:20 134:1,13 141:14,16 157:2 223:8 238:13 239:10 241:6 290:1 291:13 292:5 308:1 311:6 314:9 340:17,21 347:12 349:5,5,19 351:4,10 360:9 363:10 prescriptions 119:16 170:12,15 191:16 211:20 212:22 287:20,21 289:8 313:11,22 351:13 presence 249:8,19 present 18:5 64:14 74:14 76:8 194:11 241:14 263:16 318:19 378:6 presentation 9:1,2 9:3 58:13 70:2,11 70:16 72:21 155:6 169:14 216:5 219:3 231:6 277:2 presentations 8:2 11:10 12:1 18:2 21:19 25:18 52:22 81:16 83:6 157:18 161:14 162:14 374:19 376:20 377:7 presented 23:21 104:5 259:4,19 260:8 280:19 presenter 83:15 253:21 333:14 presenters 10:3,6 11:2 378:16 presenting 89:3 preserve 36:3	preserved 113:7 preserving 99:3 president 109:1 131:20 211:7 254:3 287:11 297:7 presiding 1:14 press 260:13 pretesting 20:13,14 pretty 7:20 157:18 165:15 166:5 168:21 255:14 prevalence 176:13 255:11 274:13,16 282:20 prevent 22:22 111:5 202:5 218:3 221:14 271:21 350:5 352:12 preventable 190:16 prevented 191:7 212:7 preventing 359:4 prevention 2:6 13:12 218:13 previous 27:10 33:14 39:14 59:13 70:22 95:8 231:5 previously 69:7 309:1 331:17 332:20 353:14 pre-NDA/BLA 94:11 pre-tested 69:20 price 261:10 primarily 95:18 98:5 120:1 219:12 345:20 primary 239:12,17 268:7 269:2 306:20 330:10 354:4 359:13 principle 78:15 153:5 principles 54:12,15 69:18 93:6,15 98:21 99:6,8	113:7 117:16 142:15 print 60:11 62:14 64:16 65:21 68:18 printed 66:13 prior 11:2 60:4 64:7 69:21,22 88:16 99:22 124:10 188:17 206:20,21 253:9 294:11 priori 249:5 prioritization 153:7,9,18 prioritizes 112:16 priority 8:15 26:20 31:12 40:22 50:17 53:8 54:4,8 98:3 288:14 376:13 private 84:10 198:2 privilege 189:1 proactively 94:19 112:10 325:20 probabilistic 112:1 probability 246:22 295:16 probably 7:4 44:6 150:5 198:21 227:10 252:10 259:9,21 262:4 279:14 302:3 359:21 378:17 379:9,11 probe 139:22 problem 29:3 115:18 141:16 181:4 241:5 252:20 278:9 334:9 336:13 338:6 340:4 problems 246:10 369:10 procedural 243:15 procedure 122:12 122:17 123:17,18 124:1,12 155:17 156:10 209:5,8
---	---	---	--	---

224:12	101:4 142:9 154:5	101:18 106:15	13:16 19:6 35:11	378:22
procedures 101:4	156:19 157:1,5	130:11 137:11	58:15,16,19,22	programs 1:20
122:11 123:21	158:11 165:2	144:16,18 176:16	59:7,21 60:5	14:7 21:8 42:17
124:7 159:4,9,20	171:15 172:19	184:3 188:20	61:17 62:3,5 66:2	57:14 59:13,16,18
296:2 307:22	173:11 174:10	192:8 195:20	66:7 67:6 68:2	60:8,14 62:22
325:7 364:17	176:15 177:15	196:1,16 202:10	89:19 93:18 94:1	63:7,10,11,13,15
proceed 194:9	189:18 192:1	207:1,12 237:19	94:8,13 95:1,5	64:9 67:20 68:12
proceeding 82:20	193:16 216:17,20	253:18 271:20	97:4 99:2,20	84:19 85:8,12
286:12 380:6	217:12 233:20	273:1,5 275:1	100:3,9 101:8	87:3,14 92:15
process 20:9 39:21	251:19 270:15	283:22 304:9	102:3 103:15,19	93:13,20 95:18
62:7 71:20 74:1	292:2,20 293:19	309:7,13 311:1,3	104:13,19 105:1,1	96:15 97:14,19
74:15 76:2 77:19	293:20 300:9	311:6,8,15 360:19	106:1 118:2 129:9	98:14 101:13,18
79:22 87:11 88:20	307:21 308:3	product's 15:22	129:19 130:17	102:11 103:11,16
94:22 112:11	322:4 323:3	86:2 90:9 100:6	131:3 138:16	104:8,17 105:11
113:14,15,16,20	329:21 343:7	product-specific	142:3,21,22	106:17 107:6,12
115:4,6 141:3	350:20 352:2	99:5 175:10	143:22 146:4,16	108:11,17 109:14
144:20 148:11	356:3 364:15	192:15	146:17 153:8	130:18 138:13
152:20 169:3	371:21	profession 248:7	178:11 179:11	139:8 141:12
178:12 188:19	processing 105:19	364:22 366:9	187:7 189:12	143:6 146:7
203:21 207:2,6	107:3	375:16,18	199:18 200:9	150:12 152:10,11
208:8,22 209:20	procure 340:6	professional 59:6,9	201:1,6 204:5,21	153:3,6 159:8
210:4 213:4	procured 340:19	87:1,20 115:10,14	205:4,11 206:20	169:6,7,10,21
214:16 215:5,10	procurement 52:18	115:20 161:6	207:10,11 208:12	170:9 171:3,4,8
217:9,13,17 223:5	77:19,22	187:3 228:6	208:17 209:12,16	171:11,18 175:7
223:21 234:5,10	procuring 74:1	229:19 239:18	209:17,22 210:12	176:1 177:3 178:2
248:16,18 249:9	produce 58:9	247:7 248:3,20	218:18 219:5,19	178:8 189:5,22
269:20 272:6	produces 302:22	250:9 251:8,17	220:9 223:4 225:3	192:16 193:13
275:20 276:8	product 22:6 46:8	274:2,20 282:9	225:5,8,14,16	194:3,10 195:8
282:16 283:7	46:10 65:9 92:5	283:8,13,20 284:3	227:16,16 230:1	198:22 199:2
286:7 293:1 294:7	92:12 94:4 112:10	305:20 318:9	232:8 233:6,7,8	200:6 202:11,13
295:21 302:11	121:22 137:16	364:11	234:8 240:4	202:16,17 205:21
304:2,3 306:4	149:22 165:12	professionals 58:2	241:17 260:21	206:19 211:17
313:1,12 314:16	166:9,13,15	111:17 161:17	263:22 277:12	212:1,2,17 219:6
315:18 316:10	172:16 179:10,20	186:6 187:19	294:15 297:21	219:11 220:9
317:14,16 321:2	180:18 181:11	188:1 213:8,10	303:8,22 307:19	225:9,15 231:14
322:6,8 328:4,15	191:1 192:16	228:15 230:2,4	310:10 311:2,4	233:19 238:14
329:15 331:12	195:3 196:3 207:3	247:4 268:4	313:3,15 315:9	241:21,22 245:18
333:3 335:17	218:6 230:11	271:16	316:9 330:6,16	262:10,19 263:15
340:22 342:16	231:7 270:6 292:6	profession's 252:19	331:1 333:12	268:13 275:19
344:15 351:11,17	292:14 296:15	Professor 109:2	335:19 336:21	285:15 292:5
356:6 357:1	310:16 312:4	profile 92:17	337:2,17 347:21	294:14 297:17
359:18 366:5	316:17 360:10	153:14 167:15	348:14 349:9,12	298:6,8 299:4,19
370:8 372:4,11	production 170:4	270:9 337:4	351:3,5,7 352:3	300:4,7,17 302:10
379:8	productive 84:5	profiles 175:8	352:17,20,21	302:19,20 303:4
processes 20:4 22:4	377:20	215:12,15	353:22 354:8	306:8,14 308:9
33:12 62:20 73:17	products 86:9	profoundest 189:3	356:11 357:3,6	309:8,18 312:14
79:1,4 80:15	91:13 98:19	program 1:19,23	370:8,9 371:20	312:17,21 314:9

314:20 318:2 320:4,19 325:21 328:2,17,21 329:7 329:10,17,22 330:4,17,21 331:9 331:12,14 333:7 337:7 345:13 346:15 347:20 350:14,19 351:3 351:21 353:8,12 353:20 355:3 356:1 357:12,15 357:21 370:5 371:18 373:21 program's 352:10 357:5 program-specific 101:3 303:16 progress 96:12 144:12 297:22 Prohaska 2:4 14:21 14:22 prohibited 268:6 project 27:15 53:13 53:21 projects 8:14,15 9:15 26:20 28:17 31:12 41:1,7 50:17 53:8,9,16 54:4,8 88:9 91:15 98:3 107:14 376:22 380:1 prominent 262:22 promise 118:4 promising 57:13 63:7 71:3 79:10 79:11 81:2 promote 85:4 99:2 253:9 promoted 87:18 promotes 94:13 promoting 252:15 253:2 promotion 249:16 prompt 27:1 proof 144:7 PROP 254:3	propagate 48:8 proper 101:5 317:10 properly 100:2 258:9 265:3 proportional 136:10 proposal 120:9 337:14 proposals 95:11 122:10 propose 126:2 149:18 proposed 35:13 105:4 178:9 181:1 181:2 260:7 263:9 proprietary 208:11 protect 131:8 267:9 protected 200:7 202:15 protecting 84:14 130:13 protection 131:10 protections 139:6 protocol 215:11 331:18 protocols 213:1 214:11 215:2,13 329:18 332:11 335:13 proven 107:16 118:11 316:2 provide 9:11 10:18 16:18 25:2,12 30:17 42:16 53:2 57:9 59:18 64:4 64:10 65:7 72:1,2 75:2,2 80:4 88:5 91:10 107:12 108:12 123:2 125:8 126:13 134:11 139:13 169:20 170:6 178:19 182:13 195:19 203:20 204:7 206:8 209:7 210:13,21 214:13	215:10 226:3 227:7 249:11,12 265:14 271:1 278:15 280:5 300:5 302:21 306:21 310:18 313:20 317:20 318:12 320:16 324:21 326:7 327:16 329:20 330:1 335:9,11,18 337:5 338:1 339:14,15 341:15 342:3,9 343:1 346:6,13 351:17 353:4,17 360:2 363:15 365:3 367:3,13,17 376:4 provided 65:13 66:9,21 108:6 111:10 205:1,9,16 207:13 208:20 210:20 236:16,20 269:18 288:21 307:7 308:10 309:20 312:10 341:2 provider 18:13 23:12 59:8 61:20 63:14 64:20 65:14 66:10 67:14 68:7 68:13 69:8 76:5 89:22 96:4 152:13 170:8,12 174:12 178:3 212:14 240:3,6 276:2 300:19 301:17 302:13 303:19 310:14 312:6,22 313:2 315:3,8,12 320:18 325:14 327:9,14 340:15 providers 18:9,10 18:15 35:5 43:7 47:20 48:11 49:15 51:22 54:21 57:15 57:16 58:1,8,21	59:4 60:2,15 62:2 63:11 65:18 66:14 66:22 87:1 115:22 121:7 127:8 128:16 135:14 143:10 145:12 146:12 175:13 177:22 195:14 246:2 249:2 280:13 282:8,14 288:6 298:13,22 299:5,7 304:15 319:5 324:7,13 326:17,19,21 327:2 338:7 343:22 361:21 363:8 provides 48:1 94:8 97:11,17 106:15 135:11 161:21 176:20 289:12 294:18 302:20 308:20 336:19 providing 53:16 67:8 70:11 102:22 105:17 130:8,19 131:10 149:6 176:4 205:20 211:13 290:17 307:13 374:22 proving 322:16 provision 288:7,7 289:1 291:2 307:21 376:15 provisions 205:14 proxy 23:11 psychiatry 124:5 public 1:6,12 6:5 7:5,22 8:4,9 10:4 11:19 17:16 27:2 27:6 31:9 46:17 47:20 50:15 82:8 82:9 85:4 96:20 104:6 129:6 131:4 132:3 136:5 190:13 194:4,5 196:13,22 203:12	206:8 210:10,13 236:13 237:15 238:3 239:8 247:18,19 263:5 267:9 287:11 297:4 303:9 305:3 306:5 374:8 377:4 377:15 publication 137:20 publicly 27:5 87:10 306:6 published 113:8 220:3 publishing 245:2 pull 373:13 pulled 282:19 pulling 245:1 purchase 326:12 purports 147:9 purpose 9:5,9 10:6 29:7 65:6 66:1 202:6 212:13 293:12 purposes 72:20 108:6 pursue 376:14 pursuing 107:17 push 186:18 194:22 301:14 put 9:7 11:5 12:19 28:5 29:12 35:4 36:1 38:18 40:10 51:15 101:4 114:15 130:11 156:20,22 157:6 162:17,19,21 164:14 208:13 259:7 266:1 337:13 puts 338:14 putting 15:4 49:17 159:22 P&T 187:17 P-R-O-C-E-E-D... 6:1 p.m 164:2 286:12 286:13 324:8
---	---	--	---	---

334:5 380:5	280:9 286:1	355:13	183:21 233:10	332:14
Q	296:22 297:22	reading 69:2	274:10	recommendations
Qs 221:2	324:11,15 345:17	243:21	reasonable 209:14	104:5 105:21
qualified 119:9	346:21 358:15,17	ready 261:4 379:13	344:7,22	132:9 168:12
336:5 343:20	366:13 371:11	real 32:17 55:1	reasons 34:17	238:5 243:4,22
quality 38:10 88:9	374:1,15 377:15	109:12 270:19	115:15 151:11	329:20 330:1
113:9 152:20,21	queue 153:20	285:1 341:20	184:8	368:22
153:6 170:1 180:3	quick 39:15 63:12	realities 194:19	reassessment	recommended
180:18 187:17	122:4 152:19	realize 133:16	153:13	138:9,14 343:13
196:11 283:12	159:2 197:21	221:12 263:17	reauthorization	recommends 86:12
322:3,6 337:9	quickly 333:20	really 6:21 13:4	23:21	98:20 302:7
quantified 224:20	quite 40:1 144:14	15:19 16:15 20:3	receipt 311:18	315:19 322:4
quantitative	185:5 228:7	20:21 22:16 27:9	322:14,20	reconcile 150:19
138:15	330:14 332:4	27:19 28:12,13,19	receive 18:19 67:20	151:3,6
quantity 176:7	quotes 18:6 28:11	32:1,14 35:3	92:22 111:12	reconciled 283:17
question 140:5,19	259:7	36:14 37:17,21	153:10 201:5	283:17
142:12 143:18	R	39:4,20 40:2,15	271:4,6,20 289:7	reconvene 380:7
144:6 146:1	R 3:19 5:16	40:22 41:5,19	307:7 312:15	record 74:13 82:20
148:16 150:3,13	racial 246:13	42:16 43:13,17	330:20 349:11,16	82:21 121:15
150:22 155:7	raise 326:14	44:22 45:4,19,22	350:6 359:19	122:3 123:10
156:10,22 157:20	raised 216:5 231:6	48:14 49:10 52:9	received 17:15	127:1 155:20
158:1,21 159:4,15	ramifications	54:11,18 55:19	68:10 71:2 79:13	156:4,7 174:20
160:15 162:15	204:17 210:21	56:1,6 57:22	176:9 233:13,15	223:2,2 244:12
165:12 166:7	ran 348:16	113:5 116:12	233:17 259:16	286:12,13 335:13
215:3 216:4 220:6	Randi 378:19	144:11,21 145:7	335:5 354:17	338:10,20 346:12
220:20 222:11	379:3	145:18,20 155:14	receiving 291:5	347:7,14 349:1
223:19 227:13	range 50:2 71:5	159:21 161:13	recess 163:5	367:21 372:3,7
231:5 233:4,4	85:20 112:19	168:8,15 169:3,5	recipient 183:17	records 47:4 48:6
272:16 273:15	226:8 275:7	185:4 199:9	recipients 335:2	50:5 76:19 120:15
275:3,4,14 276:22	282:22 283:1	202:17 203:7	reciprocal 279:14	172:10 194:22
280:2,7 281:20	ranges 274:17	205:3,12,22 206:6	recognition 114:14	197:6 276:13
282:2 284:12	rate 133:14 165:22	206:8,13 207:6	253:9	298:19 327:13
286:10 358:17	254:14,19 282:15	208:10,19 214:4	recognize 101:7	332:7
371:9 374:10	rates 254:15	219:8 223:4,5	104:12 108:15	record-keeping
375:1 376:11,21	rationale 227:18	228:1 231:5 237:4	137:8,10 248:1,15	325:17
questions 4:18,25	228:18	244:8 261:12	255:13 257:8	red 12:11 83:10
5:7,19 10:18	reach 253:8 322:17	279:17 284:18,22	268:10 307:6	254:18 255:3
11:12,15,17 12:7	reached 36:9 302:1	285:6 286:6 339:3	320:2,12 379:6	256:8 257:4
21:21 23:5 26:11	react 20:14	355:3 357:11	recognized 85:22	redesign 116:10
28:4 34:5 42:18	reaction 133:20	363:7,13 365:2	336:18	Redesigning
51:19 53:2,4	read 10:11 20:17	373:5,9	recognizes 289:11	105:16
56:22 83:6 139:19	157:9	real-time 173:18	recognizing 114:21	redistributes
139:21 140:3	readability 65:12	174:17 195:19	121:16 317:21	271:10
153:22 158:19	67:13 69:12	225:22 226:3	recommend 146:9	reduce 16:14 62:20
215:20 226:4	readable 122:15	reason 34:2 82:6	168:13 172:11	63:4,15 88:14
229:12 272:13	readily 351:20	94:7 115:13	173:12 314:14	103:21 105:15
		130:12 166:1	316:14 331:11,13	121:6 127:7

128:15 129:13 152:1 183:5 254:5 258:11 267:8 271:21 reduced 105:18 190:16 191:7 216:10 reduces 107:2 reducing 31:10 98:9 217:15 288:4 298:12 311:7 317:5 redundancies 96:20 114:16 325:16 redundancy 111:8 118:3 327:6 redundant 117:17 169:7 reenrollment 174:6 reevaluated 328:17 refer 33:13 73:2 77:8 360:17 reference 49:1 103:7 201:7 204:7 205:16 291:21 293:8 346:2 350:8 355:21 references 234:20 reference-listed 204:11 205:2,19 210:17 224:13 referred 64:21 67:2 119:20 124:3 233:9 288:17 referring 214:3 360:19 refilled 348:20 refinement 327:15 reflect 194:18 297:22 reflective 180:17 250:8 reflects 251:1 regard 142:14 143:1 219:11 277:7 361:6	369:11 regarding 93:15 94:6 98:21 103:1 132:6 134:18 231:16 300:17 302:21 305:4,16 311:12 317:13 342:15 344:14 regardless 171:13 196:2 310:7 regards 63:16 370:15 371:18 372:11 regimens 270:18 regional 161:18 246:8 287:15 regions 326:2 register 9:12 10:19 26:12 34:6 51:16 57:1 226:5 324:17 324:18 346:4 376:21 registered 12:4 236:18 356:20 registrants 245:20 registration 299:15 314:18 323:3 325:13 registries 260:3 293:18 registry 215:8 258:7 294:13 313:22 357:17,19 Regrettably 180:21 regular 193:6 270:16 300:10 379:6 regularly 17:14 regulate 304:21 306:13 regulated 86:7 112:2 309:2 regulation 238:12 regulations 181:7 regulator 178:21 192:22 229:18,18 regulatory 1:24,25	2:2 14:2,19 42:13 42:18 180:16 188:8 196:14 287:11 306:17 328:11 331:13,21 reimbursed 375:22 reimbursement 290:19 376:5 Reimbursing 290:16 reincorporate 167:11 reinforce 62:6 67:16 270:4,7 reinforcement 18:17 269:17 reinforcing 247:3 290:4 reiterate 138:19 306:11 reject 260:15 rejection 234:11 rejects 260:16 related 18:2 23:10 31:6,16 50:14 51:17 60:22 77:13 91:22 99:10 109:22 123:5 137:22 145:21 148:17 151:8 159:3 237:9 271:2 317:10 319:22 376:22 relates 30:6 55:18 89:18 315:7 relating 136:6 321:8,14 relation 182:3,18 184:6,9 185:14,16 187:5,13 220:15 220:18 221:19 228:10,12 229:7 229:20 230:10,17 267:5 relationship 20:4 186:7 269:12 307:10	relationships 249:18 343:16,21 relatively 21:6 35:18,19 117:21 172:22 186:11 release 95:4 104:21 173:16 238:19 240:8 246:20 262:8 308:20 320:7 released 17:8 147:13 165:5 166:9,15 167:20 168:1 238:1 257:22 328:19 340:12 relevance 184:12 184:16 185:22 relevant 49:18 78:22 96:8 184:15 185:18 186:1 240:22 249:18 302:21 303:3 343:12 reliability 284:6 reliable 191:11 253:9 reliance 100:19 101:12 reliant 197:4 relief 239:20 reluctant 19:5 relying 234:2,5 291:3 REM 86:9 102:7 128:9 130:3 remain 8:13 26:15 87:11 319:9 remainder 123:6 remaining 96:3 141:3 remains 84:19 138:21 181:2 237:21 239:15 321:20 Remarks 5:21 Remarks/Overvi...	4:3 remedy 195:8 remember 107:6 244:20 366:14 remembering 234:3 282:1 remind 237:6 reminded 19:15 reminders 107:2 115:19 301:14,14 removed 348:8 removing 216:15 REMs 1:4 3:7 4:3,5 4:6,8,10 5:8 6:6 9:8,11,14,16 10:14 15:2,6,10 15:17 16:3,10,11 16:14,20 17:1,3,6 17:8,9,11,14,20 18:3,11,14,15,21 19:14 20:1,6 21:4 21:8,15,22 22:2,9 23:11,13,14,17,19 24:3,3,5,7,12,14 24:17,18 25:1,4 25:11,14 26:4,8 27:12 28:5 29:17 30:1,2,4,6,7,9,12 30:20 31:6,9,10 31:18,21 32:6,7,8 32:10,22 33:5,7 33:11,16,17,19 34:1,1,3,8,15,18 35:3,4,9,11,12,16 35:18 36:1,11,15 36:17,17,18,20,21 37:2,4,5,7,11,17 38:2,13,15,21,22 39:1,4,6,8,9,14,19 40:3,4,5,7,12 41:2 41:4,6,10,12,12 41:15,20,21 42:1 42:4,7,9,13,17,19 42:21 43:4,5,9,13 44:2,2,14,18,22 45:4,5,7,10,11,13 46:1,6,7,19,22
--	--	---	--	---

47:2,8 48:4,14,15	104:19 105:1,10	175:2,5,7,14	265:2 266:5,21,22	336:11 337:1
48:16,18 49:2,6	106:1,6,10,14,17	176:13,14,18	267:11 268:1,5,5	339:21 341:3
49:11,13,14,17,18	106:18 107:3,6,7	177:2,7,10,12,17	268:13,15,16	342:13 343:3,5,8
49:22 50:1,2,9,22	107:11,13,16,19	178:1,8,9,10	270:11,14 271:2,5	345:9,13,18
51:3,4,9,13 52:3,9	108:1,5,7,9,11	179:9,10,16,22	271:18 272:1,9	346:15,18 347:16
52:10,15,16 53:11	109:5 116:9,10	180:10,15 181:9	277:8 281:7	347:20,21 348:14
54:5,7,22 55:2,5	120:8,10,17,17,21	181:14 182:20	286:17 288:2,5,9	348:17 349:3,9,12
56:7,13,15,16,21	121:2,9 122:10,19	183:2,6,8,10,16	288:13,21 289:14	349:19 350:11,14
57:8,11,14,17,21	123:6,19 124:5,18	183:20,22,22	290:16,20 291:3	350:18,21,22
58:10,12,15,15,16	125:7,16,22 126:2	184:5,8,14 185:7	292:1,1,6,11,12	351:3,21 352:2,3
58:17,19,22 59:7	126:5 127:5,11,18	185:16,21 186:8	292:19 293:2,5,7	352:10,16,17,20
59:10,13,16,18,20	128:6,8,11,17	186:15,17 187:2	293:9,14,16 294:1	352:20 353:8,19
59:21 60:8,14,21	129:9,18 130:10	187:20 188:12,18	294:3,4,17,20	354:6,8,14 355:3
61:11,17,22 62:3	130:11,17,20	189:9,12,22 190:6	295:5 296:6,7,10	355:21 356:1,3,10
62:5,22 63:3,7,8	131:3,8,9 132:6	190:18 191:5,21	296:12,20 297:17	356:14 357:3,5,6
63:10,10,13 64:2	132:20 133:17,22	192:1 193:13	297:20 298:5,6,8	357:12,15,20
64:5,9,15 65:1,6	134:22 135:7,9,10	194:14,18 195:4,8	298:15 299:11,13	358:6,11,21 361:1
65:16,21 66:1,2,7	135:16,16 136:4,7	198:19 199:1,8,11	299:19 300:4,6,9	362:2,4,12,17
67:6,20 68:2,12	136:20,22 137:14	199:18 200:11,21	300:17,18 301:4	363:18 364:3
69:5,6,9 70:4,9,13	137:19 139:8	201:4 202:3,11	302:10,11,17,21	365:11 366:5
70:20 71:21 72:3	140:7,11,14,18	203:4,8,14 204:5	303:3,7,13,20	367:8,14 368:4
72:9,10,12 73:9	141:12 142:9,15	204:10 205:21	304:20 305:4,8,18	370:2,4,7,9
73:18 74:2 75:12	142:18,19,20,22	206:10,11,19,22	306:8,14 307:19	371:18,20 372:12
75:16,17 76:19	143:6,21,22 144:7	207:5,9 208:5	308:3,7,19,22	372:16 373:15,21
77:18,21 78:2,7	144:16 145:5,6,9	209:12 210:10,12	309:7,13 310:3,7	374:7,7 377:10,11
78:16,19 79:1,5,8	145:14,21 146:6	211:17 212:1,2,10	310:10,21 311:14	378:17,20
79:16,17,20 80:3	146:13 147:1,7,15	212:13,22 213:6	312:4 313:7,12	REMS-dedicated
80:5,10,17 81:3	147:16,18 148:8,8	214:18 215:2,6,10	314:12,19,21	65:15 66:11
81:14,15 84:15,19	148:18 150:11,15	215:13 216:6,16	315:4,9,14,16,17	REMS-related
85:3,8,12,15,18	150:17 152:1,7,10	217:7 219:5,19	315:19,21 316:2,9	15:8 303:12
86:2,3,13 87:6,14	152:11,14 153:3,4	220:7 221:9	316:14 317:4,14	312:21
87:17 88:2,11,15	154:3,7,11,16	222:13 223:13	317:16 318:1	REMS-required
89:1,10,14,16,19	156:14 157:2,4,6	224:19 226:8	319:9,10,11,12,15	279:17
89:21 90:6,8,9	158:5,9,14,17	227:15,16,16,18	320:1,3,6,19	repeat 373:2
91:2,16 92:14,19	159:5,8,11,12,22	228:18,19 230:7	321:8 322:1,11,12	repeated 37:7
93:2,8,10,12,18	160:8,10,11,21	231:2,14 232:10	323:6,9,10,18,20	68:12
93:18,20 94:1,7	161:10,14 165:2,3	232:16 233:19	324:2,9,15 325:9	repetition 18:18
94:17,20 95:1,10	165:5,13,14,17,21	236:22 240:4,9	325:10,13,21	repetitive 169:9
95:16,17,18,20	166:2,9,11,14,14	242:1,21 243:21	327:1,3,10,15,17	replace 308:14
96:2,3,15 97:3,5,9	166:17 167:11,16	245:11,18 246:20	327:19 328:2,15	replicated 38:12
97:13,18 98:4,6,8	167:20,21 168:1	247:19,22 248:13	328:17,19 329:5,7	reply 226:13
98:9,12,14 99:2,6	168:10,18 169:5,9	250:10 252:18,21	329:9,12,15,17,17	report 8:16 26:17
99:10,19 100:9,18	169:21 170:9	253:2 254:10	329:22 330:4,5,16	31:11 50:16 53:22
101:12,13,22	171:4,8,10,18	257:21,22 258:4,5	330:17,21 331:1,9	129:19,22 134:6
102:2,4,10,20	172:6,8,15,20	259:3 260:8,11,13	331:12,14,16,18	137:20 138:9
103:1,11,14,16,20	173:1,13,13,18,21	260:16,21 261:8	332:10 333:7,12	182:9,10,15
104:2,8,13,16,17	173:22 174:1,12	262:8,12 264:19	334:5 335:3,5,19	205:17 239:9

352:19 379:22 reporting 132:16 181:3 187:12 229:10 reports 180:9 182:16 245:2 repository 47:16 48:1 293:6 303:11 314:13 represent 84:10 124:21 236:17 representative 59:5 366:19 369:18 representatives 107:18 130:6 286:18 372:13 represented 194:13 257:4,6 representing 259:20 278:13 represents 84:1 91:19 193:17 256:19 287:13 297:10 305:21 request 311:4 317:12 requested 130:2 requests 310:21 require 38:6,7 72:3 72:10,13 75:19 94:5 137:14 167:16 172:22 173:3 175:21 177:6,20 195:21 196:17 214:17 215:8 229:1 241:3 258:17 322:18 326:10,11 327:14 348:18 350:18 363:18 required 32:11 73:5,11,13,15,16 75:5,7,8,10 78:20 87:6 107:20 117:12 120:16 123:7 146:6 156:11 166:17	177:13 182:1,2,5 189:12 202:3 214:20 215:6 244:18 258:15 272:1 277:14 279:21 295:2 303:21 312:2,6 313:1 314:19 316:8 324:16 325:2 332:19 352:5,6 363:3 364:7,19 requirement 140:11 181:20 271:5 283:10 294:13 347:22 352:22 requirements 41:22 45:14 49:17 57:17 59:1 61:21 61:22 62:5 66:7 67:7 70:21 72:1,3 72:8,20,22 73:3 73:18 75:12,15,19 79:6,9 80:10 95:12 102:4 124:6 126:12 143:9 158:15 159:7 174:1 175:2,14,18 176:3 177:18 180:19 211:18 213:2 222:13,16 222:21 223:13 231:15 247:6 251:14 252:8 268:5,15 278:19 279:5,8,12 291:3 292:3 293:3 294:6 294:20 295:5 296:4,7,13 303:15 303:20 306:18 308:22 310:4,7,11 317:18 323:21 325:15 335:4,6 338:16,17,18 339:16,19,21 349:3,20 351:1,4	351:16 352:11,16 353:11,16,21 354:2,14 356:4,11 357:11,16 358:12 366:8 369:5,15,20 371:12,19 372:17 requires 49:15 99:21 101:16 118:8 185:13 190:12 192:2 352:4 requiring 24:2,12 107:14 research 1:22 2:12 2:16,18 6:12 84:2 128:22 129:4 131:1,17,21 133:6 133:7 238:20 241:20 321:13,21 322:19 332:18 368:2 reserve 94:21 198:13 reserved 93:11 95:18 142:19 reserving 97:18 resolution 249:12 resolve 74:17 resource 127:10 226:19,21 227:5 290:3 292:16 293:11 324:2,5,10 374:3,8 resources 9:21 29:13 59:1 97:21 101:11 145:19 213:20 297:20 303:6 304:18 305:2 320:4 323:19 374:4 respect 136:19 189:3 247:21 248:14 288:17 294:20 376:10 respectfully 310:20 311:4 Responding 239:9	response 236:12 responses 176:12 responsibilities 60:1 174:13 responsibility 66:17 103:4 177:9 320:15 329:12 responsible 3:5 170:3 177:16 253:22 254:4 269:2 responsive 251:12 251:16 252:2 273:17 responsiveness 247:17 rest 9:1 147:18 restored 168:11 restrict 149:7 346:15 restricted 97:10 136:22 138:12 149:5 204:15 309:8,18 310:12 311:2 346:20 347:16 348:17 351:6 354:6 358:22 restriction 360:18 restrictions 176:7 242:13 325:3 359:1 restrictive 95:22 176:14 278:2 restrooms 7:11 result 123:6 194:4 195:6 302:8 330:14,16 resulting 137:19 195:4 239:8 321:16 324:10 results 45:15 69:10 72:16 74:10 87:9 105:3 171:22 323:14 331:7 retail 170:2,5,10,17 170:17 175:3	177:4 222:17,20 223:11 269:7 270:21 retain 68:14 104:9 retained 90:16 retaining 301:19 retroactive 113:4 retrospectively 281:5 return 360:10 RevAssist 103:10 review 19:22 35:14 48:21 60:3 65:19 67:9 70:1 93:9 94:4,8,10,22 95:5 101:17 147:16 148:10 169:1 179:16 187:18 276:17 312:18 337:2 370:9 371:19 reviewed 58:11 reviewers 19:18,21 20:1,11 reviewing 20:2 129:18 268:16 revise 229:7 revised 181:4 249:11 revision 179:22 revisions 153:1 232:7 Revlimid 103:10 105:11 353:9 rewrite 181:6 re-initiation 355:8 rheumatoid 166:13 rich 332:15 richness 127:1 275:12 right 40:15 43:5 44:6 46:8 82:14 83:16,17 134:16 198:14 202:10 205:15 208:11 211:5 215:19 218:22,22 271:15
--	---	--	---	---

271:20,20 280:16 280:17 283:15 284:13 287:3 347:20 363:2 371:1 rigid 56:1 331:21 rigorous 39:4 51:9 85:7 137:6 138:6 249:6 322:6 RISC 24:8 risk 1:3 2:1,2,4,6,9 13:12,19,22 14:3 14:14 19:19 21:5 22:1,8 25:14 32:11,21 35:17 57:6 59:20 61:4 63:21 66:2,4,6,16 67:6,16 70:7 86:11,14 91:12 92:16,18 93:8 94:2,19 95:6,21 97:22 98:3 99:10 99:16 100:5,14,16 103:9 104:1,7 105:22 109:14,17 109:18 110:2,14 110:22 111:4,20 112:1 113:1,22 114:8,19 116:13 116:21 118:7,13 118:17 129:14,14 129:20 130:14 131:7 132:3 134:7 135:1 136:9 137:21 138:6,16 138:20 145:11,13 145:20 147:9 148:1,3 153:14,17 161:17 164:22 166:4,22 167:8,14 168:2,6,9 172:18 172:22 175:8 179:5,7 180:13,14 185:6,15 186:16 188:14,20 189:14 189:18 190:14,15 190:17 192:7,18	193:1,4,22 195:10 195:16 196:1,16 198:22 206:3 215:7 216:9 217:15 218:4 219:14 229:17 230:7,12 232:11 236:9 241:14 258:11,21 264:12 264:14,15 265:19 265:21 266:18,19 268:2 270:5 284:15,16 285:5 287:8 300:2 310:1 320:13 321:4 322:2 334:11 362:9 365:12 riskier 130:11 RiskMAP 103:9 116:14 RiskMAPs 199:1 220:8,8 266:21 risks 15:16,18 16:2 16:7 22:3,6,11 25:6 34:17,19,20 39:1 51:2 55:13 58:22 59:19 61:10 64:11 67:5 69:15 85:19 86:7,10 92:12 96:9 98:18 99:5 100:7 101:5 103:18 104:11 109:21,21 112:14 117:12 129:11,13 134:4,18 135:18 137:12,17 139:1 143:14 144:2 145:1 147:9 151:8 152:2 154:14 165:18 167:6 169:5 172:17 173:2,3 179:20 184:20 191:6 197:10 216:7 217:7 221:12,16 227:9 251:22 253:10 257:15	265:10,13 267:2 267:12 295:9 301:5 316:4 321:19 326:14 362:5 363:6 risk-benefit 25:9 89:2 risk-intensive 110:16,21 111:3 118:13 road 317:11 robust 127:5 128:13 148:11 role 63:13 70:19 71:18 76:1 92:15 188:19 189:7 190:8 192:22 224:5,8 239:13 268:3,10 297:15 304:19 306:15,20 317:22 321:14 329:9 330:10,14 334:7 339:4 368:8 roles 59:22 192:3 369:12 roll 230:1 room 1:12,12 6:8 11:9 235:13 252:4 302:4 344:11 root 113:3 rosiglitazone 44:11 rotations 363:5 roughly 211:16 round 164:9 route 253:15 278:12 routine 97:12 110:9 144:17 145:13 186:21 327:16 routinely 325:19 royalties 205:8,10 210:3 royalty 205:12 RPC 242:20 rule 155:19 181:2,2 181:3 375:4	rulemaking 209:5 209:8 224:12 rules 242:22 243:1 263:14 370:18 378:12 run 21:2 225:6 running 191:10 285:21 359:6 rural 60:18 278:5 Rx-Female 125:11 Rx-Male 125:2 R.N 3:5 5:6 R.Ph 1:16 3:8,15 3:17 4:4 5:10,13 5:15,22 <hr/> S <hr/> safe 22:8 33:2,14 42:14 61:1,12 65:8,17 66:15 67:18 72:15 74:8 74:14 76:7,9,21 79:19 80:1,12 92:12 93:12 95:19 103:12 113:11 135:10 143:7 170:4 174:2 175:12 176:17 188:15 190:2,19 196:17 199:14 200:1 241:11 257:11 263:13 264:18 268:17 284:17 285:18 293:15 294:10 297:16 302:16 313:17 319:3 329:6 335:12 337:5 343:1 safeguard 327:21 safeguards 212:4 safely 64:13 154:6 237:19 267:4 298:11 307:4 308:1 313:11 344:4 366:11 safest 238:17 319:6	safety 1:17,21 2:5 6:11 14:10 15:1 15:21 18:18 23:2 58:21 84:14 85:4 92:3,9,21 94:17 103:3 110:1,14 112:22 129:22 132:21 135:12 136:6,17 137:5,12 137:13 139:6 144:7 155:1,2,3,4 155:8 164:22 167:15 169:5 170:2 171:2 179:2 179:11,20 180:3 180:18 181:8,14 181:17,21 182:8 182:16,20 185:5 189:2,6 191:19 196:20 197:13 212:3,14,19 215:11 228:21 232:20 253:15 267:10,22 269:14 271:19 301:14 302:12 303:9 310:1 318:17,21 319:8 320:22 321:10 322:17 329:19 331:4 335:15 337:13 341:4,5 347:8 355:3,5 357:13 365:16 safety-related 186:9 sake 98:15 salads 7:19 sample 322:19 samples 204:11 sandwiches 7:18 Sara 4:13 Sarah 2:12 83:14 83:16,20 91:4 saturation 302:2 savings 127:17 saw 28:11 165:21
---	---	--	--	--

348:19	121:3 128:10	self-study 240:19	290:15 307:11,17	325:18 326:1
saying 36:15	153:5 179:15	Seligman 2:22 4:23	367:4 375:21,22	327:6,9 345:18
143:13 146:16,22	181:8 214:1	188:5,6,7 216:4	376:5,9,15	351:22 369:1,6
159:13 217:8	section 2:11,19 3:1	217:19 220:1	serving 44:10	seven 12:1 83:3
219:19,21 220:4	3:8 4:13,20 5:4,9	226:12 231:4	session 10:5 19:18	119:10,14 130:4
says 116:14 165:9	8:10	Senate 259:13	20:22 27:2,6 82:2	337:18,20
205:5 206:4	sections 69:14	send 46:19 222:3	89:4 162:15	severe 133:21
260:17 376:17	318:7	339:22 360:4	272:14 290:4	166:17 289:17
SBLA 168:17	secure 314:15	Senior 297:6	368:15 376:20	severity 190:17
scale 313:20	security 110:1	sense 36:10 42:5	377:14	216:11 335:1
scenario 360:7	see 11:22 18:15	46:13 145:6 225:7	sessions 8:1 10:8	sex 132:18 133:5,19
scenarios 350:13	37:6 42:3,9,11	359:2 375:2,5,9	11:19,21 17:17	134:8,19 136:13
350:15	44:9 52:15 55:1	sent 107:20 304:1	27:17 289:21	shading 69:14
schedule 162:12	63:6 68:15 71:7	340:16 370:11	290:17 368:13	shape 216:11
scheduled 7:3,15	107:19 124:14	Sentinel 196:11	set 35:13 37:21	share 17:10 40:11
schedules 299:20	125:8 126:10	separate 232:10,15	56:9,21 71:11	47:12 57:11,13
school 198:4	140:2 151:10,20	301:7 319:18	81:8 93:14 98:20	64:5 71:1,2 85:14
230:19,20,20,21	151:21 157:18	321:3 325:17	116:20 122:10	86:5,10,15 89:5
364:6,19	163:2 169:10	340:22 359:14	177:20 240:20	103:1 116:16
schools 312:12	182:17 185:10	separation 249:15	249:4 299:22	131:5 157:14
science 21:5 35:17	201:8 214:21	September 8:17	317:4 359:17	160:19 164:12
39:11 99:15	215:1 224:5 236:2	26:17 379:21	363:20 368:5,14	165:8 172:18
132:12	254:17 255:2,6	sequential 40:1	370:17,19	174:16 189:10
sciences 119:6	266:8 276:13	series 121:20	sets 29:1 79:18	197:8 199:17
297:11	284:10 331:19	124:20 125:2	setting 35:1 37:13	200:22 201:8
scientific 214:22	363:13,14 371:8	207:15	76:2,11,11,12	203:17 204:9
301:8	371:20	serious 22:1 34:18	77:1,14 78:6,6,17	205:6 206:4,14
scientists 133:9	seeing 319:18	58:21 137:12	80:8 87:18 119:21	208:17 209:15
scope 177:3 243:2	seek 282:7	237:15 251:22	127:10 155:9,11	221:18 225:4,8
245:16 248:21	seeking 50:19	316:21 317:5	184:11 189:16	235:2 239:4 254:8
321:14 368:8	254:15,20 255:4,8	321:19	190:13 192:19	287:5 305:15
scoring 113:4	257:5	seriously 306:19	294:22 327:4,19	323:18 350:21
screen 275:6	seen 36:17,17 58:14	serve 6:13 15:7	351:1 354:3 356:2	372:16 373:4,8
screening 57:17	59:14 69:3 79:10	44:8 90:21 119:22	357:10,22 369:5	shared 99:7 100:1
Scripts 2:24 211:4	198:20 222:5	179:4 213:18	369:14,16,16	198:19 199:3,8,20
211:8,8,19 213:9	256:5,7 340:13	270:12 290:2	settings 3:7 4:10	199:22 201:6
se 191:21	sees 123:8	291:20 293:7	5:8 35:6 37:18	202:11 203:8,10
seamless 304:2	select 33:4 51:2	306:10 311:17	38:4 39:2 52:12	204:21 206:5,10
374:12	354:7	319:3 367:1	52:14 53:18 70:9	206:19 207:9
search 17:2	selected 20:15,16	served 213:7	70:12,15,20 71:5	208:5 209:2,12,14
second 93:10 95:15	32:9	290:15 341:7	71:11,19 72:5,12	209:22 210:16
114:20 122:7	selections 117:4	serves 9:19 294:1	75:22 76:3 78:12	224:1,3,7 226:1
125:21 126:22	self 237:11 250:8	service 119:15	79:7 81:4,18	226:19 231:17
146:1 160:15	self-attestation	170:11 307:16	85:21 98:11	320:6 357:15
167:10 175:1	311:16	309:19 310:5,17	222:17 269:3	358:11 372:9
191:22 210:7	self-regulation	services 2:22 119:5	270:3,22 286:17	shares 203:3
secondly 118:11	248:7	119:11 170:8,13	286:19,21 297:13	237:16

sharing 41:7 54:8 108:13 109:6 160:3 161:11 162:1 199:11 205:4,7 208:1,11 299:1,11	193:12 203:10 211:21 220:19 297:19 320:2 365:12 significantly 175:6 220:13 258:21 311:7 314:16	348:2,5 349:22 358:4 Sir 220:2 site 106:16 299:16 311:11 360:4,5,9 360:9 sites 356:15 360:3,6 360:21 369:11,19	168:16 societies 59:6,9 87:1 society 2:17 3:15 131:16,21 132:10 132:16 133:5 136:3,19 137:5,18 138:14,20 183:12 318:8,15,22 society's 138:8 246:3 soft 260:16 software 172:14 sole 309:14 solely 96:3 253:15 solicit 61:4 solid 269:19 272:9 solution 106:13 165:20 168:4 173:18 288:18,19 291:1 292:17 308:11 336:12 solutions 104:15 167:19 173:8 197:2 221:17 237:22 291:16 301:11 302:8 305:7 338:6 solve 334:9 338:6 solving 344:18 somebody 233:11 279:10 373:12 somebody's 264:14 somewhat 39:22 44:8 109:8 250:17 367:14 some-odd 190:1 soon 355:16 sophisticated 157:10 SOPs 154:1,11,12 154:20 157:11,19 158:7 325:7 sorry 231:10 273:13 286:10 302:6 sort 20:15 28:22	74:22 80:12 110:7 125:10 148:22 149:20 151:21 152:3 199:3,11 200:12,13 202:2 202:18,20 203:6 205:7 208:7 209:13 210:13 219:4,8 222:15 224:3,12,15 225:3 231:17 281:4,16 374:14 379:8 sorts 43:16 53:1 162:9 360:13 373:4 sought 17:15 200:4 262:16 sound 100:11 sounds 159:21 231:15 368:13 source 180:3 231:13 251:20 291:17,19 293:8 306:20 324:13 sources 357:9 space 265:22 span 43:13 speak 8:9 11:20 27:2,6 81:2 93:21 109:4 129:3 131:13 132:5 161:9 165:8 245:9 277:5 286:20 296:19 321:7 333:18 377:2 379:16 speaker 2:11,19 3:1 3:7 4:12,19 5:4,9 83:13 128:21 131:15 169:16 197:15 211:3 235:16 236:18 305:11 318:4 345:6 377:14 speakers 2:10 7:6 11:11 12:4,9 83:3 83:7 164:11
sharp 255:4,7,10 256:7,22 Sheehan 2:14 4:14 102:17,18,19 141:8 142:4 sheets 59:10 shift 34:11 shifted 192:8 ship 349:20 shipment 309:18 shoot 257:10 265:1 shop 90:5 shopping 258:10 short 64:22 67:2 255:12 shorten 126:18 shortened 82:6 shortly 162:22 show 64:6 122:4 182:20 244:22 280:18 307:12 showed 206:20 220:12 showing 254:18 256:16 shown 69:5 307:5 shows 116:16 254:14 side 112:3 133:21 155:2 204:18 369:5 sidebar 375:12 sides 275:11 sign 6:19 8:8 11:20 27:5 230:19 379:17 signal 179:16 signed 67:15 263:7 377:5 significant 133:10 186:9 189:9,21	239:12 203:10 211:21 220:19 297:19 320:2 365:12 significantly 175:6 220:13 258:21 311:7 314:16 silence 6:17 Silver 1:13 similar 39:1,1,2,8 42:9 44:10 47:1 63:15 86:6,10,14 104:3 158:11 160:20 167:22 172:17 205:11 215:10,11 275:21 276:7 299:20 337:6 343:2 344:1 350:20 351:4 353:8,13 357:16 358:11 371:13,16 similarities 175:8 Similarly 108:3 191:13 simple 42:8 127:20 171:3 185:19 187:5 247:5 simpler 49:5 93:3 simplification 301:1 simplified 105:13 simply 34:17 187:6 194:7 212:10 214:6 252:14 335:15 338:1 simulations 111:11 single 35:10 49:1 49:20 63:14 96:18 105:7 106:16 195:10 199:17,20 200:22 203:8 209:12 224:1,7 252:5 255:6 288:15 289:18 293:5 295:14 303:15 308:13 331:13 347:18	348:2,5 349:22 358:4 Sir 220:2 site 106:16 299:16 311:11 360:4,5,9 360:9 sites 356:15 360:3,6 360:21 369:11,19 situation 104:16 167:1 208:4 225:12 341:20 situations 104:1 175:10 193:16 199:19 354:19 six 12:3 17:10 164:11 170:18 363:4 size 19:16 28:12 37:15 55:21 135:21 139:3 326:1 331:17 skills 243:12,15,17 Slatko 2:6 13:10,11 25:20 29:15 140:19 141:20 142:11 272:16 374:18 376:16 377:8,11 sleep 134:13 slide 19:19 23:9 24:2 25:19 26:1,1 33:14 60:7 122:16 124:15 142:15 206:21 210:6,7 256:15,16 259:7 332:3 347:17 350:9 355:20 slides 18:4 21:17 22:15 24:20 25:16 28:12 72:2 83:16 162:16,21 222:7 234:19 379:10,11 slot 12:5 small 43:21 44:4 285:4 smartphone 301:13 sNDA 165:13	168:16 societies 59:6,9 87:1 society 2:17 3:15 131:16,21 132:10 132:16 133:5 136:3,19 137:5,18 138:14,20 183:12 318:8,15,22 society's 138:8 246:3 soft 260:16 software 172:14 sole 309:14 solely 96:3 253:15 solicit 61:4 solid 269:19 272:9 solution 106:13 165:20 168:4 173:18 288:18,19 291:1 292:17 308:11 336:12 solutions 104:15 167:19 173:8 197:2 221:17 237:22 291:16 301:11 302:8 305:7 338:6 solve 334:9 338:6 solving 344:18 somebody 233:11 279:10 373:12 somebody's 264:14 somewhat 39:22 44:8 109:8 250:17 367:14 some-odd 190:1 soon 355:16 sophisticated 157:10 SOPs 154:1,11,12 154:20 157:11,19 158:7 325:7 sorry 231:10 273:13 286:10 302:6 sort 20:15 28:22	74:22 80:12 110:7 125:10 148:22 149:20 151:21 152:3 199:3,11 200:12,13 202:2 202:18,20 203:6 205:7 208:7 209:13 210:13 219:4,8 222:15 224:3,12,15 225:3 231:17 281:4,16 374:14 379:8 sorts 43:16 53:1 162:9 360:13 373:4 sought 17:15 200:4 262:16 sound 100:11 sounds 159:21 231:15 368:13 source 180:3 231:13 251:20 291:17,19 293:8 306:20 324:13 sources 357:9 space 265:22 span 43:13 speak 8:9 11:20 27:2,6 81:2 93:21 109:4 129:3 131:13 132:5 161:9 165:8 245:9 277:5 286:20 296:19 321:7 333:18 377:2 379:16 speaker 2:11,19 3:1 3:7 4:12,19 5:4,9 83:13 128:21 131:15 169:16 197:15 211:3 235:16 236:18 305:11 318:4 345:6 377:14 speakers 2:10 7:6 11:11 12:4,9 83:3 83:7 164:11

286:16 292:8 298:14 376:22 speaking 57:7 64:1 198:11,12 267:4 282:16 334:6 350:21 speaks 80:7,12 special 293:19 310:12 378:15 specialists 263:1 specialization 213:12 specialized 213:13 353:7 specially 72:6,6 specialties 89:7 213:11,18 specialty 119:5,17 126:10 148:21 149:2,9,13,13,15 149:15 150:1 170:10,13,17 176:2,10,21 211:10,12 212:20 222:18 270:11,15 270:16,18,21 272:21 273:2,6 309:15 310:13 329:1,10 332:17 335:2 353:6 354:18 specific 18:1 24:1 34:18 38:4 45:13 51:13 60:22 72:3 72:19 80:9 86:5 100:14 104:15,16 113:18 138:4 147:2 172:19 185:7 190:2 196:17 234:12 243:9,22 244:5 247:9 254:13 266:1 271:2 276:11,11 279:8 295:6 309:7 310:16 315:9 316:3,16 323:19	324:21 348:14,18 357:5 361:16 362:17 363:17 370:12 specifically 9:11 30:13 136:20 143:6 151:8,9 243:3 268:14 277:21 313:4 360:19 370:4 specification 181:21 182:20 228:21 specifics 26:10 85:19 specified 315:16 spectrum 196:20 speed 82:7 215:9 spelled 209:9 spend 15:9 25:15 29:5 70:10 83:4 286:8 377:22 spending 29:21 30:18 337:18 spent 183:11 232:6 315:12 SPL 46:7,11,12,21 47:6,10,13,22 48:7,15,17 49:9 49:16 121:22 159:6 231:19 292:7,9,11 314:13 spoke 335:10 359:13 spoken 12:7 273:16 340:7 sponsor 62:4 86:2 88:21 94:5 99:21 167:20 196:3 sponsored 262:20 sponsors 19:22 35:13 46:19 62:1 67:22 69:4,7,22 88:16 89:15 93:7 94:2,21 99:8 101:19 130:1,18 146:6,9 147:15	148:6 169:1,12 181:20 192:10,17 193:2 spontaneous 180:9 spread 12:2 spring 1:13 134:12 Spurgeon 2:12 83:14,17,19,20 spurred 133:22 139:21 Stabi 3:21 5:17 345:7,8,9 369:22 370:1 371:15 372:20 373:17 stability 99:3 stable 291:7 Stacie 3:10 5:11 297:2,6 305:10 staff 11:9 12:22 73:14,21 75:9 94:14 312:3 369:19 stage 29:1 56:22 147:16 252:3 staged 153:11 stages 27:15 251:4 251:5 273:18 stakeholder 10:3 10:17 15:12 17:15 17:19 18:5 20:20 21:1 24:10 26:8 27:8,14 28:8,11 37:3 39:12 50:20 85:16 118:5 137:19 188:11 193:7 195:13,17 196:9 259:6,7 317:12 326:20 stakeholders 9:10 10:13 11:3 12:2 18:1 19:4,11 26:3 26:5 27:11,18 28:3 33:3,15 36:9 36:16,18 37:10,18 40:17 44:20 46:16 49:11,21 51:18 52:21 54:15,21	56:11 57:12 62:9 62:17,21 64:5 70:3 79:4,14 85:2 86:16,19,21 88:9 91:1 93:3 97:6,20 101:22 102:10 110:15 114:17 145:20 152:12 162:2,4 172:12 189:13 190:10 192:4 193:14 194:13 196:21 197:1 229:16 259:10 268:7 272:19 288:13 293:9 298:2 302:8 304:13,17 305:7 308:21 320:10 323:5 326:1 328:4 stance 339:19 341:16 standard 33:6 46:13,16 80:19 86:21 93:14 98:20 99:8 101:17 105:21 113:21 125:16 128:18 130:4 292:6,7,9 293:14 298:8 299:22 307:22 329:21 331:12,21 332:5 337:14 375:2 standardization 2:11,19 4:12,19 6:6 8:2 13:3 18:2 19:12 21:16 22:13 22:19,20 23:6 24:13,14 25:19 26:18 28:13,15,19 29:16 30:4,9,15 31:9,13,16,21 32:1,3 33:10 34:1 34:13 36:6,12 37:14,22 38:20 39:17 43:17 49:4 49:8 55:1 78:16	81:12,19 83:2 85:14,22 86:4 87:11 88:14 89:4 89:20 91:11 93:13 98:12,15,16 102:8 103:2,22 104:14 108:14,16 109:5 109:10 110:8 118:19 121:2,9 132:6,19,20,22 133:2 135:3,6,8 135:12,19 139:2,4 150:8 152:8 164:10,13,15 169:21 172:2 175:5 178:11 183:9 188:12 215:4,5,13 216:19 236:9 248:14,16 248:17 287:7 293:16 296:16,21 304:20 305:8,18 308:3 313:10 319:11 323:13,13 334:13 344:7 350:18 378:17,20 standardize 9:16 28:10,16 30:1,12 34:8 38:14 40:3 44:22 45:5 53:10 54:7 55:6,20 62:17 91:16 94:1 98:8 150:14 151:14 165:3 166:20 182:18 183:8 215:7 250:4 288:2,13 298:5 306:7 317:16 323:5 standardized 32:13 33:18 38:22 39:8 39:9 41:12 42:21 47:8 48:13,14,22 49:20 51:8,10 86:15,20 87:5,8 90:2 95:1 104:9 105:10,13 110:17
--	--	---	--	--

110:21,22 111:20 114:2,6,7 118:16 128:9 136:8 152:1 156:13 168:22 171:9,19 172:15 249:5 288:16 292:1 293:6 313:7 313:12 317:14 323:16 342:13,17 353:12 357:21 standardizing 1:3 4:5 9:13 29:17 30:16,17,20 31:6 31:17 32:3,7 33:16,17 34:12,15 39:19 41:2,6 42:21 49:13 81:3 85:8 88:11 98:3 173:10 294:2 350:11 standards 55:4,15 56:1,9,13,14,16 137:5 138:11 174:16 180:16 181:1 242:18 248:8,10 249:9 290:12 303:11 314:10 323:1,11 start 6:15 12:10 30:14,21 41:5 44:1 46:9 55:9 82:11,12,14 109:6 121:12 126:19 140:3 155:15 164:17 272:14 286:22 325:6 358:16 359:8 369:22 380:3 started 202:15 215:22 286:15 371:16 374:14 starting 6:4 122:8 126:10 155:5 180:4 216:22 255:21 357:2 374:14 starts 32:9 156:9	274:2,3 354:10 357:4 startup 73:2 state 53:14 68:12 91:21 109:12 180:17,22 181:22 184:17 230:5 246:3 255:7 279:4 306:12 309:2,5 312:11 338:17 347:9 stated 9:12 53:14 62:21 77:20 105:2 182:13 183:8 190:18 298:14 313:8 329:14 343:4,11 statement 213:17 312:20 343:11 statements 65:12 66:8,20 67:12 342:15 states 84:12 122:18 134:2 180:8,22 181:10,19 182:2,5 214:8 238:10,13 244:19 254:11,18 254:19 256:13 269:1 274:14 278:18 279:15 302:14 351:8 352:18 statistically 134:4 statistics 279:2 status 174:4 statute 146:5 201:18,22 205:5 statutory 21:7 25:3 stay 248:11 355:18 staying 215:19 steer 42:22 steering 15:8 24:8 27:13 30:7 step 29:4 40:13 41:15 49:12 97:4 134:16 155:16 183:10	Stephen 2:21,21 4:22 178:16 steps 30:19 33:6 34:19 103:8 106:20 115:7 141:3 145:11 156:11 171:14 212:15 217:14,20 218:5 364:2,4,15 365:20 366:2 Steve 188:4 stewardship 86:2 stick 7:17 233:21 stickers 191:15 sticking 378:8 stigmatize 260:3 stimulate 26:22 stimulated 82:17 stimulates 157:19 stint 198:3 stipulates 199:15 stock 214:7 354:9 371:3 stocked 349:6,7 stop 90:5 261:9 storage 338:10 store 356:16 372:5 stores 3:9 170:17 170:18 269:7 287:2,13,14,16 356:18 stormed 116:20 straight 159:14 225:16 236:19 266:6 straightforward 68:15 117:22 165:16 166:6 168:21 357:12 strategic 1:23 13:16 293:10 strategies 1:4 91:13 93:9 94:20 95:22 129:12,21 130:20 130:22 131:8 132:4 137:22 236:10 238:21	275:2 287:9 334:12 strategy 274:11 stratify 264:15 284:15 Stream 236:14 streamline 52:2 102:10 174:10 289:1 293:1,20 streamlined 90:11 168:22 329:15 331:9,15 streamlining 62:20 90:15 288:5 strength 250:15 strengthen 268:4 strengthening 92:6 stress 313:6 strict 261:8 strictly 114:22 stringent 310:3 strive 197:12 striving 240:14 strong 86:1 295:15 308:12 318:20 strongly 168:13 288:14 293:9 structure 77:1,14 299:21 structured 46:7,9 46:14 47:2 49:19 94:8 121:22 172:16 231:7 structures 215:6 struggle 374:5 struggles 189:4 Stubbings 2:15 4:15 119:1,3,4 140:6,10 148:16 149:2 154:21 158:2,5 160:5 161:5 students 236:6 318:12 studies 180:10 307:5,12 309:16 study 116:15,19	136:12 193:21 237:3 261:21 311:5 312:17 stuff 378:21 styles 52:7 60:16 62:15 subcommittee 367:7 subconsciously 110:4 subject 244:1 325:4 submission 95:14 165:15 180:5 182:19 314:12 submissions 20:1,3 165:3 169:1 submit 90:17 162:10,16 181:20 234:19 344:21 345:4 372:19,21 373:18 submits 309:21 submitted 11:1 47:14 69:4 165:14 171:5 182:9 236:11 262:17 submitting 70:1 102:13 122:13 suboptimal 234:21 subsequent 72:2 199:6 202:16 subsequently 166:14 subset 44:5 substance 274:13 282:21 283:20 substances 299:21 substantive 207:13 Sub-optimal 228:4 sub-populations 132:15 sub-process 115:6 success 104:19 130:20 173:20 178:6,8 189:15 190:12 191:21,22 193:10,18 194:17
---	--	--	---	--

196:5 217:2 218:18 219:5 247:12 successes 37:2,6,8 successful 99:20 107:16 189:12 217:8 281:6 303:22 313:14 334:18 successfully 147:8 173:15 190:8 194:1 242:19 312:19 367:8 suffered 135:2 sufficiency 361:18 sufficient 157:5 311:21 362:8 sufficiently 87:12 suggest 22:1 98:2 110:19 114:4 209:3 263:12 290:11 299:17 302:17 suggested 216:6 225:21 304:10 373:3 suggesting 152:14 223:20 suggestion 146:2 suggestions 9:15 199:4 299:6 373:18 suggests 88:1 304:12 summaries 63:12 summarize 27:8 125:14 summarized 350:9 355:19 summarizes 371:11 summary 242:7 272:1 summer 136:18 summit 161:19 supermarkets 287:14 supplant 301:17	supplement 301:16 supplier 325:1 suppliers 48:2 supply 136:1 280:12 321:2 326:11 342:3 351:14 354:17 support 16:19 47:3 58:18 61:2,15 67:8 87:15 104:14 176:21 238:20 240:7 241:2 242:19 245:10,11 248:10 249:10,14 272:8 285:19 288:9 292:9,9 298:4 300:22 309:13 317:15 338:12 339:5 supported 104:8 175:19 supporting 174:9 195:8 238:16 supports 49:3 86:18 88:8 91:14 96:16 98:7 99:17 104:4 239:21 242:14,18 suppose 262:20 359:8 supposed 200:21 201:12 203:9,17 203:22 204:1 205:6 206:9 209:11 supposedly 262:6 Supreme 186:10 sure 27:4 38:13 48:19 52:15 55:4 55:8,14 77:21 114:17 141:8 142:4 144:5 146:14 148:9 150:16 151:5 155:12 158:13 222:8 230:13 237:17 242:21	280:4 285:22 302:5 336:12 364:1,4,12,16,22 366:10 370:9 371:22 375:17 379:1,13,15,17 Surgeon 4:13 surprising 109:16 surrogate 185:20 surrounding 308:9 310:14 surveillance 63:22 92:7 94:16 177:8 229:9 367:16 surveys 100:20 191:19 Survival 246:15 sustained 246:20 switch 9:7 synthesis 133:15 194:5 system 3:20 9:17 16:12,15,21 17:10 17:20 21:10 22:5 23:4 24:4 31:8 32:20 33:21 48:9 55:12 73:20,22 77:2,6,12,16,17 77:18 79:21 80:6 80:17,22 84:21 88:19 91:18 95:3 97:20 101:10,14 101:15,20 102:4 102:12 107:8 108:1 119:6,8 120:8,11,18,21,22 121:13,15 123:13 123:22 125:17,22 127:8,21 128:5,8 136:1 138:6 140:15,21 141:1 141:19 152:16 154:6,14 159:10 159:14 160:13 169:9 170:21 172:9 179:19 180:1 183:13	184:22 188:22 189:19 191:10,17 192:2 194:11 195:10,22 197:3 199:20,22 200:22 201:9 212:10,12 223:3 224:1,7 227:2,11 229:6 234:9 242:17 245:22 246:3,3,6 246:8,13,18 247:1 247:22 249:3 250:15 252:9 267:8,22 269:16 271:9 280:18,19 282:6,9 283:4 299:9 303:15 313:7 314:1 315:2 319:14,18 320:6 321:3 326:21 330:2,8 333:16 336:1,20 337:15 338:13 339:6,6,11 339:19 345:11,19 346:8,19 347:1,2 347:5,14,19,22 348:3,12 350:2,21 352:14 356:9 357:15 358:4,10 359:11 361:13 363:9,16,22 364:1 367:9,20 369:2,21 370:3,14,20 376:2 378:5 systematic 43:15 112:9,14 118:16 319:16 systematically 118:12 systems 33:11 47:13 48:6 50:5 52:18 53:18 73:16 73:17 76:17,18,20 77:22 79:17 80:15 80:16 88:3 103:13 106:3 108:2,5 109:3 120:15	121:17,19 126:8 126:12,16 127:2 128:10,13,18 136:10 149:17 154:9 161:12 174:8 175:3,20 176:19 183:7 191:14 195:2 196:7 197:5 222:14 223:1 227:4,8 240:5 243:1 248:3 250:10 251:8 270:22 272:20 276:1 281:11 288:4 289:2 292:21,22 294:4,8 298:20,20 304:15 318:13 319:2 323:15 326:6,9,14 326:15 327:12 332:7 334:2,8,14 335:7,14 338:8,14 341:19 342:20,21 343:19 344:19 345:1 358:11 363:20 366:16 367:12 systems-wide 367:14 system's 247:5,17 250:2 system-based 171:19 326:18 system-related 102:1 S-E-S-S-I-O-N 164:1 <hr/> T <hr/> table 4:1 5:1 326:21 tables 66:9,21 tablets 68:20 tackle 29:2 260:14 tailored 37:17 195:17
---	---	---	--	---

take 25:8 29:4,10 36:19 45:20 49:12 50:10 61:13 74:21 106:4 125:5 132:7 134:15 141:15 198:14 199:5 201:15 219:8 220:17 245:2 278:7 286:2,3 290:3 297:18 298:11 301:10,15 306:19 320:1 323:22 324:17 333:5 336:8 342:13 359:17 364:7 374:16	30:5,10,19,22 31:20 34:2 48:13 51:5 70:8 150:6 183:2 198:20 202:7 208:10 225:9 230:3 266:22	tell 9:4 36:16 37:3 140:20 183:14 184:1	196:7 218:11 324:7	358:14 368:10,19 372:22 376:16 377:19,20 378:8 378:16 379:2 380:2
106:4 125:5 132:7 134:15 141:15 198:14 199:5 201:15 219:8 220:17 245:2 278:7 286:2,3 290:3 297:18 298:11 301:10,15 306:19 320:1 323:22 324:17 333:5 336:8 342:13 359:17 364:7 374:16	talks 199:12 203:9 283:14	tells 175:9 201:5 228:11	testable 282:4 tested 69:7 127:14 127:19 335:6	thankful 328:16 Thankfully 134:5 thanks 118:20 162:6 223:17,18 225:17 227:12 360:12
306:19 320:1 323:22 324:17 333:5 336:8 342:13 359:17 364:7 374:16	target 22:22 59:3 104:2	temperature 235:10,12	testimony 171:6 testing 64:7 69:5,10 87:9 93:16 98:22 137:2 168:6 175:17 283:3	themes 78:14,15 theoretically 206:12
342:13 359:17 364:7 374:16	targeted 15:19 118:3 143:9 146:10 176:11	ten 11:14 12:14 83:4,8,11 134:1 272:13 358:15 370:5	tests 43:9 74:20 218:10 276:11	theory 207:12
takeaway 118:6	targeting 32:22	tend 219:1 342:7	text 45:9 65:11 66:8,20 67:11	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
taken 80:19 136:5 163:5 212:16 355:11 364:2,5 365:20 375:16	targets 242:15	tension 147:21	Thalomid 44:14 103:8 105:11 353:8	therapy 126:19 175:16 218:8 302:15 307:18 311:10 338:3 340:15 349:16 350:7 351:18,22 352:12 354:13,16 355:8,15 358:2
163:5 212:16 355:11 364:2,5 365:20 375:16	task 179:4 350:12	ten-minute 12:5	thank 15:3 29:18 57:2,3 63:18 70:5 82:15 91:3,4,9 102:14,15,22 108:18,19 118:21 119:3 128:18,20 129:2 131:12,14 131:19 139:12,14 139:15,16 142:11 144:5 148:13,15 156:17 157:21 162:12 163:3 165:7 169:14,15 169:19 178:13,15 178:18 188:3,4,9 197:7,14 211:1,2 215:16,17,18 225:18 234:15,17 235:5 245:4,5,8 253:19,20 254:1 266:12,13 272:10 272:11 274:1 275:15 287:3,4 296:18 297:1,5,18 298:3 304:16 305:9,10,13,14 318:2,3 328:5,6 328:13 333:10,13 333:17 344:9,11 345:2,3,16 358:13	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
355:11 364:2,5 365:20 375:16	taught 264:12 274:15 284:15	teratogenic 104:7 138:7 173:3	Thalomid 44:14 103:8 105:11 353:8	therapy 126:19 175:16 218:8 302:15 307:18 311:10 338:3 340:15 349:16 350:7 351:18,22 352:12 354:13,16 355:8,15 358:2
365:20 375:16	Tavakoli 2:8 4:9 13:20,21 63:19,20	Teratogenicity 221:13	thank 15:3 29:18 57:2,3 63:18 70:5 82:15 91:3,4,9 102:14,15,22 108:18,19 118:21 119:3 128:18,20 129:2 131:12,14 131:19 139:12,14 139:15,16 142:11 144:5 148:13,15 156:17 157:21 162:12 163:3 165:7 169:14,15 169:19 178:13,15 178:18 188:3,4,9 197:7,14 211:1,2 215:16,17,18 225:18 234:15,17 235:5 245:4,5,8 253:19,20 254:1 266:12,13 272:10 272:11 274:1 275:15 287:3,4 296:18 297:1,5,18 298:3 304:16 305:9,10,13,14 318:2,3 328:5,6 328:13 333:10,13 333:17 344:9,11 345:2,3,16 358:13	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
takes 13:4 17:2 154:14 244:22 272:4	teach 251:22 284:13	term 46:9 161:20 258:17	Teratogenicity 221:13	therapy 126:19 175:16 218:8 302:15 307:18 311:10 338:3 340:15 349:16 350:7 351:18,22 352:12 354:13,16 355:8,15 358:2
154:14 244:22 272:4	teaches 264:4	terfenadine 220:11	term 46:9 161:20 258:17	Theresa 1:13,16 4:4 5:22
talk 20:17 25:18,20 29:16 30:14 31:22 32:6 33:10 34:10 34:11 39:17 42:12 42:20 45:19 50:6 50:9 57:20 64:3 70:13 120:9 146:5 185:9 198:18 201:7 209:13 216:13 224:15 229:9 241:14 323:2 329:11 340:5 377:8,9	teaching 264:8 285:17	termcommunity.... 161:21	thank 15:3 29:18 57:2,3 63:18 70:5 82:15 91:3,4,9 102:14,15,22 108:18,19 118:21 119:3 128:18,20 129:2 131:12,14 131:19 139:12,14 139:15,16 142:11 144:5 148:13,15 156:17 157:21 162:12 163:3 165:7 169:14,15 169:19 178:13,15 178:18 188:3,4,9 197:7,14 211:1,2 215:16,17,18 225:18 234:15,17 235:5 245:4,5,8 253:19,20 254:1 266:12,13 272:10 272:11 274:1 275:15 287:3,4 296:18 297:1,5,18 298:3 304:16 305:9,10,13,14 318:2,3 328:5,6 328:13 333:10,13 333:17 344:9,11 345:2,3,16 358:13	thing 33:9 34:13,21 35:8 36:7 37:1,9 38:9 40:2 43:2 114:15 125:11 127:12 179:8 208:9 217:22 218:22,22 224:3 257:8 286:5 343:11 365:22 373:11
29:16 30:14 31:22 32:6 33:10 34:10 34:11 39:17 42:12 42:20 45:19 50:6 50:9 57:20 64:3 70:13 120:9 146:5 185:9 198:18 201:7 209:13 216:13 224:15 229:9 241:14 323:2 329:11 340:5 377:8,9	team 304:8	termination 93:17 99:1	Thalomid 44:14 103:8 105:11 353:8	things 17:22 19:1 19:21 20:10,17 22:2,16 27:16,19 31:5,15 33:18 35:8 38:5,19 44:16 46:3,20 48:15 50:13 55:16
34:11 39:17 42:12 42:20 45:19 50:6 50:9 57:20 64:3 70:13 120:9 146:5 185:9 198:18 201:7 209:13 216:13 224:15 229:9 241:14 323:2 329:11 340:5 377:8,9	teams 35:14	terminology 42:8 43:1 105:21	thank 15:3 29:18 57:2,3 63:18 70:5 82:15 91:3,4,9 102:14,15,22 108:18,19 118:21 119:3 128:18,20 129:2 131:12,14 131:19 139:12,14 139:15,16 142:11 144:5 148:13,15 156:17 157:21 162:12 163:3 165:7 169:14,15 169:19 178:13,15 178:18 188:3,4,9 197:7,14 211:1,2 215:16,17,18 225:18 234:15,17 235:5 245:4,5,8 253:19,20 254:1 266:12,13 272:10 272:11 274:1 275:15 287:3,4 296:18 297:1,5,18 298:3 304:16 305:9,10,13,14 318:2,3 328:5,6 328:13 333:10,13 333:17 344:9,11 345:2,3,16 358:13	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
50:9 57:20 64:3 70:13 120:9 146:5 185:9 198:18 201:7 209:13 216:13 224:15 229:9 241:14 323:2 329:11 340:5 377:8,9	technical 301:8,20	terms 22:2 42:13 76:16 78:4 146:17 146:19 151:16 155:18 198:17 199:2,14 208:10 216:14 221:4 227:19 232:16 338:17 340:3,9 358:22 367:16	Thalomid 44:14 103:8 105:11 353:8	therapy 126:19 175:16 218:8 302:15 307:18 311:10 338:3 340:15 349:16 350:7 351:18,22 352:12 354:13,16 355:8,15 358:2
70:13 120:9 146:5 185:9 198:18 201:7 209:13 216:13 224:15 229:9 241:14 323:2 329:11 340:5 377:8,9	technicians 297:12 318:11	Teratogenicity 221:13	Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
185:9 198:18 201:7 209:13 216:13 224:15 229:9 241:14 323:2 329:11 340:5 377:8,9	technologies 190:3 243:13 291:4 298:18 313:19 356:1	terminology 42:8 43:1 105:21	Thalomid 44:14 103:8 105:11 353:8	therapy 126:19 175:16 218:8 302:15 307:18 311:10 338:3 340:15 349:16 350:7 351:18,22 352:12 354:13,16 355:8,15 358:2
201:7 209:13 216:13 224:15 229:9 241:14 323:2 329:11 340:5 377:8,9	technology 48:3 87:16,18,22 105:13 107:4 194:20 222:22 223:12 244:11 299:2 301:10 314:1 358:7 364:1	terms 22:2 42:13 76:16 78:4 146:17 146:19 151:16 155:18 198:17 199:2,14 208:10 216:14 221:4 227:19 232:16 338:17 340:3,9 358:22 367:16	Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
216:13 224:15 229:9 241:14 323:2 329:11 340:5 377:8,9	technology-assist... 316:6	terrific 186:12	Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
229:9 241:14 323:2 329:11 340:5 377:8,9	teeth 260:11,14	Terry 6:10 29:19 30:1 36:8 81:7 148:15 178:18 305:13	Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
323:2 329:11 340:5 377:8,9	telehealth 302:9	test 53:10 69:22 72:16 88:10 173:4	Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
340:5 377:8,9			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
talked 18:8,9 20:1 34:22 50:7 51:19 127:13 128:7 159:5 184:14 199:10 210:8 228:19 231:6 267:6 269:8 277:3 277:6 338:11,17 343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
34:22 50:7 51:19 127:13 128:7 159:5 184:14 199:10 210:8 228:19 231:6 267:6 269:8 277:3 277:6 338:11,17 343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
127:13 128:7 159:5 184:14 199:10 210:8 228:19 231:6 267:6 269:8 277:3 277:6 338:11,17 343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
159:5 184:14 199:10 210:8 228:19 231:6 267:6 269:8 277:3 277:6 338:11,17 343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
199:10 210:8 228:19 231:6 267:6 269:8 277:3 277:6 338:11,17 343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
228:19 231:6 267:6 269:8 277:3 277:6 338:11,17 343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
267:6 269:8 277:3 277:6 338:11,17 343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
277:6 338:11,17 343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
343:15 374:20			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13
talking 23:6 29:21			Thalomid 44:14 103:8 105:11 353:8	therapies 61:10 92:21 96:11 176:10 192:6 309:9,11 327:1 364:13

56:5 73:7 74:5 75:4,16 76:17 113:17 147:22 150:19 151:4 154:4 156:5,15 159:7 160:6 164:13 167:17 183:3,18 184:1 186:21 199:4 203:11 209:1 216:15 218:15,20 221:19 223:10 225:10 226:2 229:15 232:10 235:1 272:18 278:1 359:11 think 7:8 13:6 16:12 26:5 27:16 28:2,10,14 32:2 32:10,16,19 33:1 33:9 34:14 35:21 37:20 38:4,18 40:9 44:21 47:5,7 53:3 81:19 83:7 83:12,14,16 96:12 110:5 111:1,14,17 140:22 142:13 144:14 145:3,4,18 147:5,20 148:4 150:9 152:9,16 153:22 154:2,8,13 155:15 156:9,13 156:14 157:3,13 157:22 158:5 159:4 160:5,11 165:16 166:6 185:19 199:4 217:21 218:19 219:2 222:16,19 224:7 226:2,14,20 226:22 227:4,9,20 228:11,13 229:3 229:11 230:16,22 231:1,12,18 232:21 253:1 256:18 259:8 260:21,22 264:7	267:19 277:20 278:12,19 279:2,7 279:8 280:8 281:13 284:8,12 302:2 334:19 336:10,15 338:9 338:15,22 341:9 342:12 344:22 358:21 361:5 365:7,9,19 366:4 366:5 367:18 369:3 371:8 373:2 373:19 378:12 thinking 13:3 26:22 32:13 78:5 82:17 117:16 157:17 167:18 208:3,4 third 93:13 98:7 103:14 121:4 122:7 126:20 167:12 193:10 214:17 thirdly 128:12 153:12 third-party 86:22 Thirty-five 120:2 thought 11:6 19:8 38:6 133:5 208:7 217:17 229:13 thoughtful 162:13 thoughtfully 29:9 189:20 thoughts 36:11 151:2 226:9 273:4 362:16 370:19 thousands 212:22 325:18 346:1 three 18:4 21:17 24:20,21 39:20 52:22 141:12 142:13 152:19 171:7 183:1 275:22 286:4 319:22 321:8 339:11,16 357:9 three-day 355:9	THURSDAY 1:8 tied 191:2 tiers 176:14 299:19 tightly 138:12 Tikosyn 355:2 time 7:2 11:12 12:11 18:10,19 21:13 25:15 27:21 29:6,11,21 30:18 36:19 55:15 64:14 73:5 74:6,22 81:21 82:5,10 83:5,12 94:22 99:3 101:11 104:9 107:3 108:18 109:8,11 114:3 116:17 126:18 139:18 145:19 148:10 153:11,15 153:16 158:19 161:2 162:8 167:1 171:7 174:22 177:1 196:8 198:15,15,21 206:14,18 207:8 208:14 210:19 215:19,20 218:6 223:14 232:6 244:22 245:3 255:1,12 256:5 270:19 272:12 285:21 286:6 297:19 299:6 300:14 303:6 304:17 305:1 315:12,17 318:2 320:20 324:12 326:14 333:18 345:2 350:10 352:18 358:13 359:17 370:7 377:3,22 378:2,3 timeframes 20:7 timely 7:21 88:5 96:8 107:2 171:15 187:13 timer 12:8	times 105:19 127:10 204:15 276:15 time-consuming 176:3 time-wise 7:9 timing 269:9 271:15 TIRF 160:11 173:16 223:4 233:6,17 234:8 294:1,4 304:8 350:21 title 57:19 titled 137:21 238:2 239:9 titles 105:22 today 6:14 7:1,4 29:12,21 31:3,20 34:3 40:20 50:18 53:5 57:9 58:13 63:18 64:2 108:18 118:10 120:9 130:6 132:21 165:2 168:15 170:6 171:3,7,10 179:9 197:8 199:10 200:7 205:18 210:8 212:10 225:10 254:2 266:21 267:7,14,16 268:9 269:8 286:15,20 292:8 296:19 298:14 315:17 318:19 320:8 321:9 328:14 329:11 343:10,12 345:6 365:11 today's 26:7,13,22 29:1 34:4 90:20 214:5 333:9 Toigo 1:14,16 4:4 5:22 6:3,10 15:3 81:8 82:22 83:18 91:4 102:15 108:19 118:21	128:20 131:14 139:15 148:13 150:2 153:21 156:17 158:4,18 161:3 162:11 164:3 169:15 178:15 188:4 197:14 211:2 215:17 220:2 221:21 222:5,9 223:17 225:18 227:12 231:3 232:22 234:15,17 245:5 253:20 266:13 272:11 273:14 275:16 276:21 280:6 284:8 285:20 286:14 297:1 305:10 318:3 328:6 333:13 345:3 358:14 361:3 366:13 368:10,19 371:5 372:18,22 376:17 told 11:7 18:17 36:13 260:2 263:8 tolerance 285:14 toll-free 291:12 Tom 247:16 tomorrow 7:2,5 8:1 8:3 11:19 85:8 155:6 235:15 314:7 328:14 332:3 344:14 376:19 377:6,16 377:17 379:16 380:3 tool 58:10,20 59:18 61:8 65:3 96:19 144:21 145:2 147:11 217:3,8 289:20 302:16 toolkit 33:19 39:10 39:10 tools 3:1,7 4:6,8 5:4 5:8 18:3,11 19:14
---	---	---	--	---

24:14 32:8,15 33:5,8,11,16,19 33:21 34:4,9 39:2 39:3,7,8,10 40:8 42:9,11,21 45:12 48:10 49:6 50:22 51:3,6,14,17,20 52:4,12 55:6 56:21 57:8,10,12 57:15,20,21 58:1 58:7,14 61:2 64:2 64:4,6,10,15,18 66:3,13,21 68:18 81:17,17 86:13,18 87:6,8,13 93:18 96:1 98:4 99:2,10 100:2,18 101:8,18 102:3 110:17 114:16 115:1,21 116:21 117:7,8,11 117:15 118:2,18 143:15,17 145:13 148:2 150:11 160:9,10 186:3 193:16 195:3,16 196:2 216:17,20 217:12 226:20 227:7 235:7 264:13 267:1 275:5 276:11 284:15 285:17 286:17,20 293:7 319:22 321:18 326:3 330:18 345:18 352:2 373:4,7 top 153:20 366:6 topic 6:22 89:6 109:5 244:9 279:7 296:20 topics 10:7 11:5 109:22 243:9,22 346:3 topic-specific 279:16 total 175:21 215:13 totality 93:20 100:8	142:22 146:3,15 147:8 touch 58:13 330:12 touched 303:10 track 49:5 62:1 67:22 226:2 281:3 281:11,14 313:2,4 tracking 73:20 176:6 tradeoff 23:2 traditional 182:15 287:13 train 51:21 73:13 75:8 trained 72:9 73:14 111:17 234:4,6 361:9 363:1,9 training 45:12 58:16 59:17,19 60:3,6,9,15,19,19 62:7,10,11 63:8 64:20 73:21 90:14 109:19 111:9,10 124:17 154:9 172:5 174:2 191:8 215:9 242:16 244:5 268:15 272:1 277:4,8,17 280:9,13,14 293:20 294:5,15 299:14 311:18 312:3,13 313:5 315:8 361:17 363:2 transactions 106:18 108:2 transcript 8:21 transcription 379:9 transcripts 8:18 transition 78:5 106:3 346:14 transitions 78:4,7 120:13,18 125:20 126:17 140:16 156:2 327:2 translate 100:14 280:20,21 283:8	translated 281:8 282:11,11 304:9 translation 281:1,4 transmission 313:21 transmucosal 173:15 transparency 118:19 135:5 169:12 177:6 178:5 316:10 transparent 306:5 352:17 354:2 transportation 340:3 treat 76:14 263:18 284:13 treated 184:17 treating 187:18 264:1 treatment 84:22 124:3 138:5 184:11 243:14 254:15,20 255:5,8 257:5 258:20 264:17 269:13,20 270:18 272:4 337:2 treatments 139:7 243:13 tree 113:3 125:3 tremendous 106:22 tremendously 142:7 trial 185:20 354:8 trials 109:9 180:6 tricky 43:13 tried 11:5 273:12 tries 45:22 trigger 172:19 295:3 trouble 282:1 troubling 338:4 true 181:16 251:1 264:18 285:6 329:13 truly 133:9 341:7	356:12 trump 137:13 trusted 307:10 343:16 try 7:16 19:1,3 43:3 45:3 46:4 143:4 159:2,12 168:15 201:15 216:19 256:16 333:19 336:3 trying 6:20 29:2 34:14 37:21 44:21 154:12 157:3 207:4 208:5 217:22 220:18 221:11,14 232:17 232:18 235:12 261:8 317:2 337:7 343:3 362:1 375:4 377:18 tuned 228:10 turn 6:17 12:10,13 56:18 81:6 284:17 341:20 turned 255:3 turning 83:13 turns 264:17 tutorial 113:8 twice 250:19 two 7:22 9:2,4 11:19 12:4,10 25:16 31:18 32:5 37:22 38:4 44:9 66:5,19 67:10 83:10 120:1,11 142:16 150:19 151:3 164:9 173:1 182:6 198:3 199:18 225:8,15 255:15 261:14 279:1 355:6 377:7 378:15 two-day 236:7 two-parter 159:1 two-way 187:8 231:17 type 17:1 113:19	167:11 168:17 180:12 278:2 types 71:9,10 98:18 334:20 369:6 typically 104:17 268:8 <hr/> U <hr/> UBC 266:18,19 UHC 366:19 367:7 367:19 UI 119:7,7,15 124:3 UIC 154:1 344:14 ultimate 217:15,21 ultimately 32:21 203:1 207:16 209:7 281:10 293:1 unable 200:5 unavoidable 22:21 uncertainty 110:8 unclear 43:16,20 uncommon 357:7 uncover 133:10 undergo 150:17 underlie 247:8 248:20 251:18 275:8 underlies 274:12 274:19 underlying 89:2 115:13 180:7 288:8 understand 6:21 24:16 28:18 36:21 38:3 49:22 78:2 93:4 144:19 147:22 151:15 186:14 201:14 206:2 208:20 210:18 247:8 258:20 269:12 274:21 275:1 281:7 332:10 341:3,8 344:3 362:1 376:3
--	--	---	--	--

understandability 69:13	173:8 194:14 200:14 275:21	299:12 313:18 317:8	363:6 365:6 useful 32:4 42:16	253:4,6 307:6 317:9
understandable 183:18	281:17 296:13 326:7 367:18	urges 238:10 292:3 urging 238:12	193:19 250:20 277:16 289:9	values 174:20 vantage 194:15
understanding 20:8 35:1 40:5 67:16 77:7 94:5 99:7,22 100:1,20 147:17 148:5 168:18 186:6,17 192:4 201:1,9,14 208:18 210:15 224:4 227:17 251:10 281:2 285:2,9 290:18 311:15 314:2 321:15	uniquely 336:5 United 3:5 84:11 134:2 180:22 181:10,19 182:1,5 214:8 254:11 256:13 266:14,18 269:1 274:14 unit-dosed 351:15 universal 190:5 195:11 university 2:15 3:20 109:3 119:1 119:6 161:8 227:1 333:15 334:1,8 335:6 336:17 339:12 341:18 342:21 343:18 344:16,18 345:1 366:15,21	usage 303:1,4 use 22:8 23:16 33:2 33:12,14 39:3 42:14 49:16 56:12 56:14 57:14 61:1 61:12 64:9,12 65:9,17,20 66:3 66:15 67:18 72:15 74:8,14 76:7,9,21 79:19 80:1,12 84:21 86:9 92:14 93:12 95:19 101:6 103:12 107:1 109:10,13 111:22 114:1,5 115:6 116:12 118:16 121:16 122:9 135:10 142:5 143:7 144:2,7 167:6 171:6 174:2 175:12 176:17 188:16 190:2,19 191:1,15 196:17 199:15 200:1 202:2 216:17 217:12 238:18 241:6,11 247:11 248:11 253:11 255:16,21 260:15 261:17 263:2 264:12 267:4,21 268:17 275:1,6 281:3 283:11,22 284:15 285:17 293:15 294:10 297:16 302:16 303:18 308:13 313:17 316:20 317:10 318:17 319:2,3,6,13,17 319:18 322:18 326:15 329:6 346:15 352:6	320:17 usefulness 321:16 user 87:9 171:18 219:14 uses 79:20 322:5 usual 325:1 usually 58:10 60:2 65:10 66:18 67:10 183:19 369:16 Utah 262:1 utilization 87:16 187:16 188:2 191:4 330:18 utilize 126:22 145:4,12 182:7 221:4 313:19 368:1 375:19 utilized 108:5 187:7 221:2 307:19 358:7 utilizing 88:12 utmost 84:16 U.S 91:22 102:20 164:22 188:8,22 287:22	variability 70:14 70:15 81:16 variables 185:19 326:13,13 variance 284:1 Variants 250:14 variation 22:21 36:4,10,13 38:1 85:17 98:13 246:9 246:9 251:1,11 275:12 variations 35:21,22 45:1 varied 34:16 35:9 37:12 66:5 180:3 293:17 varies 34:22 42:2 variety 17:16 52:6 52:14 59:7 60:8 68:17 109:22 162:2 193:12 298:5 359:11 various 60:16 97:15 98:10 110:5 113:1 126:9 127:22 146:22 226:19 251:4,5 291:15 295:10 325:13 327:19 362:2 365:14 vary 34:17,21 40:6 42:6,6 45:4,7 75:21 varying 314:19 vast 84:10 vegetables 19:2 vehicle 327:7 vendors 20:5 48:3 172:14 316:6 verbal 307:1 verification 74:17 303:20 304:5 313:16 322:13
undertake 177:9 200:15	unknown 309:21			
underway 314:8	unnecessary 36:4 38:1 98:13 171:11 295:2 308:4			
under-served 120:1	unneeded 355:18			
undesirable 365:9	unplanned 138:7			
undoubtedly 212:7	unreasonable 178:3 213:2			
undue 84:20 156:5 296:11 319:12 327:18	untapped 127:10			
unforeseen 218:14	unusable 117:10			
unfortunate 256:2 286:5	unusual 81:22 117:1 268:13			
unfortunately 146:4	unwanted 218:14			
unified 96:18 203:1	unwarranted 295:12			
uniform 173:9 292:12 293:14	upcoming 241:10 241:16			
unintended 139:4 365:8	update 9:8 15:5,10 41:11 182:8,16 372:2			
unintentional 336:14	updated 153:8,17			
unique 71:12 78:17 103:19 108:12 135:18 166:22	updating 54:10 upper 124:14 urge 288:14 293:9			

323:3	262:14	182:18 183:21	welcome 6:5 11:20	window 351:4
verified 72:14		185:20 194:7	27:7 164:3 234:16	wishes 250:11
74:13 233:11	W	197:11,21 200:22	373:16	wishing 302:5
304:1	wait 360:5,9	209:2,18 234:5	well-defined	withdrawn 134:2
verifies 123:9	waiver 201:20	250:4 266:5 273:5	190:13	withstand 196:7
verify 74:7 76:21	203:2 207:9,17	281:14 284:13	well-designed	women 2:17 128:22
79:19,22 156:5,7	walk 81:9 114:9	285:18 294:19	321:21	129:5 131:2
156:8 310:21	141:2 164:8	334:10 335:22	well-documented	132:15 133:3,12
324:20 349:2	walked 82:16	336:3 337:14	111:22 112:3	133:19 134:5,15
356:10,16	want 8:7,13 27:1	338:2 343:2	well-equipped	134:15 135:2,21
verifying 72:17	29:9 36:2 40:21	361:17 362:6	336:20	136:12 137:4
74:10,10 349:19	43:8 45:18 48:18	367:13	well-established	151:8,9,19 246:16
versions 60:12	51:5 55:20 68:17	ways 34:8 40:10	139:5 167:15	246:16
versus 37:15	79:8 82:8,11	50:20 51:21 52:5	well-informed	women's 2:18
138:22 154:15	116:12 138:19	53:10 70:4 85:2	265:13	131:17,21 133:7
157:2,8 183:9	139:22 140:3	159:21 160:2,2	well-known 227:21	wonder 140:8
215:8 222:17	151:20,21 152:4	161:10,22 172:4	well-trained 336:6	wondered 222:14
225:8,16 277:21	165:7 198:18	189:14 255:15	went 82:20,21	wondering 143:2
279:22 342:16	206:7 208:17	264:7 288:2,12	113:17 198:4	277:10 369:13
352:1 358:1,2	224:4 227:8 228:1	291:1 329:14	216:13 217:17	words 358:22 370:3
vexing 188:21	235:2 251:13	weak 260:21	220:12 286:12,13	work 23:6 24:9,11
Vice 211:6 287:10	267:15 268:2	285:11	340:20 374:10	24:13,15 25:1,19
297:6	275:16 336:11	wears 275:21	we're 286:14	25:21 26:9 27:20
vice-versa 371:4	338:5 348:7,13	weather 164:5,6	white 1:12 239:6	29:22 30:3,4,6,10
victims 261:22	373:2 379:16,21	380:4	246:16 343:4	31:2,19 37:12,16
view 106:18 112:15	wanted 8:2,4 25:21	web 10:16 63:14	wholesaler 148:21	39:18 42:17 53:20
129:8 184:5 189:8	27:4 117:3 263:15	293:5 374:4	149:3,4,11,15	53:21 54:16 55:11
212:11	263:21 266:7	webcast 6:9 378:8	150:1 359:13,15	55:22 84:17 86:12
viewpoint 181:17	284:9 285:22	webinar 241:10	359:15 361:2	102:9 110:9,10,15
views 85:14 165:8,9	373:11	website 8:20 10:10	wholesalers 126:11	158:12 161:14
189:10 197:8	wants 215:21	17:1,3 47:18	149:9 310:15,17	185:5,6 189:1
318:19	272:14	62:22 63:3 65:16	316:6	193:3 197:22
vigorous 214:21	warnings 186:8	66:12 69:9 90:9	wide 50:1 52:6,14	199:16 201:16
virtue 295:7 364:8	warrant 89:8	134:20 162:18,22	71:4 85:20 296:5	203:22 204:1
visual 291:11	Washington 132:1	167:22 168:3	298:5	207:16 209:11
vital 105:5 107:6	wasn't 19:7 146:14	202:10 234:1	widely 112:6 160:3	210:4 216:21
191:9 239:13	waste 118:1	290:11 291:8	widespread 376:11	223:10,11 226:8
volume 213:13	watch 250:17	314:15 357:3,4,6	376:12	228:11,14 229:8
311:6	254:21 376:17	358:8	wild 109:12	242:22 288:9,12
voluntary 83:22	waters 367:8	websites 59:10 65:2	willing 156:20	290:11 292:4
239:21 241:4	way 41:8 43:15	68:20 290:13	157:21,22 222:1	293:10,13 304:6
242:11 262:9,19	45:3 46:1 47:7	web-based 88:19	234:18 307:7	304:13 314:3,7
264:21 277:3,12	48:4,9,13 51:10	121:11,12 197:5	373:8 376:3,4	325:12 326:2
277:16,20 278:11	51:10 110:2,9,10	225:22	willingness 191:12	333:11 344:11
279:22 280:3	111:18 120:19	week 278:16	378:4	364:9,10 372:14
344:17	125:7 144:22	379:11	Willy 377:9	376:7 378:5 379:4
voted 260:10 262:8	149:18 166:20	weighing 138:22	wind 260:20	workability 212:17

workable 295:21 316:4	worry 257:18	\$	199 4:23	215 4:25
workday 337:19,21	worst 360:7	\$50 84:8	1990 133:8 170:21	23,000 306:1
worked 27:10	wound 266:4	1	1990s 254:14,16	235 5:4
154:11 193:20	wrap 12:15 44:22	1 2:11 4:13 86:6	257:1	24 26:1 245:20
201:1 216:18	266:3	89:14 189:16	1991 198:1	24-hours 310:4
235:2 286:7 304:8	wrapping 83:12	274:14,18	1992 249:11	245 5:5
workflow 18:13	write 8:16 278:6	1,000 119:16	1994 113:13	25 1:9 105:19
36:20 79:3,5,17	351:13	1,100 91:19	1997 134:3 250:1	260:10 347:21
87:20 124:16,19	writing 65:8	1,400-bed 346:8	1998 103:6	250,000 268:21
124:21 141:18	154:19	10 260:10	1999 179:4 229:16	254 5:5
171:10,14 172:19	written 8:12 26:15	10:30 82:12,14,21	255:1 266:20	26 380:7
173:19 174:10	69:2,17 102:13	102 4:14	2	26,000 170:16
176:20 222:21	122:14 171:6	109 4:15	2 2:19 4:20 87:7	266 5:6
223:6,11 307:22	221:1 236:11,20	10903 1:13	89:20 189:17	27 190:1 211:18
308:4 313:10,13	289:4,10 290:22	11 119:9	2,000 246:2	272 5:7
331:16 332:8	291:6 307:1	11:50 7:16	2.1 268:22	287 5:10
375:7	308:14 321:18	11:52 163:4	2.6 268:20	29 4:5
workflows 171:20	wrong 113:16,17	111,000 236:5	2.7 287:19	297 5:11
298:16	115:8 283:16	115 211:20	2:54 286:12	3
workforce 336:6	wrote 136:19	119 4:16	20 15:10 170:22	3 87:15 90:4 189:20
working 15:8,13	148:21	12 106:4 117:11	279:6	3.8 287:18
17:14 22:17 24:22	Y	178:22 274:15,18	200 17:6	3:11 286:13
27:16,19 37:11	year 103:13 105:9	324:11 371:11	2000 134:3 198:1	30 92:1 116:20
41:16 99:12	182:11 183:12	12:45 7:16	198:21	117:8,14 351:13
130:22 147:1	211:20 228:14	12:53 164:2	2002 113:7 246:11	305 5:12
148:6 151:12,18	259:13 278:21	12:55 163:3	2003 181:2	31 1:12
161:10 183:12,16	279:18	129 4:17	2004 249:11	318 5:13
192:17 197:9	years 18:7 21:4	131 4:17	2005 103:10 255:1	32 271:14
199:2 206:11,13	23:19 108:11	132,000 287:19	2007 10:15 16:4	328 5:15
208:1,21 223:4	110:18 133:18	133,000 245:22	135:17 188:18	333 5:16
233:6 242:20,21	170:22 178:22	139 4:18	2008 17:7 103:11	345 5:17
266:19 305:5	182:6 183:1 189:1	14 117:9 279:8	189:10	35 120:3 261:19
323:5 337:19	189:2,22 194:7	15 82:3 346:10	2009 137:18 255:6	358 5:19
workload 187:3	198:4,20,21	15-minute 7:13	257:22	36 96:1
308:4 329:16	214:19 220:4	286:3	2009-2010 324:4	376 5:22
workplace 108:2	246:18 298:2	1503 1:13	374:5	4
works 29:14 55:10	318:15 328:16	16 117:8 279:7	2010 137:20 259:5	4 88:13 90:11 190:3
141:7 194:8	363:1,4	16th 8:18 26:17	260:9 320:5 343:4	4:30 7:3,4 376:18
212:10 217:3	yellow 12:10 83:9	379:21	2011 97:1	4:37 380:5
workshop 51:12	yield 292:12	164 4:21	2012 84:7 104:6	40 12:2 278:18
world 32:18 38:21	young 255:17	169 4:21	136:18 245:22	279:6,18
109:13 197:4	Z	170 346:10	2013 1:9 16:22 96:1	40,000 318:10
250:7 263:1	zero 220:13 274:18	178 4:22	262:10 380:8	41,000 287:17
300:18	283:18	18 117:15	2015 95:5	43 170:17
worldwide 103:5	zip 276:20	188 4:23	20993 1:13	44,000 345:22
worried 263:10		1980 245:14	211 4:24	46 278:18

49 130:4
495-bed 119:9

5

5 190:7
50 96:3
505(b)(2) 202:4
57 4:7

6

6 4:4
6:00 324:8 334:4
60 8:19 279:6
379:10
600-physician
119:12
62,000 297:10
63 4:9
65,000 175:4
66 17:9

7

7,500 170:16
7:30 7:1
70 4:11 171:4
189:22 318:15
72 17:9 96:2 287:21

8

8:30 1:13 380:3,7
8:33 6:2,4
80 282:14
81 211:16
83 4:13
88 17:11 211:16

9

9:48 82:20
90 259:16 264:10
282:14
91 4:14
92 262:1

C E R T I F I C A T E

This is to certify that the foregoing transcript

In the matter of: Risk Evaluation
and Mitigation Strategies

Before: FDA

Date: 07-25-13

Place: Silver Spring, MD

was duly recorded and accurately transcribed under
my direction; further, that said transcript is a
true and accurate record of the proceedings.



Court Reporter

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

(202) 234-4433

www.nealrgross.com