

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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FOOD AND DRUG ADMINISTRATION (FDA)

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PRESCRIPTION DRUG USER FEE ACT (PDUFA)
REAUTHORIZATION

+ + + + +

PUBLIC MEETING

+ + + + +

MONDAY
OCTOBER 24, 2011

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The Meeting convened in the Great Room at the Food and Drug Administration, Building 31, Room 1503B/C, 10903 New Hampshire Avenue, Silver Spring, Maryland, at 9:00 a.m., Patrick Frey, Moderator, presiding.

PRESENT:

- PATRICK FREY, Acting Director, Office of Planning and Analysis, FDA, Moderator
- JANET WOODCOCK, MD, Director, Center for Drug Evaluation and Research, FDA
- THERESA MULLIN, PhD, Director, Office of Planning and Informatics, FDA
- WADE W. ACKERMAN, Office of Chief Counsel, FDA
- JANE A. AXELRAD, JD, Associate Director for Policy, Center for Drug Evaluation and Research, FDA
- EDWARD COX, MD, MPH, Director, Office of Antimicrobial Products, Center for Drug Evaluation and Research FDA

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PRESENT(Cont'd):

JOHN K. JENKINS, MD, Director, Office of New Drugs, Center for Drug Evaluation and Research, FDA

ROBERT A. YETTER, PhD, Associate Director for Review Management, Center for Biologics Evaluation and Research, FDA

JEFF ALLEN, PhD, Executive Director, Friends of Cancer Research

MARC BOUTIN, JD, Executive Vice President and COO, National Health Council

DIANE DORMAN, Vice President, Public Policy, National Organization for Rare Disorders

DANIEL PERRY, President and CEO, Alliance for Aging Research

SALLY GREENBERG, Executive Director, National Consumers League

KATE RYAN, MPA, Program Coordinator, National Women's Health Network

CELIA WEXLER, Washington Representative, Union of Concerned Scientists

DIANA ZUCKERMAN, PhD, President, National Research Center for Women and Families

MARCIE BOUGH, PharmD, Senior Director, Government Affairs, American Pharmacists Association

BARRY D. DICKINSON, PhD, Director, Science and Biotechnology, American Medical Association

MARISSA SCHLAIFER, MS, RPh, Director, Pharmacy Affairs, Academy of Managed Care Pharmacy

KASEY K. THOMPSON, PharmD, Vice President, Office of Policy, Planning and Communications, American Society of Health-System Pharmacists

ANDREW EMMETT, Managing Director, Science and Regulatory Affairs, Biotechnology Industry Organization

DAVID WHEADON, MD, Senior Vice President, Scientific and Regulatory Affairs, Pharmaceutical Research and Manufacturers of America

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

2 (9:01 a.m.)

3 MR. FREY: Okay, good morning and
4 welcome to this public meeting on the
5 Reauthorization of the Prescription Drug User
6 Fee Act, known as PDUFA. Thank you for
7 joining us today. I am Patrick Frey, Acting
8 Director of the Office of Planning and
9 Analysis in the Center for Drug Evaluation and
10 Research at FDA and I will be your moderator
11 for the day.

12 First let me briefly review some
13 background information to explain the purpose
14 of this meeting. The legislative authority
15 for the current iteration of PDUFA was part of
16 the FDA Amendments Act of 2007. This
17 authority will expire in September 2012.

18 FDA began the process to
19 reauthorize PDUFA for the next five year
20 period by holding a public meeting and opening
21 up public comment period in April 2010.
22 Following that, FDA began regular concurrent

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1 discussions with industry and public
2 stakeholders, including patient advocates,
3 consumer advocates, healthcare professionals
4 and scientific and academic experts. These
5 discussions lasted from July 2010 through May
6 2011. After administration clearance, the
7 package of proposed recommendations that
8 resulted from these discussions was posted on
9 FDA's website on September 1st.

10 The purpose of today's meeting is
11 to discuss these proposed recommendations and
12 offer the public the opportunity to present
13 its views on the recommendations. A
14 transcript of this meeting will be posted to
15 the docket and on FDA's website within about
16 one month. The public also has opportunity to
17 provide written comments to the public docket.
18 The deadline for these submissions is October
19 31st, 2011.

20 By January 15, 2012, FDA must
21 transmit its final recommendations for PDUFA V
22 to Congress.

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1 Now turning to the agenda for
2 today, I think we will have ample time to hear
3 what you have to say. We will begin with
4 remarks from Dr. Janet Woodcock, Director of
5 CDER, followed by a presentation of the
6 proposed recommendations for PDUFA V from Dr.
7 Theresa Mullin, Director of CDER's Office of
8 Planning and Informatics.

9 We will allow some time for
10 clarifying questions regarding FDA's
11 presentation but I will ask that any
12 commentary be reserved for the open comment
13 period in the afternoon.

14 The FDA presentation will be
15 followed by four panels of stakeholder
16 representatives, patient advocates, consumer
17 advocates, healthcare professionals, and the
18 regulated industry. Each panelist has been
19 asked to provide their comments on the
20 proposed recommendations in about ten minutes
21 or less and I will do my best to keep things
22 moving.

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1 If we happen to have left over time
2 at the end of a panel, we will take any
3 clarifying questions you may have.

4 After the stakeholder panels, we
5 will proceed to the open public comment
6 session where 11 people have indicated a
7 desire to speak so far. If you decide you
8 would like to say something, please let me
9 know and we will add you to our schedule for
10 that session.

11 We are also webcasting this meeting
12 to a handful of people. So I will be checking
13 in with our webcast moderator periodically to
14 see if there are any questions from those
15 folks.

16 Lastly, we have a short break
17 planned in the morning and lunch is scheduled
18 from 12:00 to 1:00. The kiosk in our lobby
19 will be serving food and drink for purchase
20 during the lunch hour and the restrooms are
21 located outside the room down the hall and
22 beyond the kiosk.

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1 That is all I have right now. I
2 think I will turn it over to Dr. Woodcock for
3 her remarks.

4 DR. WOODCOCK: Thank you, Patrick.
5 And let me add my welcome to all of you who
6 have worked alongside of us during this
7 challenging process of the PDUFA V
8 negotiation.

9 We are nearing the end of our part
10 of the negotiation process. After final
11 public input and evaluation by FDA, a package
12 will go through the administration clearance
13 and then to Congress who will have the
14 responsibility of passing reauthorizing
15 legislation if this program is to continue
16 beyond September of 2012. I think you are all
17 aware of this timetable.

18 I am personally very supportive of
19 the proposals that have been negotiated. I
20 think they are a very good package. On the
21 process side, I think that increasing the
22 opportunities for communication in an

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1 organized manner during the review process
2 will improve transparency and help us reach
3 clarity in an efficient manner. And so I
4 think this provision that we have put in for
5 more interactions during review with the
6 applicant will be very helpful. We have to
7 recall that today's applications often are
8 very complex and there are additional
9 processes that were added by the Amendments
10 Act that have increased the number and types
11 of interactions and activities that must go
12 on.

13 Additionally on the process side,
14 the proposal for a staff at FDA to assist
15 small or first-time sponsors I think is a very
16 good one, as we have all gotten bigger and the
17 process has become more complicated that those
18 interactions have become difficult for the
19 smaller sponsors or those who are just
20 starting out, again because of its complexity.
21 So I think this is a great idea and will
22 really help those innovators who are just

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1 getting into the game for the first time. But
2 I also think that the drug development
3 proposals are equally important alongside the
4 process proposals. I am quite excited about
5 that.

6 As you all know, there is much
7 controversy on all sides about drug
8 development. Some people say our standards
9 are too high and preclude innovation and
10 others say our standards are too low and lead
11 to insufficient safety or greater excess
12 uncertainty for marketed products. And so we
13 are always in between these two poles. And of
14 course when people are advocating very opposed
15 viewpoints, it is quite likely that neither
16 side can be right and that there is some
17 middle ground that we can reach.

18 And I think, and I have said this
19 for a long time, the only way out of this
20 dilemma really for us, for drug developers,
21 for advocates, is improving the science of
22 clinical development so that we can actually

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1 reduce uncertainty in an efficient way. And
2 these proposals get to that.

3 The controversies I'm talking about
4 are caused by the huge amount of scientific
5 uncertainty about human response to drugs.
6 Despite enormous effort and expenditure in
7 drug development programs, there is still a
8 lot we don't know about how a drug is going to
9 perform in the market when a drug is approved.
10 And this is no one's fault. This simply has
11 to do with our lack of understanding of human
12 biology and also human behavior to some
13 extent.

14 And we still have great difficulty
15 in the development program assessing and
16 characterizing the range of human responses to
17 a drug. So we need to improve clinical
18 assessment science if we are going to get any
19 better at that and actually satisfy both sides
20 of this argument because improved scientific
21 abilities in drug development will allow us to
22 let drug development proceed in an efficient

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1 manner but it also will result in more
2 knowledge at the end of the day. So I think
3 both groups could be satisfied.

4 So the proposals that we are seeing
5 today and discussing not only pertain to drug
6 development science, they also move toward the
7 science of what I call patient-centered drug
8 development. And this is the type of drug
9 development that actually incorporates patient
10 values into understanding the benefits and
11 risks and the outcomes. It works toward
12 developing patient-reported outcome
13 instruments so we can directly collect from
14 the people who experience the drug and who
15 experience the disease and what the impact of
16 the disease and the drug are on them.

17 And also, in a separate way, we are
18 continuing our focus on individual responses,
19 rather than mean responses. And this is
20 partly what people are calling personalized
21 medicine. We know that one of our sources of
22 ignorance is that you give a drug to people.

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1 Some people respond and some don't. Some do
2 just fine and yet others have serious adverse
3 events. What we need to understand is why
4 that happens to those individuals. That will
5 enable us, as I said, to be both more
6 efficient and have safer and more effective
7 drugs. So the personalized medicine piece is
8 extremely important and we will continue to
9 push on that. And that is part of patient-
10 centered drug development because it really
11 focuses on what happens to the individual, not
12 just what happens to a population of patients.

13 And finally at the end of the day,
14 we are going to be working more if these
15 proposals go through, on our qualitative
16 benefit-risk assessment. Now to do such an
17 assessment, you have to have this information
18 that I have just been talking about and you
19 have to have it in a way that you can weight
20 it with the patient values and then we put it
21 into our framework and try to determine, from
22 a patient's point of view, will the benefits

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1 outweigh the risks for any given intervention.

2 So this is a huge step forward and
3 Patrick and his colleagues are working on this
4 in their spare time away from PDUFA. And I
5 think this will really revolutionize our
6 communication about drugs and responses to
7 drugs.

8 So these are my thoughts about the
9 PDUFA V proposals but today really we want to
10 hear your assessment and we are eager to hear
11 what you have to say.

12 Now in closing I would like to
13 remind everyone we started this at the very
14 beginning we said the PDUFA negotiation is not
15 about policy. We don't negotiate policy with
16 the industry and the other stakeholders in
17 this manner. Policies are off the table.

18 Now as this negotiation, which is
19 on process and procedures and resources, as
20 this negotiation is coming to a close, there
21 are proposals circulating by various people,
22 external folks, and some in Congress on

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1 various important policy matters and
2 evidentiary standards for drug approval. And
3 so this is, I think from the FDA point of
4 view, we would be most hopeful that we have a
5 PDUFA program that can go through cleanly and
6 actually get reauthorized so that we have a
7 PDUFA program on October 1 of next year.
8 However, we have to face reality that there
9 are many individuals and groups that have
10 additional policy-type proposals that they
11 would like to move forward along with this
12 legislation.

13 This meeting today is not intended
14 to entertain as policy proposals. As I said,
15 that is a different process outside of this.
16 But I would say if these are moving forward
17 and they do become prominent, that your voices
18 should be heard in those debates alongside the
19 others who might be raising policy issues.

20 So I thank you very much and I hope
21 you have a very productive day.

22 MR. FREY: Thank you Dr. Woodcock.

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1 Now we have Theresa's presentation on the
2 PDUFA V recommendations. And while she is
3 getting set up, if I could ask the FDA panel
4 at the head table to introduce themselves real
5 quickly. Push to talk on the mikes.

6 MS. AXELRAD: I'm Jane Axelrad, the
7 Associate Director for Policy CDER.

8 DR. YETTER: Bob Yetter, Associate
9 Director for Review Management, CBER.

10 DR. JENKINS: Good morning. I'm
11 John Jenkins. I'm the Director of the Office
12 of New Drugs in CDER.

13 DR. COX: Good morning. Ed Cox,
14 Director of the Office of Antimicrobial
15 Products in CDER.

16 MR. ACKERMAN: Good morning. Wade
17 Ackerman in the Office of Chief Counsel.

18 DR. MULLIN: Well good morning.
19 I'm Theresa Mullin, Director of the Office of
20 Planning and Informatics in the Center for
21 Drug Evaluation and Research.

22 And so I will just proceed. I have

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1 a half an hour and I thought for those of you
2 who have been following this process closely
3 and I know many of you, maybe most of you
4 have. I wasn't going to take you through
5 blow-by-blow with this presentation but I
6 wanted to recap it for everyone here.

7 So I think as everyone who has been
8 in PDUFA discussions before is aware, this
9 program was put in place because the U.S. was
10 behind. U.S. patients were not getting access
11 to the medicines that were available to
12 patients in Europe and elsewhere in the world
13 in the early 1990s. And they were among the
14 most vocal advocates for putting in place a
15 program that would provide more resources and
16 a more predictable process so that they would
17 have access to safe and effective medicines
18 sooner. This is particularly true of patients
19 in the AIDS and the cancer communities.

20 And so PDUFA is structured so that
21 the fees are additive. They are put on top of
22 a base of appropriated funds and FDA has

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1 agreed to specific performance commitments
2 that are possible because of those additional
3 resources. And the result has been a success
4 by and large. Here we have the approval phase
5 which represents the FDA review phase time.
6 And this slide shows that that has dropped by
7 nearly 60 percent since the beginning of the
8 PDUFA program. Patients have earlier access
9 to medicines, about 1500 new biologics and
10 drugs are available now.

11 And so here is a brief history of
12 PDUFA. The first authorization from 1993 to
13 1997 and that was really focused on the
14 backlog of applications that had built up over
15 time and putting in place some initial
16 performance goals to eliminate the backlog and
17 to begin to do a more reliable and predictable
18 review and getting a response back to
19 companies. Not necessarily an approval, but a
20 response.

21 PDUFA II from 1998 to 2002 was part
22 of the FDA Modernization Act and the focus

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1 there was further shortening some of the
2 review timeframes and adding sets of goals
3 related to what are called process and
4 procedures, meeting goals, so meeting with
5 sponsors during the development phase, special
6 protocol assessments, and a variety of other
7 development phase interactions.

8 PDUFA III was reauthorized as part
9 of the Bioterrorism Preparedness and Response
10 Act of 2002. And there was a significant
11 increase in funding to help cover the cost of
12 all those meetings and other commitments that
13 were made under PDUFA II and then in addition
14 for the first time, FDA was able to use fee
15 funds to take a look at what happened to the
16 safety experience after approval for up to the
17 first three years. But what we -- And we also
18 began to look at the first cycle GRMPs, Good
19 Review Management Practices during PDUFA III
20 to increase our communication with sponsors
21 during that first review cycle.

22 In PDUFA IV we extended the period

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1 and basically allowed a limited look at what
2 happens to a drug in terms of safety after it
3 is on the market, and that can be supported
4 with PDUFA funds. And there were some other
5 enhancements as well, further enhancements to
6 the pre-market review, modernizing the post-
7 market safety system and other enhancements.

8 And in addition to these other
9 things, so here is a trajectory of the
10 resourcing for PDUFA. And as you can see,
11 there has been a pretty steady increase in
12 resources. These are the sorts of goals that
13 are -- This is the structure of a lot of our
14 review goals. Ninety percent of, for example,
15 priority applications will be reviewed and
16 acted on within six months. Ninety percent of
17 standard applications within ten months. And
18 so we receive the whole cohort of submissions
19 in a given fiscal year, we apply those
20 performance goals to all submissions that come
21 in. And this is our target for what
22 percentage are going to be met within those

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1 timeframes. Because 100 percent is not
2 realistic. There can be issues and quality
3 variations in the applications and other
4 things arise. So we consider 90 percent to be
5 both an ambitious target but a realistic one
6 as well.

7 This is a chart that I think shows
8 the success of this program. One of the major
9 reasons for putting the user fee program in
10 place so was that U.S. patients would have
11 earlier access to medicines available to
12 people elsewhere in the world. And this chart
13 shows a fairly unambiguous pattern of
14 increased access to medicines first in the
15 U.S. and a success by that measure, undoubted
16 success of PDUFA in getting drugs to U.S.
17 patients earlier.

18 In addition to the Title I of FDDAAA
19 which reauthorized PDUFA, that's PDUFA IV the
20 current authorization, the FDA Amendments Act
21 included a number of other provisions and
22 other titles that had an impact on the review

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1 process because they were also relating to
2 some aspect of human drug review.

3 And I don't know if you can read
4 this in detail but essentially the three
5 titles that I am talking about are Title IV -
6 Pediatric Research Equity Act, Title V - Best
7 Pharmaceuticals for Children; and Title IX -
8 The Enhanced Authorities Regarding Post-market
9 Safety of Drugs. The Agency was given new
10 requirements for review related to pediatric
11 applications and a number of new authorities,
12 as well as new requirements for post-market
13 safety. And these were to occur within that
14 same time frame that I showed you earlier, the
15 90 percent being accomplished within those
16 timeframes that were established back in PDUFA
17 II, so ten years earlier. The timeframes from
18 ten years earlier were still in place and
19 there were new authorities and new
20 requirements for process that were being
21 inserted into those timeframes.

22 And so not surprisingly this had an

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1 impact on our performance, especially early
2 on. As you can see, the Agency's performance
3 in terms of review of new drug applications,
4 biologic licensing applications, and efficacy
5 supplements is back up to the pre-FDAAA
6 period. But sometimes you will hear, I know
7 that there have been publications out there,
8 about the drop in performance in 2008 and
9 2009. And indeed there was a drop in our
10 review performance. And it is for those
11 reasons and its return to those pre-FDAAA
12 levels at this point.

13 And this is another indicator of
14 the performance and the improvement over time
15 that PDUFA has allowed to occur. The 19
16 months was the median time to approval in 1993
17 and now we are down to a median time to ten
18 months. And again, you can see short-term
19 impact of the FDAAA implementation in '08 and
20 '09.

21 While this current PDUFA expires
22 next September 30th and we are still refining,

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1 continuing to refine the processes that we
2 have in place currently in PDUFA. We are
3 still refining the implementation of our
4 additional authorities and requirements under
5 FDAAA, and as Patrick mentioned, we have been
6 engaged in the requirements for PDUFA V
7 reauthorization as specified by the statute.
8 Many of you have been involved in this over
9 the past year and we have been very
10 appreciative of all the great input you have
11 given us in this process. And so Patrick went
12 through this process. I don't need to do it
13 again.

14 Our goals for reauthorization were
15 to continue to ensure the sound financial
16 basis for this program. Without that, we
17 don't have a steady staffing of the program.
18 And without continued reliable staffing levels
19 of this program, we can't make commitments to
20 the performance goals. It all ties together,
21 the financial basis underlies everything else
22 that we can accomplish.

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1 We want to stick to the fundamental
2 goals that this program was intended to be
3 about, continue to improve the science as Dr.
4 Woodcock mentioned. The quality of the
5 evidence that we get in submitted applications
6 on our end make it a more predictable and
7 efficient process.

8 And we want, in particular over the
9 past years, we have striven to have our
10 stakeholders feel that the priority concerns
11 that they had raised with us were being
12 addressed through this package. Many, many
13 issues were raised in that April meeting. A
14 number of them were important issues that,
15 nonetheless, felt outside the scope of the
16 PDUFA discussions that we have tried to talk
17 about and provide information and be
18 responsive and hear those concerns anyway to
19 be addressed elsewhere.

20 We have tried to at least address
21 the priority concerns we were hearing within
22 the confines of this package. And we wanted

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1 to continue to focus enhancements on improving
2 the efficiency and effectiveness of this
3 program and maintain the public confidence in
4 the program.

5 In that first meeting in April of
6 2010 a number of concerns were raised. I am
7 going to just quickly go over those now
8 because these were really themes that informed
9 the set of proposed enhancements that FDA
10 developed more details around and that a
11 number of which did make it into this final
12 package of recommendations.

13 Patient advocates told us they
14 wanted us to continue to speed development and
15 focus on regulatory science to make that
16 happen, look at innovative trial designs,
17 develop more drugs for rare diseases, get
18 information, provide them with clear
19 information on benefits and risks but also we
20 heard pretty clearly that patients in
21 particular want to have a chance to weigh in
22 more on the risks that are acceptable for

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1 treatments for the disease that they are
2 suffering from. They wanted to provide input
3 to us on REMS designs and ensure that they
4 don't become unduly burdensome and prevent
5 patient access to medications.

6 Consumer advocates were concerned
7 that we strengthen our system of oversight for
8 clinical trials, provide better information,
9 more understandable information on drug safety
10 and effectiveness, and an easier way to report
11 adverse event reporting to FDA when there is
12 problems with medications.

13 Health professionals were largely
14 concerned about the implementation of the
15 Title IX requirements around REMS. They
16 wanted something more effective than the
17 current forms of medication guides, MedGuides
18 I should say. They wanted REMS to be more
19 standardized. The healthcare system is
20 complex and burdensome enough from the views
21 of many of these people. They wanted REMS to
22 be as streamlined and standardized as possible

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1 and to obtain pharmacists and other health
2 provider input on the design of those systems.

3 Industry wanted a more efficient
4 process, get the post-FDAAA, deal with those
5 challenges, have offices work seamlessly on
6 the FDA side of this, provide more transparent
7 benefit-risk standards, and ensure consistency
8 in terms of what the Agency does and a
9 predictable timeframe with REMS request.

10 So this discussion, as Patrick
11 said, continued from July of 2010 through May
12 of 2011 and a number of enhancements resulted
13 from these discussions.

14 One of the largest, I guess in
15 terms of impact across products with today's
16 standards, scientific standards is the so-
17 called Enhanced Review Program for New
18 Molecular Entity NDAs and Original BLAs. This
19 is intended to address this concern about all
20 of the additional components and requirements
21 that are now shoe-horned into the process and
22 those timeframes. A lot of manufacturing

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1 facilities have moved overseas, as have
2 clinical trials. These inspections have to be
3 conducted within those same goal timeframes.

4 And what an analysis indicated, we
5 did a statistical analysis looking at all of
6 the approval data or rather process data and
7 what characteristics of application review
8 were associated with approval on the first
9 cycle of review and what was associated with
10 not getting approved on the first cycle,
11 looking at data from 2003 through 2009 we
12 found interestingly that those applications
13 that missed their PDUFA date, that was the
14 highest predictor of getting approved on the
15 first cycle.

16 Which is to say, review teams would
17 hold on to the application, continue to work
18 through with the sponsor to try to address
19 issues that they could tell were addressable
20 in that first cycle. And so rather than
21 kicking it back and meeting their PDUFA goal
22 which might have been you think what somebody

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1 would want to do to achieve their goals,
2 instead the review teams were holding on to it
3 to work through those issues in order to
4 achieve a first cycle approval.

5 This was very telling to us and I
6 think the industry negotiators found that to
7 be interesting. And while it does suggest a
8 little more time to allow those issues in
9 greater communication in that first cycle, if
10 the issues can be addressed in the first
11 cycle, they may be able to be addressed and
12 achieve a first cycle approval, instead of
13 having to go through multiple subsequent
14 cycles because those communications couldn't
15 occur.

16 So that is what that program will
17 allow, more time for more communication in a
18 more predictable way in that first cycle for
19 this cohort of applications.

20 Then we have a number of
21 enhancements that come under the heading of
22 regulatory science and expediting development.

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1 One, as Dr. Woodcock mentioned, is this
2 increasing the communication with sponsors
3 about a range of issues that they may be
4 concerned about that are affecting their
5 ability to move forward with an efficient
6 development program, talking more with
7 sponsors during development, developing a set
8 of best practices and methods for meta-
9 analysis that we would be using in FDA's
10 reviews, you know, we could be recommending
11 that sponsors use in their submissions to us.

12 A greater capacity to review
13 applications that include biomarker data and a
14 capacity to allow FDA to review a biomarker
15 qualification package so that there are more
16 qualified biomarkers available for use in
17 clinical trials.

18 And another form of patient-focused
19 drug development is this development of more
20 patient-reported outcome tools for different
21 diseases, validated tools for collecting
22 patients, reported experience with how well a

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1 drug is treating their symptoms and so on. If
2 these are validated, we can use them as part
3 of the evidence of benefit.

4 So more work in that area
5 increasing our capacity to support the
6 development of drugs for rare diseases,
7 enhancing that benefit-risk qualitative
8 framework, and also having a systematic
9 process of engaging with patients to hear more
10 about their views about risk and the risks
11 associated with therapies to treat their
12 condition.

13 We have some initiatives to
14 modernize post-market safety, including
15 standardizing the elements of REMs, which we
16 heard would be so desirable and we had, in
17 fact, identified that already as an area of
18 great importance to us through a series of
19 public meetings that FDA had held; using
20 Sentinel to try to evaluate safety questions
21 that come up and to see how well that Sentinel
22 capability can serve to answering questions

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1 about a particular risk that appears to be a
2 potential risk for a marketed product;
3 requiring electronic submissions and
4 standardized data to greatly improve our
5 efficiency and the quality of applications;
6 and then in terms of the sound financial
7 basis, modifying our inflation adjuster and
8 looking at the current workload adjuster and
9 making sure that it does capture the most
10 important elements of workload.

11 This is just quickly to show you a
12 summary page of the resources added to the
13 program to cover those enhancements.
14 Approximately 40 million dollars is being
15 added to the program, most of that to cover
16 additional staffing, with about 4.3 million
17 dollars of that total for contract-related
18 funding. This brings the total estimated
19 program revenue to about 712.3 million dollars
20 in the first year of PDUFA V.

21 The next steps in the process are
22 to analyze the comments that we hear today and

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1 those that we received through the docket,
2 revise the recommendations as we need to based
3 on those comments, and transmit this to
4 Congress by the statutory deadline of January
5 15, 2012 so that Congress can begin its work
6 and we can have timely reauthorization.
7 Thanks.

8 MR. FREY: Okay, are there any
9 clarifying questions for the FDA presentation?

10 (Pause.)

11 MR. FREY: All right, seeing none,
12 I can dismiss this panel for now. They will
13 be back during the open public comment period
14 in the afternoon.

15 And if we can have the panelists on
16 the patient panel come up, we will get started
17 with that.

18 The first speaker on patient panel
19 will be Jeff Allen. Jeff is the Executive
20 Director of the Friends of Cancer Research.

21 DR. ALLEN: Good morning. Thank
22 you for the invitation to be here with you

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1 this morning.

2 I would like to I think just start,
3 I have a couple slides that just have,
4 hopefully what will be, a little bit of a
5 snapshot of the kind of PDUFA experience of
6 the oncology community as a bit of a case
7 study through the process. But first I would
8 like to thank the FDA representatives that
9 were here earlier today and their respective
10 teams for really engaging the broad community
11 in a new process of communication over the
12 last several months that I hope has been
13 valuable for all parties. And I know it has
14 for myself and my other colleagues here as
15 well.

16 This first slide just shows a
17 couple of different examples of the immediate
18 impact of the PDUFA program that Dr. Mullin
19 discussed with you earlier. In the top left
20 panel, A shows the immediate reduction times
21 after the first PDUFA reauthorizations in
22 cardiovascular disease, B in oncology, panel D

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1 in anti-infective, and perhaps not the same
2 impact on CNS disorders.

3 But what I would like to do is
4 spend a little bit of time today on the
5 continued impact of the PDUFA program in
6 oncology because this trend has continued over
7 the subsequent reauthorizations of PDUFA. And
8 what you see now is since 2003, the average
9 approval times for new molecular entities,
10 NDAs in oncology, is right around six months.

11 So this is trending in a positive direction
12 for those who are awaiting new medicines in
13 oncology, which is perhaps one of the most
14 robust pipeline of new drug developments but
15 perhaps one of the most complex as far as new
16 molecular mechanisms and shrinking populations
17 due to refinements based on molecular biology.

18 Dr. Mullin mentioned in her
19 presentation that one of the goals of the
20 original PDUFA reauthorization was compared to
21 the benchmarks of other countries. So what
22 you can see here that under the current

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1 timeframes, the approval of new oncology drugs
2 is approximately half the time as it is in the
3 EMA. And in fact comparatively the United
4 States is approving more drugs in oncology
5 sooner. And of all the 27 drugs since 2003
6 that were approved in both the EMA and the
7 U.S., they were all available to U.S. patients
8 first.

9 A couple of the review mechanisms,
10 again looking specifically into new molecular
11 entities in oncology, the first is the use of
12 accelerated approvals which arguably is a very
13 strong and important program for life-
14 threatening disorders like oncology. You can
15 see in this top panel that almost a third of
16 all drugs since 2003 for cancer have been
17 improved through this important mechanism.
18 Some will cite that since 2008 perhaps this
19 number has been going down. This is likely
20 for a number of reasons, which could be
21 debated for review standards or even choice of
22 the sponsor for using this program as

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1 frequently as it was in 2003 to 2007.

2 The two other areas of the PDUFA-
3 established standard review, I think this is
4 remarkable that 35 out of 38 of the newest
5 oncology were approved within that ten-month
6 time frame. And I think this gets to the
7 importance of the first cycle descriptions
8 that Dr. Mullin just provided. And as far as
9 priority reviews, which may be identified as
10 some of the most important products, only
11 about half of those were hitting that six-
12 month time frame, which perhaps speak to the
13 extension of the two months on top of that.

14 Now I don't raise these points for
15 the purpose of saying that everything is good
16 in the world and there are not bigger problems
17 that need to be addressed as we move forward
18 with this reauthorization but really to point
19 out that the current, really the current state
20 of developing new medicine is nearing an
21 unsustainable crisis. The fact that it take
22 15 years and over a billion dollars to get a

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1 new drug to market is something that our
2 healthcare system cannot sustain and not
3 something that any of us in this room want to
4 see continue. But I think it is important to
5 note how small of a sliver that FDA review
6 time period is. So all of the facts that I
7 have shared with you about the continuing
8 decreasing time in oncology new molecular
9 entity approval is such a small component of
10 the challenge that we are all facing here.
11 And in order to truly address this problem, I
12 hope that we can move forward with these
13 discussions and the reauthorization process to
14 try and address some of those areas, both on
15 the left and the right of that FDA review time
16 period. And I really would like to commend
17 the negotiators on both sides; my colleagues
18 who have provided input along the way because
19 I think what are seeing here is a direct
20 attention to the scientific programming that
21 is essential to shrink the poles of this
22 particular diagram.

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1 The last reauthorization process
2 which was largely focused on safety
3 information and creating better systems of
4 post-market surveillance, which hopefully will
5 inform the pre-market side as well. And I
6 think what you need for this particular
7 reauthorization process is the amount of
8 attention that has been paid to for meeting
9 management for that small sliver but also for
10 scientific programming.

11 And I won't go through the guidance
12 documents that have been described but really
13 commend the agency and the industry for
14 finding unique ways to address those
15 scientific challenges not only through
16 additional guidance document but really trying
17 to implement new review processes and new ways
18 for communicating scientific information both
19 coming into the Agency and going out through a
20 series of workshops, through interactions with
21 the public that hopefully we will be able to
22 shrink the times on this slide that you see

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1 here and address the true challenges with the
2 development of new medicine as much as we can
3 in this particular process.

4 One area that I would like to
5 mention that I think is something that we can
6 all look to to try and create better
7 efficiencies for these in and out
8 communications of scientific expertise is the
9 current dealing with conflict of interest and
10 advisory committees. And these two graphs, it
11 didn't do it justice to combine them all but
12 this is available on the new FDA-TRACK website
13 where you can see on the left-hand side the
14 target number of caps that are permissible by
15 FDA and those waivers that are granted for
16 Advisory Committee Members and contrast that
17 with the common pink goal line with the large
18 number of Advisory Committee Members.

19 And I raise this to you not to say
20 something blanket that go ahead allow more
21 conflicts, that is not the point here, but I
22 think as we look at new processes for getting

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1 scientific input into the FDA that perhaps
2 scientific expertise should have a renewed
3 commitment, rather than just judging in
4 conflict or granting of waivers initially.

5 I also think there is other ways
6 through examining the Federal Advisory
7 Committee Act to look at unique ways in which
8 the Agency can interact with the public, with
9 the scientific community in order to really
10 refine some of these programs.

11 I will stop there today. I look
12 forward to everyone else's comments. And
13 thank you very much for the chance to be with
14 you today.

15 MR. FREY: Thanks, Jeff.

16 Marc Boutin will be our next
17 speaker. Marc is the Executive Vice President
18 and Chief Operating Officer at the National
19 Health Council.

20 MR. BOUTIN: Good morning. I can
21 see we have got a tough crowd here today. I
22 know we have got a lot of information to get

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1 through but let me start again. Good morning,
2 everyone!

3 (Chorus of good morning.)

4 MR. BOUTIN: That's much better.
5 Thank you.

6 As many of you know, the National
7 Health Council provides a united voice for
8 people with chronic disease and disabilities.

9 We focus on systemic issues and the
10 development of new treatments as one of the
11 core issues of the National Health Council and
12 that more than 50 national patient advocacy
13 organizations work on.

14 About a year and a half ago many of
15 the folks in the room heard from patients.
16 They talked about how it was patients who
17 chained themselves to the FDA and NIH more
18 than two decades ago. It was patients who
19 demanded access to treatments that were still
20 in clinical trials and under review. We were
21 told we couldn't have access to those
22 treatments because we didn't know if they were

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1 safe or effective. But the patient community
2 pushed back and said you know what, I'm going
3 to be dead in a year. I want access to those
4 treatments. And the beginnings of early
5 access began and an environment was created
6 that allowed for the first PDUFA
7 authorization.

8 And during the subsequent PDUFAs we
9 have seen tremendous success. The development
10 of medicines for people with chronic diseases
11 has speeded up and we have had a specific
12 focus of looking at the context of the disease
13 and the context of the treatment.

14 But you also heard a year and a
15 half ago from patient advocacy organizations
16 that said they were becoming more frustrated.

17 There was this emerging frustration amongst
18 many people with chronic diseases who felt
19 that they were not getting access to
20 treatments as quickly as they would like and
21 we felt they were being denied access based on
22 a benefit-risk paradigm that they completely

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1 did not understand. And as a result, the
2 patient community engaged in the PDUFA
3 process. And I echo Jeff's comments that the
4 opportunity to engage with FDA during this
5 process over the last year and a half has been
6 tremendously beneficial for us, and I hope for
7 the FDA and industry, and I hope it is
8 reflected in the agreement.

9 As we worked with FDA, we
10 identified several priorities. And I am going
11 to identify three that were key to many people
12 with chronic conditions. First nowhere in the
13 world is a developed, structured, objective,
14 framework for assessing benefit-risk.
15 Benefit-risk happens in the minds of the
16 reviewers but it is not articulated in a
17 framework that is agreed upon by all
18 stakeholders. There is no opportunity for
19 transparency, communication, or dialogue
20 around that benefit-risk framework and, as a
21 result, there is a lot of confusion.

22 So we asked for the creation of an

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1 objective qualitative benefit-risk framework,
2 one that would put the benefits and risk in
3 the context of the therapeutic indication, one
4 that would allow for different weights
5 depending on that therapeutic indication, one
6 that would look at the variability amongst
7 patients and the uncertainty that would exist
8 as products came to market. It is a process
9 that allows us to develop a benefit-risk
10 framework that truly works for both patients
11 and consumers. Many of you have heard me
12 speak about the spectrum of patients and
13 consumers. We are the same stakeholder but
14 depending on where you fall on that spectrum,
15 your perspective of benefit-risk can shift
16 dramatically. If you are somebody with hay
17 fever, your tolerance for risk, variability,
18 uncertainty for a new medicine to treat your
19 hay fever is virtually zero. But if you are
20 now diagnosed with ALS, Lou Gehrig's Disease
21 and you are told you have about two years to
22 live, your tolerance for a risky medication

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1 for that condition is dramatically different.

2 That doesn't change your perspective on the
3 hay fever medication.

4 Second, that qualification and use
5 of biomarkers and patient-reported outcomes.
6 This is tremendously important to the patient
7 community. When we spoke with folks at FDA
8 and folks from industry at the beginning of
9 this process, there was a lot of discussion
10 about going back to where we were. Let's go
11 back to the timeframes we had. Let's make
12 sure we are doing it as fast as we did it in
13 the past. Well I will tell you that is not
14 good enough for people with chronic
15 conditions. They want the process to go
16 faster and we saw opportunity and regulatory
17 science to develop metrics and tools to make
18 the process more effective, more efficient,
19 and allowed the delivery of safe and effective
20 medicines to people who need them.

21 Lastly, the development of
22 treatments for rare disease. My colleague

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1 Diane Dorman will be speaking to this issue,
2 I'm sure, but for the millions of people with
3 rare diseases, the challenges of developing
4 treatments are significant. The opportunity
5 for new resources and flexibility in the
6 science in developing those treatments is of
7 huge importance to many millions of people
8 with chronic conditions.

9 Let me simply say that PDUFA V
10 offers us an opportunity for the first time in
11 the world to develop a benefit-risk framework
12 that will transpire transparency, provide a
13 framework for meaningful dialogue, and allow
14 us to make benefit-risk work in the
15 therapeutic context for both patients and
16 consumers and at the same time promote
17 regulatory science to over time speed the
18 delivery of the development of medicines for
19 people who need them.

20 I want to, as well, thank the FDA
21 and industry for hearing our concerns and for
22 addressing them in a meaningful way in PDUFA

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1 V. And I say to everybody in the room, let's
2 get it done. Let's get it done fast.

3 Thank you.

4 MR. FREY: Thanks, Marc. Sounds
5 good.

6 Diane Dorman is next. Diane is the
7 Vice President of Public Policy at the
8 National Organization for Rare Disorders.

9 MS. DORMAN: Thank you very much.
10 I want to thank the Food and Drug
11 Administration for providing NORD the
12 opportunity to speak today regarding our
13 position on reauthorization of PDUFA.

14 Since 1983, NORD has served as the
15 voice and advocate for the 30 million men,
16 women, and children in the United States
17 affected by one of the 7,000 known rare
18 diseases. NORD's mission is to ensure that
19 this nation is one where people with rare
20 diseases can secure access to drugs and
21 biologics that extend and improve their lives,
22 enabling them to be successful members of

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1 society.

2 One of our objectives is to ensure
3 that there continues to be a social,
4 political, and financial culture of innovation
5 that supports both the basic and translational
6 research necessary to create effective
7 therapies for all rare disorders and support a
8 regulatory environment that encourages
9 development and timely approval of safe and
10 effective treatments for individuals with rare
11 diseases.

12 NORD views PDUFA reauthorization as
13 the unique opportunity to develop a
14 comprehensive series of recommendations to
15 advance orphan product development. The rare
16 disease community believes that engaging
17 Congress and FDA officials in the process will
18 lead to practical and detailed recommendations
19 that can be implemented throughout the
20 development process from concept to access.

21 Of significance in the draft is the
22 rare disease initiative that will enhance the

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1 development of drugs and biologics for the
2 treatment of rare conditions. NORD supports
3 these efforts and looks forward to the
4 opportunity to work with the Agency to
5 guarantee success of this initiative.

6 The agreement that is currently
7 written completes the staffing and
8 implementation plan for the CDER rare disease
9 program within the Office of New Drugs and
10 establishes a CBER rare disease liaison within
11 the Office of the Center at CBER.

12 Among other things, the CBER and
13 CDER offices will develop and disseminate
14 guidance and policy related to orphan product
15 development and work with center reviewers to
16 improve their understanding of the unique
17 challenges of study design, end points, and
18 statistical analysis of orphan product
19 development.

20 Missing in the draft agreement is
21 increased coordination between two other key
22 centers. Although regulatory schemes differ

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1 between CDER, CBER, CFSAN, and CDRH, there are
2 underlying themes of commonality:
3 geographically disbursed small patient
4 populations, and of course the challenges of
5 trial design. Because NORD felt this also
6 includes humanitarian use devices and medical
7 foods for inborn errors in metabolisms and
8 other rare conditions, increased collaboration
9 between all centers is critical to move the
10 product to the development of orphan products
11 for rare diseases.

12 I would now like to talk a little
13 bit about the Advisory Committee conflict of
14 interest issue. During FDAAA negotiations,
15 NORD argued that because patient populations
16 are very small, few companies are willing to
17 take on the financial risk of developing
18 orphan products and there are a limited number
19 of researchers conducting this research
20 identifying experts not financially conflicted
21 to sit on an advisory committee would be
22 difficult, if not impossible.

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1 These concerns were realized in
2 2008 when it took the FDA nearly six months to
3 identify an expert to review a lifesaving
4 therapy to treat infantile spasms. To address
5 those concerns, NORC has joined forces with
6 over 50 organizations who are deeply concerned
7 about the issue of the current conflicts of
8 interest statutory provisions and their impact
9 on the appointment of experts, particularly
10 researchers and patients as special government
11 employees on FDA advisory committees and as
12 otherwise needed.

13 As a group, the organizations
14 promote efforts to bring better treatments and
15 cures to those struggling with diseases. Many
16 of these conditions have no adequate
17 treatments and, therefore, it is imperative
18 that we challenge hurdles that impede the
19 quality and efficiency of the treatment
20 development process. It is our belief that
21 protections must be in place where persons are
22 appointed to positions where their own

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1 financial interests might influence the
2 service to the federal government.

3 However, it is also our strong
4 belief that the current conflict of interest
5 statutes that apply to the FDA have resulted
6 in a system that is out of balance to the
7 point that conflict avoidance is the primary
8 driver of who serves on advisory committees,
9 regardless of the extent of the conflict and
10 the uniqueness of their expertise or the
11 government's need for their services.

12 As you know, FDA SGEs are subject
13 to an additional layer of statutory conflict
14 of interest divisions beyond those that
15 already govern SGEs for all other departments
16 and agencies in the executive branch.
17 Specifically under current law, the FDA must
18 analyze potential committee members pursuant
19 to Section 712 of the Food, Drug, and Cosmetic
20 Act in addition to the government-wide
21 provisions found in the Federal Advisory
22 Committee Act and the Ethics in Government Act

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1 of 1978. This additional FDA-specific
2 provision appears to drive the FDA to look
3 only for individuals to serve as SGEs who have
4 virtually no financial ties to an issue that
5 might be addressed by a given advisory
6 committee.

7 While that may sound wise at first
8 glance, in fact those with expertise in a
9 given area often have unforeseeable and
10 unavoidable ties to the community as a result
11 of their expertise. Yet under the current
12 structure, the FDA is not allowing those
13 individuals to serve as SGEs, despite the fact
14 that by doing so the FDA is being deprived of
15 expertise by those who are best qualified.

16 Accordingly, we support any effort
17 to eliminate the additional conflict of
18 interest restrictions that apply only to the
19 FDA. It is our conviction that the existing
20 provisions in the Federal Advisory Committee
21 Act and the Ethics in Government Act of 1978
22 are adequate to safeguard against conflicts of

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1 interest while still allowing those with
2 necessary expertise and perspective to serve
3 on those very important committees.

4 In fact, the specific standard for
5 SGEs found in U.S. Code recognizes that
6 potential SGEs may have conflicts of interest
7 but allows for this service nevertheless when
8 the need for their services outweigh the
9 potential for a conflict of interest created
10 the financial interest involved. That
11 standard is clear, reasonable, and balanced,
12 and appropriately recognizes that some
13 potential SGEs may come to the FDA with ties
14 to the community that may pose some conflict
15 of interest but that the primary issue must be
16 the government's need for their services.

17 The main goal of these committees,
18 after all, is to help the FDA to make the best
19 decisions possible. The FDA can only do that
20 if it has the best, most well-informed
21 researchers, clinicians, and patients advising
22 them.

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1 Now I am going to go on to risk
2 tolerance in the patient community. Earlier
3 this year, NORD convened a meeting of like-
4 minded members of the patient community to
5 discuss the willingness or reluctance of
6 patients and their families to tolerate a
7 greater degree of risk in the use of therapies
8 to treat chronic and rare conditions. Our
9 goal was and continues to be to develop a
10 proposal which we have already submitted to
11 the FDA as to how the patient community can
12 communicate on a more frequent and periodic
13 basis with medical reviewers and other
14 relevant FDA staff as they are making risk
15 tolerance and other decisions regarding
16 specific product applications while making
17 policy decisions. Thirty-two organizations
18 who signed the letter submitted to CDER on
19 September 27th are in full agreement that it
20 is essential that patients have the
21 opportunity to provide such input to product
22 and policy decisions made by the FDA,

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1 particularly with regard to risk tolerance
2 associated with the use of specific products.

3 Mechanisms currently exist for
4 patients and other external audiences to
5 provide input to the FDA, for example, the
6 public sessions of advisory committees but the
7 input does not necessarily occur at the time
8 that risk tolerance and other critical issues
9 are being deliberated and does not necessarily
10 represent a broad spectrum of patient views.

11 As the FDA commits to a more
12 patient-centric posture and as patients
13 themselves become more knowledgeable and
14 sophisticated about diseases and their
15 treatment options, we advocate that more
16 systematic approaches be established at FDA to
17 enable contributions from the patient
18 community at the time that critical decisions
19 on risk tolerance are being made and from a
20 representative sample of patient views. We
21 believe the process should be well-defined and
22 well understood within the review divisions

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1 and provide a universally applied opportunity
2 for patients to make such input.

3 We are conscious that FDA reviewers
4 and other relevant FDA staff may have demands
5 on their time but strongly believe that a new
6 process for input will improve product
7 analysis and approval and access to necessary
8 treatments in a timely manner. We recognize
9 that risk tolerance and other critical
10 decisions are made at any points during the
11 regulatory life cycle of a product from
12 initial clinical trials to marketing.
13 However, at some point in the review process
14 when risk assessments are made, patient
15 contributions will be of value to the FDA
16 decision-makers.

17 We also recognize continuous
18 interaction with the patient community is not
19 always feasible. At the same time, the
20 patient community believes that specific
21 milestone events should be designated at the
22 times at which FDA as a matter of policy seeks

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1 full input from the patient community.

2 We do not seek to create a
3 burdensome or a time consuming process.
4 Rather, we want to be sure that patients
5 across the country, whether they belong to a
6 patient organization or not, have the
7 opportunity to share their views with the FDA.

8 Our hope and expectation is that the kinds of
9 information that patients and patient
10 organizations can share with the FDA will
11 contribute towards its decision-making in
12 assessing the benefit-risk equation for new
13 products, as well as the amount of risk
14 patients at various stages of their condition
15 are willing to take, the quality of life
16 challenges they face, the ways they receive
17 information about the proper use of their
18 therapies, how often they see and receive
19 information from their physicians, and other
20 information that FDA medical reviewers and
21 other relevant FDA staff made better from
22 going directly from patients.

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1 So in closing, I want to thank the
2 FDA for giving NORD the opportunity to address
3 our concerns related to reauthorization. We,
4 along with the organizations we work with to
5 address conflict of interest and risk
6 tolerance issues welcome the opportunity to
7 work with the Agency.

8 Now on a different note, as a
9 member of the Board of Directors, I would be
10 remiss if I failed to mention the Alliance for
11 a Stronger FDA. The Alliance has over 180
12 members spanning from not-for-profit
13 organizations, patients, research, advocacy
14 organizations, associations representing
15 health professions and industry, and
16 individual companies. The Alliance works to
17 ensure annual appropriations that will
18 adequately fund the FDA's essential mission
19 and we believe that the American people expect
20 there is no other Agency that performs this
21 critical work.

22 I invite you to learn more about

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1 the Alliance and to join forces with it to
2 ensure that the FDA is adequately funded
3 through appropriations. Thank you.

4 MR. FREY: Thank you, Diane. The
5 last speaker on this panel will be Daniel
6 Perry, President and CEO of Alliance for Aging
7 Research.

8 MR. PERRY: Good morning. Thank
9 you very much, Patrick Frey and Theresa Mullin
10 for the invitation to join today's panel of
11 patient representatives and for the
12 opportunity to comment on the proposed
13 reauthorization of the latest version of the
14 Prescription Drug User Fee Act.

15 On behalf of the Alliance for Aging
16 Research I extend my sincere appreciation to
17 all of the employees of the FDA who are here
18 today and to all of your colleagues for the
19 challenging and extremely important jobs that
20 you do every day. Quite obviously, the impact
21 of your work is felt by millions of older
22 Americans and tens of millions more who aspire

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1 someday to be older Americans.

2 The Alliance for Aging Research is
3 a private not-for-profit organization now in
4 our 25th year working for public policies to
5 promote medical and scientific research in
6 human aging and in the chronic diseases that
7 accompany it all too often, so that we might
8 all realize better health and quality of lives
9 as we grow older.

10 We are all familiar by now with the
11 unprecedented and consequential graying of
12 nations, the aging of populations around the
13 world. In January of this year, the first of
14 some 77 million American Baby Boomers began
15 turning age 65. For many years, our
16 population has been producing approximately
17 6,000 new senior citizens every day and adding
18 them to America's Medicare roles. Beginning
19 this year, we went from 6,000 to 10,000 people
20 celebrating a 65th birthday each and every day
21 and we will stay at that higher level now for
22 the next 18 years.

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1 As people grow older, many will
2 experience increasing risks of chronic age-
3 related ailments: coronary artery disease,
4 stroke, heart failure, type II diabetes,
5 cancer, bone and joint disabilities, vision
6 loss, and neurological disorders such as
7 Parkinson's and Alzheimer's disease. Unless
8 we discover and put to work in a more
9 effective means to prevent, postpone, or
10 reduce the impact of diseases of aging, the
11 U.S. faces what we call a silver tsunami of
12 age-related infirmities and disabilities that
13 carry enormous social, cultural, and economic
14 costs.

15 At the alliance for aging research,
16 we view the federal agencies that monitor
17 public health and invest in aging research and
18 regulatory science as America's most important
19 defenses against the coming of this silver
20 tsunami. FDA's processes for evaluating and
21 approving new and innovative therapies for
22 chronic diseases are critical to allow

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1 discoveries to move from basic science and to
2 become the next medical breakthroughs. We
3 recognize that the FDA can only realize this
4 vital role if proper resources and policies
5 are in place.

6 The current proposal under
7 consideration for PDUFA V is a positive step
8 toward enabling the Agency to conduct more
9 patient-focused scientifically sound and
10 timely reviews. My organization has been a
11 regular participant in the monthly stakeholder
12 engagement process, as are others who are here
13 today. While patient organizations were not
14 at the same negotiating table with industry
15 and the FDA, we feel that the Agency took
16 seriously the directives from Congress and
17 FDAAA to consult with members of the patient
18 community on their views regarding the user
19 fee program.

20 From the time the Agency held its
21 first public meeting in April 2010, concerns
22 presented by patients' advocates were received

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1 by the Agency staff and appropriately included
2 in the enhancement proposals put forth by FDA
3 in the negotiations. These issues included
4 accelerating drug development through greater
5 focus on regulatory science, supporting the
6 development of innovative clinical trial
7 design, reevaluating how the Agency assesses
8 benefits and risks of therapies and how it
9 communicates benefit-risk information, and
10 ensuring that REMS, risk evaluation and
11 mitigation strategies do not serve as a
12 barrier to patient access.

13 For the past five years, the
14 Alliance for Aging Research has shared a
15 coalition of more than 50 national nonprofit
16 groups focused on regulatory and scientific
17 issues related to one disease, Alzheimer's.
18 This coalition is called ACT-AD, which stands
19 for Accelerate Cures and Treatments for
20 Alzheimer's Disease. Our coalition is made up
21 of organizations representing the interests of
22 Alzheimer's patients and their families, older

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1 Americans, women's health groups, care givers
2 healthcare providers, and researchers. Much
3 of our coalition's work on Alzheimer's focuses
4 on how to select patients for clinical trials
5 for treatments effective at the earliest stage
6 of the disease; how to appropriately balance
7 the potential benefits of new therapies
8 against the ever-present level of risk of harm
9 from the treatments; how to approach the
10 generalized ability of results from a specific
11 trial population to the larger patient
12 population; and how to measure the clinical
13 benefits of treatment for patients at the
14 earliest discernable stages of the disease.

15 ACT-AD has identified the selection
16 of end points in clinical trials as a
17 critically important part of successful drug
18 development. With respect to end points that
19 capture patient-reported outcomes, reliability
20 has been a problem, which results in high
21 failure rates for these types of trials. We
22 are encouraged that the FDA would like now to

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1 devote more resources under PDUFA V to both
2 increase their capacity to address trials that
3 include PROs and engage in public consultation
4 about qualifying PROs.

5 We are pleased to see that FDA will
6 utilize PDUFA V fees to increase its capacity
7 to advance the use of biomarkers and
8 pharmacogenetics in drug development. This is
9 becoming more critical as evidence accumulates
10 supporting the use of biomarkers in order to
11 decrease drug development time. FDA likely
12 will continue seeing an increase in
13 applications, including the use of biomarkers
14 in Alzheimer's clinical trials.

15 We support FDA's commitment in
16 PDUFA V to developing a framework for
17 enhancing risk-benefit decision-making that
18 systematically and openly gathers input from
19 patients. CDER and CBER are committed to this
20 agreement for a total of 20 meetings over four
21 years to receive input from patients and their
22 representatives on disease, severity, and

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1 unmet medical needs. These meetings, many
2 focused on individual diseases, will be
3 extremely valuable to the patient community.
4 However, we regret that the original
5 enhancement proposal of half again as much, 30
6 meetings over four years was not agreed to in
7 the negotiations.

8 There are many diseases and patient
9 organizations for which risk-benefit tradeoffs
10 are critical to helping chronic and terminally
11 ill patients achieve the outcomes they want
12 from the treatment, but it improved quality of
13 life, increased length of healthy life, or
14 other objectives. If there is no flexibility
15 or available funds to consider additional
16 meetings under PDUFA V, we hope the FDA will
17 consider committing staff and resources to
18 scale up to a point where the Agency can
19 consider additional meetings either supported
20 by appropriated funds or obtained in the next
21 reauthorization round.

22 It is also not entirely clear how

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1 the FDA will analyze the proceedings from
2 these meetings and translate them into
3 operative procedures and decision-making. The
4 initial enhancement proposal detailed how this
5 information would be utilized including for
6 new and updated guidance. We are not certain
7 this is still the Agency's intent. Therefore,
8 we urge the FDA to clarify its plans for
9 incorporating what it learns from these
10 audiences into new or updated official
11 guidance.

12 For those diseases with an
13 established patient representative program,
14 such as cancer and Alzheimer's, there has been
15 an avenue for patient voices to be heard in
16 the medical product development process. We
17 are pleased that PDUFA V supports increased
18 utilization of the patient representative
19 program. We strongly feel that early and
20 frequent patient consultations will lead to
21 more balanced evaluation of new products,
22 particularly for FDA staff that do not

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1 regularly interact with or treat patients with
2 a particular disease or condition.

3 We further hope that tighter
4 conflicts of interest rules through FDAAA do
5 not act as a barrier to FDA's access to needed
6 expertise either from patients or medical
7 experts when the Agency needs the best advice
8 that it can get.

9 We believe that policy changes made
10 during PDUFA IV, such as those concerning REMS
11 for new drugs could help regulators and
12 clinicians to acquire more data on the known
13 and unknown risks the drugs present and allow
14 FDA and industry to manage those risks
15 appropriately in the post-market space.
16 Currently, many conversations about managing
17 risks are happening too late in the reviewing
18 process and responsible for delays in drugs
19 coming to market. We are pleased with reforms
20 in PDUFA V to improve REMS. By starting
21 safety conversations earlier, these changes
22 will help sponsors and the Agency to identify

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1 safety issues in trials and make necessary
2 adjustments.

3 And to echo Diane Dorman's
4 comments, I, too, serve as a founding member
5 of the Alliance for a Stronger FDA. The
6 Alliance for a Stronger FDA has taken on the
7 role of educating Congress on the urgent need
8 for adequate resources for FDA and how
9 unfunded mandates have put a heavy burden on
10 the Agency in recent years.

11 In light of the difficult
12 appropriation's outlook for the foreseeable
13 future, we understand that there is a need to
14 remain true to what is in the PDUFA V
15 agreement so FDA can maintain a sound
16 financial basis. The merits of the current
17 agreement certainly warrant wide-spread
18 support. However, we hope that FDA has plans
19 in place and will continue to work with
20 patients and other stakeholders to address
21 those issues put forward in the initial
22 enhancement proposals but not retained in the

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1 current agreement.

2 In particular, we would like to see
3 further effort and resources devoted to
4 ensuring the quality of adaptive trial designs
5 and resources devoted to informed optimal dose
6 selection.

7 Thank you for the opportunity to
8 share these comments on PDUFA V, the current
9 reauthorization process. I welcome the
10 opportunity to provide additional comments and
11 look forward to looking with the Agency on
12 initiatives that will help us move forward
13 swiftly to new treatments that are both safety
14 and with efficacy. Thank you.

15 MR. FREY: Thank you very much,
16 Dan. Are there any questions in the room,
17 clarifying questions for this panel or on the
18 webcast?

19 (Pause.)

20 MR. FREY: Okay, seeing nothing, I
21 think we are at our break and we are ahead of
22 schedule. The break is 15 minutes. So if you

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1 can be back here by 10:25, we will start with
2 the consumer panel at that time.

3 (Whereupon, the foregoing proceeding went off
4 the record at 10:13 a.m. and
5 resumed at 10:35 a.m.)

6 MR. FREY: The first speaker on the
7 consumer advocate panel will be Sally
8 Greenberg. Sally is the Executive Director of
9 the National Consumers League.

10 MS. GREENBERG: Okay, well the
11 podium is better for sound but I am vertically
12 challenged so I hope everybody can see me.

13 So good morning. On behalf of the
14 National Consumers League I would like to
15 thank the FDA for the invitation to share a
16 consumer-oriented perspective on proposed
17 recommendations for the reauthorization of the
18 Prescription Drug User Fee Act, known as PDUFA
19 V.

20 The National Consumers League was
21 established in 1899 and it is the nation's
22 oldest nonprofit consumer education and

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1 advocacy organization. NCL provides
2 government, businesses, and other
3 organizations with the consumers' perspective
4 on numerous policy issues. From the first
5 pure Food and Drugs Act passed in 1906 to the
6 more recent FDA Modernization Act, NCL has
7 been working often alongside this Agency to
8 ensure that the public is adequately
9 represented and protected and that our
10 medications are safe and effective.

11 It is in this context that NCL
12 expresses concern that many of the
13 recommendations for this reauthorization of
14 PDUFA are focused on reducing perceived
15 barriers to new drug approvals, rather than on
16 protecting and promoting the health of
17 patients and consumers by ensuring access to
18 safe and effective medications.

19 The other consumer groups
20 represented on this panel, all members of the
21 patient, consumer, and public health
22 coalition also share these overriding

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1 concerns.

2 NCL believes that we should have a
3 drug approval process that provides timely
4 access to safe and effective drugs while
5 reducing exposure to harmful drugs that pose
6 undue risk. We recognize that PDUFA must
7 balance the needs of consumers who are
8 concerned about serious side effects with the
9 concerns of patients who may be facing a life-
10 threatening illness where time is of the
11 essence. Thus, while it is important having
12 efficient and timely approval process there is
13 still in our view too little emphasis on
14 performance goals aimed at improving the
15 safety and efficacy of drugs.

16 We continue to be concerned that
17 the public has too little opportunity to fully
18 engage in the PDUFA process. While we
19 appreciate the FDA's efforts to keep
20 stakeholders informed about the negotiations
21 and to solicit our input on the proposals
22 under discussion, consumer and patient groups

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1 were not present during the negotiations. And
2 as a result, several patient and consumer
3 protection initiatives that were put forward
4 were never discussed in the formal dialogue
5 with industry. We believe that the PDUFA
6 proposal should not move forward without these
7 additional provisions.

8 And I am going to address several
9 of those issues right now. First, direct-to-
10 consumer advertising of prescription drugs.
11 NCL has long been interested in ensuring that
12 consumers receive accurate and useful
13 information about their healthcare, including
14 information about the safe and effective use
15 of prescription drugs. With over four billion
16 dollars spent a year on DTC ads and over 91
17 percent of Americans reporting that they have
18 seen or heard advertisements for prescription
19 drugs, DTC ads have become an integral part of
20 communicating information on prescription
21 drugs.

22 Consumers are continually exposed

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1 to these ads and it is imperative that the FDA
2 have the staff and the resources to ensure
3 that the ads are accurate and not misleading
4 before they reach the public. As we have
5 mentioned in previous testimony before this
6 Agency, we recommend that FDA be granted the
7 authority to require that all DTC ads undergo
8 review before public dissemination. This
9 would enable Agency staff to work with
10 industry to revise materials where needed so
11 that misleading information does not reach
12 consumers. Without the authority to make
13 review a condition of broadcasting, product
14 sponsors have no incentive to submit their ads
15 for Agency review.

16 NCL urges the FDA to make the
17 review of ads for newly approved drugs a top
18 priority. FDA should also consider placing a
19 moratorium on all DTC advertising for new
20 drugs, especially those deemed to have
21 inadequate safety information. Based on
22 available safety data, the Agency should be

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1 given latitude in determining that the
2 appropriate length of the moratorium on a
3 product-by-product basis.

4 NCL would support adding a third
5 provisional status for some new drugs which
6 would allow limited exposure of a product to
7 appropriate patients. This would mitigate the
8 likelihood of inappropriate use and
9 overexposure, while additional post-approval
10 safety data collection is ongoing.

11 In order to conduct such oversight
12 of DTC advertising, we suggest that user fees
13 be allocated to support hiring of additional
14 staff to review ads and respond to industry
15 feedback in a timely fashion. There is
16 currently a dangerous imbalance between the
17 volume of DTC advertising and the resources
18 available for monitoring and reviewing the
19 advertisement. This imbalance becomes even
20 greater when considering the growing number of
21 internet and social media advertising for
22 prescription drugs.

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1 As consumers increasingly turn to
2 the internet for health information, it will
3 be more important than ever for FDA to have
4 the resources to ensure that consumers receive
5 balanced information about the drugs
6 advertised to them.

7 Let me take a moment to talk about
8 adverse event reporting in MedWatch. Because
9 reports of adverse events from consumers and
10 healthcare professionals may be the first
11 indication of a drug's safety problem, it is
12 important that consumers are able to easily
13 report any adverse events with medical
14 products and that the FDA is able to capture
15 and act upon that information. We are
16 encouraged by the improvements that FDA is
17 making to the MedWatch forum for consumers.
18 If FDA wants to encourage voluntary consumer
19 reporting of adverse events, the Agency must
20 ensure that reporting mechanisms are consumer
21 friendly.

22 While we support FDA's provisions

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1 of the MedWatch forum, we are concerned that
2 those revisions will fail to address the fact
3 that complaints entered into MedWatch are
4 rarely used because of how the information is
5 captured by the FDA. We understand that the
6 information electronically collected on
7 MedWatch is not able to be easily transferred
8 to a usable electronic format so the trends
9 could easily be identified. The MedWatch
10 system is not an active surveillance system.
11 It is in fact a passive program. We suggest
12 that these issues be resolved so that MedWatch
13 can effectively serve as an early warning
14 system in a larger post-market safety
15 surveillance system.

16 Let me talk a moment about off-
17 label prescribing. While off-label use of
18 medications can sometimes be beneficial, the
19 majority of medications so prescribed have no
20 valid scientific evidence in support of such
21 prescribing. A recent review by the Agency
22 for healthcare research and quality found that

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1 while antipsychotic drugs are used for many
2 off-label indications, for the majority of the
3 medications there was little evidence of
4 benefits and in some cases, there are serious
5 adverse effects.

6 From a consumer perspective, many
7 people are likely unaware that they are even
8 being prescribed off-label drugs. Consumers
9 should be informed about the following if they
10 are prescribed drugs off-label: availability
11 of alternatives; second, a body of evidence
12 supporting product use; third, approval,
13 status and use in other countries; and fourth,
14 implications for insurance coverage.

15 Finally, we urge that the PDUFA V
16 funds be directed to examining the safety of
17 off-label prescribing and the implications of
18 the lack of consumer awareness and
19 understanding of the practice.

20 In conclusion, we believe that
21 proposed recommendations must do more to
22 ensure the safety of patients and consumers

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1 and the scientific integrity of the drug
2 review process.

3 Thank you for giving the NCL the
4 opportunity to present our views on this
5 important hearing related to the
6 reauthorization of the Prescription Drug User
7 Fee Act. Thank you.

8 MR. FREY: Thank you, Sally.

9 Next up we have Kate Ryan. Kate is
10 a Program Coordinator at the National Women's
11 Health Network.

12 MS. RYAN: Good morning, everyone.

13 Well first I want to say that I am from the
14 National Women's Health Network, which is a
15 nonprofit advocacy organization that works to
16 improve the health of all women. Our goals is
17 bring the voices of women consumers to policy
18 and regulatory decision-making bodies, such as
19 the FDA and we are supported by our members
20 and don't take financial contributions from
21 drug companies, medical device manufacturers,
22 insurance companies, or any entity with a

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1 financial stake in women's health decision-
2 making. We are also a member of the Patient
3 Consumer and Public Health Coalition, along
4 with the other speakers on the consumer panel.

5 I also want to start by thanking
6 the FDA for the opportunity to speak today
7 about the fifth reauthorization of PDUFA. We
8 have also been very involved with the
9 stakeholder meetings and I greatly appreciate
10 the ways in which we have been able to
11 contribute to the development of this program.

12 In particular, I want to talk today
13 about the way the program can be strengthened
14 as it relates to ensuring the safety and
15 effectiveness of drugs for women. Women rely
16 on the FDA to ensure that the drugs they use
17 will only be approved and made available if
18 they are safe and effective and that the
19 approved drugs that we manufactured and
20 marketed according to the highest safety
21 standards.

22 As some of you sure know, the

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1 network has a long history of working with the
2 FDA and while we often play the role of
3 critic, we are staunch advocates of the
4 critically important contribution of the
5 Agency. Our criticisms come from our
6 commitment to improving the FDA's ability to
7 protect the public from exposure to
8 unnecessary medical risks caused by unsafe
9 drugs. And I offer our comments today in that
10 spirit.

11 I would like to begin by addressing
12 the reauthorization process itself,
13 specifically the transparency efforts that
14 were included by Congress in PDUFA IV to
15 better engage patient and consumer advocacy
16 groups in this process. The meetings we have
17 attended over the last year have been
18 incredibly informative and have given us
19 valuable opportunities to ask questions and
20 discuss concerns about issues of importance to
21 our constituencies. We also appreciate that
22 the agency used this forum to share and

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1 discuss with us the FDA's proposals for
2 potential enhancement in PDUFA V. These
3 insights have allowed us to better participate
4 in this go around of PDUFA.

5 That said, however, our meetings
6 with the Agency included little substantive
7 information about the negotiations themselves
8 or specific areas of focus or problems within
9 the negotiations with regulated industry. The
10 lack of specificity in combination with delays
11 in meeting minutes severely hindered our
12 ability to provide timely and relevant
13 comments on the ongoing negotiations. We
14 believe the proposed recommendations reflect
15 this power dynamic which is why we have and
16 will continue to advocate for a seat at the
17 table.

18 After reviewing the proposed
19 recommendations, we are disappointed that the
20 proposed recommendations fail to address
21 specific concerns we have raised about the
22 safety and efficacy of drugs and the health of

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1 patients and consumers. We recognize that
2 some of these recommendations definitely have
3 the potential to benefit patients by speeding
4 up the approval process and improving the
5 chances the drugs will be available to them
6 when they are needed. There is too little
7 evidence, however, on performance goals aimed
8 at improving the safety and efficacy of drugs.

9 Drugs must only be approved with
10 adequate evidence to support their safety and
11 efficacy and that that must be supported by a
12 robust post-market surveillance system to
13 ensure that drugs found to be dangerous are
14 removed from the market as quickly as
15 possible. The PDUFA V proposals that we
16 shared with the FDA during the negotiation
17 process but which did not make it into the
18 recommendations, focused on specific patient
19 safety and consumer protection initiatives,
20 some of which, granted, are being worked on by
21 the FDA but without, we believe, adequate
22 support.

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1 In particular, our recommendation
2 supported an integrated and robust safety
3 surveillance system going from the passive
4 reporting through MedWatch to active safety
5 surveillance with Sentinel. If included, we
6 believe our proposals would allow the FDA to
7 more quickly and efficiently identify problems
8 and take action to protect the health and
9 safety of American consumers. The proposals I
10 will outline identify key safety initiatives
11 where this additional support is needed.

12 As Sally said with regard to
13 MedWatch, we believe it is an important first
14 step and one that has been used more often in
15 recent years, which we think is important in
16 terms of having the advisory committees, for
17 example, looking at and reassessing the safety
18 and effectiveness of products that have been
19 on the market for some time. However -- Well
20 actually I will also say we have been working
21 very closely with the FDA on developing the
22 new consumer friendly MedWatch form and have

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1 really appreciated the way in which the FDA
2 has engaged patient and consumer stakeholders
3 in the development of this form.

4 While it looks great, it's not
5 finished yet but it looks good thus far, we
6 also really want to support what Sally had
7 said regarding needed resources to update the
8 FDA's IT capabilities and allow its
9 biostatisticians to use MedWatch in a more
10 efficient and speedy manner.

11 We would also like to discuss
12 active surveillance. I will get into sentinel
13 a little bit later but specifically we think
14 that there are ways in which it could be used
15 both in its pilot form when it is scaled up to
16 assess off-label prescription of drug use
17 which Sally addressed has very little
18 evidentiary basis.

19 We believe that the FDA could use
20 Sentinel to determine where off-label drug use
21 is occurring and conduct low-cost
22 observational research to determine the safety

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1 and effectiveness of such uses. The results
2 of this research could be used to guide
3 regulatory action and if the results of the
4 research were made public, allow prescribers
5 and patients to make more informed decisions.

6 We also strongly support expanding
7 the Agency's capacity for monitoring direct-
8 to-consumer advertising. There continues to
9 be a dangerous imbalance between the volume of
10 DTC advertising both on TV in print ads and
11 with the exponentially increasing number of
12 internet and social media ads. And we believe
13 that resources need to be made available for
14 monitoring and reviewing these drug promotion
15 campaigns in a timely manner. Given this
16 growing burden of monitoring drug promotion
17 efforts, it is essential that the FDA be
18 provided with adequate funds to support the
19 staff and the resources necessary to ensure
20 the consumers reach a balanced understanding
21 of the drugs advertised to them.

22 I would also like to address

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1 proposals that were included in the package,
2 and particularly appreciate the proposed
3 recommendations that allocate user fees for
4 post-market safety activities, such as the
5 Sentinel initiative.

6 We commend the Agency's progress in
7 developing Sentinel. We believe that broader
8 use of an active risk identification and
9 analysis system such as this has the potential
10 to fundamentally transform post-market safety
11 surveillance and dramatically improve the
12 safety of prescription drug use in the United
13 States. We are very disappointed, however,
14 that this proposal does not explicitly commit
15 the Agency to scaling up Sentinel's successful
16 pilot stage to a more full and robust system
17 that would enable the FDA to realize its
18 potential.

19 In addition, we are concerned about
20 the discussion of focus on expected risks,
21 rather than on a broader approach, that would
22 enable the Sentinel initiative to provide

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1 preliminary data on unexpected adverse
2 reactions. We would urge implementation of an
3 implementation plan, including a timeline for
4 progress with Sentinel.

5 We also appreciate the Agency's
6 support for their clinical trial oversight
7 proposal and are disappointed that it did not
8 get into the package. We would continue to
9 advocate for that, as we believe that clinical
10 trial oversight and the FDA's ability and
11 authority to conduct inspections, both
12 domestically and abroad is essential.

13 As it has been discussed regarding
14 advisory committees, I also want to address
15 some of the concerns raised.

16 First, within the proposed
17 recommendations there has been discussion that
18 there would be a decreased number of drugs
19 that go to advisory committees for review.
20 Some of our concerns revolve around the fact
21 that the information that is made available to
22 the public before and advisory committee

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1 meeting provides patients and consumers with
2 vital information, in particular the FDA
3 executive summaries that are associated with
4 those drugs. And so we would urge the Agency
5 to make that information available, even if
6 the decision is made not to go to an advisory
7 committee meeting.

8 Second, we are extremely concerned
9 about the efforts we have already seen to
10 loosen conflict of interest guidelines for FDA
11 advisory committee meetings. We don't want to
12 keep needed expertise from the Agency,
13 however, we believe there are an adequate
14 number of un-conflicted experts to be found
15 and we also believe that the waiver system is
16 such that it is, in the case of rare diseases,
17 if the only experts are conflicted experts,
18 that there are waivers in place already to
19 address concerns like that.

20 I would like to conclude by saying
21 that we believe the proposed recommendations
22 should do more to ensure the safety of

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1 patients and consumers as well as the
2 scientific integrity of the drug review
3 process.

4 We do appreciate the efforts of the
5 Agency to work towards those ends but believe
6 that as long as patients and consumers are
7 excluded from the negotiations themselves, the
8 concerns and priorities of these principle
9 stakeholders will get less attention than they
10 deserve.

11 We will continue to advocate for
12 these interests and improve the proposed
13 recommendations for PDUFA V by supporting
14 these proposals and ensuring the Agency is
15 provided with sufficient resources to carry
16 out these initiatives.

17 Thank you for your time.

18 MR. FREY: Thank you, Kate.

19 The next speaker is Celia Wexler.
20 Celia is the Washington Representative of the
21 Union of Concerned Scientists.

22 MS. WEXLER: Good morning and I

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1 always ask, can you see me, not can you hear
2 me. But I think that you can.

3 Thank you for inviting me to
4 participate in this consumer perspective
5 panel. The Union of Concerned Scientists with
6 more than 350,000 members and supporters
7 throughout the country is one of the nation's
8 leading science-based non-profits working for
9 a healthy environment in a safer world.
10 Within our coalition, UCS lobbied for passage
11 of the Food and Drug Administration Amendments
12 Act when PDUFA IV was reauthorized in 2007.

13 And we have already said that we
14 certainly appreciate the FDAAA required public
15 participation requirements that the FDA has
16 fulfilled. We would have preferred, you know
17 that we had had a seat at the table during the
18 negotiations. Nevertheless, the periodic
19 meetings were helpful and a good first step.
20 And we very much appreciate Theresa Mullin,
21 who has always been accessible to us, very
22 good about asking questions and understanding

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1 that our job as advocates is to push the
2 Agency when it is being pushed the other way.

3 However, that all said, I come to
4 this meeting as a journalist. I am a former
5 journalist. So what I pay attention to are
6 words and what I always come through after I
7 read a document are a lot of questions. And
8 this is, I think, the way I am going to
9 approach this document.

10 We were surprised by the tone of
11 the document. We have no complaints with the
12 notion of improving the review process. But
13 repeatedly this document elevates "timely
14 access" to new drugs as the Agency's highest
15 priority, with very little emphasis placed on
16 either drug safety or efficacy. We are
17 concerned that the tone of this agreement
18 could have a very negative impact both on
19 patients and on FDA scientists, particularly
20 those charged with application reviews.

21 We know that this program is about
22 achieving more efficiency and better

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1 communication for the review process for new
2 drugs and biologics. Nevertheless, we are
3 concerned that this program is so wedded to
4 adhering to timelines and schedules, it sends
5 the strong message that promptness trumps all.

6 For example, on page ten of my copy
7 of the draft performance document, the FDA
8 proposes to establish a tracking system to
9 document review team performance for several
10 key milestones. The milestones focus
11 exclusively on the extent to which reviewers
12 adhere to a strict schedule. There is no
13 mention of the need to keep to these
14 milestones while adhering to the highest
15 safety standards and basing the review on the
16 best available science.

17 Similarly on page 11, the FDA gives
18 first priority to "improving the efficiency
19 and effectiveness of the first cycle review
20 process and decreasing the number of new
21 review cycles." It is only at the end of this
22 long list that safety is even mentioned and

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1 then parenthetically. Indeed, a search of
2 this entire document reveals that the FDA uses
3 the terms timelines or timely a total of 37
4 times while the term of safety or safe occur
5 only 27 times.

6 This concern about tone would not
7 be so serious if the FDA did not propose
8 certain changes that we fear may send a
9 message to FDA scientists, particularly
10 reviewers, that the Agency is most concerned
11 about achieving speeding consensus, rather
12 than exploring safety questions that may cause
13 a slip in timelines. And we have some reason
14 to be wary. In the past ten years, there have
15 been well documented cases of FDA scientific
16 staff whose concern about the safety of
17 certain drugs were downplayed or dismissed by
18 the Agency, ultimately causing great harm to
19 tens of thousands of patients. In several
20 instances, FDA scientists who disagreed with
21 FDA managers found their work environment so
22 toxic that they left, robbing the Agency of

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1 the dedicated talented staff it needs. That
2 is why it is so crucial that the FDA do
3 nothing to sustain an environment that sends
4 the message to Agency scientists that their
5 views are not welcome if they in any way
6 hamper the efficiency of the drug review
7 process. We say that knowing that morale at
8 FDA has improved considerably but still
9 feeling that the morale is vulnerable.

10 Here are a couple of our specific
11 concerns. There is the use of an independent
12 contractor to assess the quality and
13 efficiency of biopharmaceutical development
14 and regulatory review programs. This document
15 states that the contractor must have expertise
16 in assessing these types of review programs,
17 which makes sense, but it doesn't offer any
18 more details. And secondly, the plan to train
19 certain staff to serve as dedicated liaisons
20 in the drug review program. The FDA states
21 that the liaison staff will include
22 individuals with expertise about the drug

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1 review process and, in some cases, be on
2 detail from the review divisions. And the
3 liaisons will be there to facilitate general
4 and in some cases specific interactions with
5 sponsors and develop training programs for
6 review staff that address best practices for
7 communication, presumably between the sponsors
8 and the staff.

9 Instituting a new program to
10 improve the communication between the Agency
11 and industry sponsors isn't a bad idea.
12 Indeed, you know more effective communication
13 is a good thing. So is facilitating the
14 approval process.

15 However, without more explanation,
16 if I were an FDA scientist, these two
17 recommendations would be worrisome and would
18 raise many questions. What will be the core
19 values that drive the assessment of the
20 independent contractor the FDA hires? How
21 will that contractor's assessment affect job
22 reviews at the Agency? And what will the role

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1 of the liaison staff truly be? Will liaisons
2 be facilitators or industry advocates? Will
3 they not only be good and expert communicators
4 but will they also have a demonstrated
5 commitment to drug safety? And will their
6 role shepherding an application through the
7 process continue all the way through post-
8 market phase so that if there are problems or
9 safety concerns, those problems can be
10 addressed as quickly as any glitches or hold
11 ups that occur while the drug was being
12 initially reviewed?

13 The FDA in this document observes
14 that not all drugs or biologics may need
15 review by an advisory panel. And Kate
16 expressed some of our concerns about that and
17 our plea that if you do not use an advisory
18 panel that the information that would have
19 been available remain available. We also
20 think it is very important that when you
21 decide not to use it, you disclose your
22 reasons. And certainly we would hope it

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1 wouldn't be just to save time.

2 The FDA must send a strong signal
3 to its scientists and review teams that drug
4 safety remains the Agency's highest priority.

5 The Agency must make clear that dissenting
6 opinions on a drug review team are welcome and
7 must be addressed, even if they slow down the
8 review process.

9 And just to add to what was talked
10 about in terms of conflict of interest, and I
11 am going a little out of turn, we strongly
12 believe that it would be a mistake to loosen
13 conflict of interest standards at the FDA.
14 You know, there is nothing to prevent an
15 advisory panel from hearing from the world's
16 greatest experts, despite their conflicts from
17 asking them questions from getting a
18 presentation from them and then having them
19 leave the room. Because as you know, the
20 advisory panels operate like juries and the
21 people with the biggest stake in the outcome
22 have a lot of influence.

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1 We also believe that you have to
2 demonstrate that there is a shortage of
3 expertise. There were two conflicts on the
4 diabetes drug review panel last year on
5 Avandia. And you know what? There is no
6 shortage of people with expertise on diabetes
7 or on cardiovascular issues. There were many
8 conflicted experts on panels weighing the
9 benefits of Vioxx. And again, we are talking
10 about a pool that is pretty large for experts
11 dealing with pain and again for experts
12 dealing with heart problems. And really no
13 one benefits from the use of conflicted
14 experts.

15 And Susan Wood, who you remember
16 from the FDA as I think Director of the
17 Department of Women's Health, has done studies
18 that have established that there may be 50,000
19 academics and physicians in teaching hospitals
20 and universities throughout the country. And
21 she believes that pool is probably big enough
22 to give you what you need. Certainly for

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1 orphan drugs, as Kate mentioned, there is a
2 waiver system and we have no problem with
3 that.

4 I think the last thing that we want
5 to talk about is conflict of interest, a
6 couple of ways to resolve some of the issues
7 we brought up. First of all when it comes to
8 your independent contract, conflict of
9 interest counts there as well. The conflict
10 of interest guidelines should be firm and
11 without exception. The FDA shouldn't retain a
12 firm that has had any financial ties over the
13 last three years with a company whose products
14 must go through an FDA review process.
15 Individuals retained by the firm should do the
16 work for FDA as well as their spouses and
17 adult children also must be free of these
18 financial ties. And the look-back period
19 should, again, be three years.

20 The FDA must publicly disclose the
21 criteria on which it will select an
22 independent contractor, the names of companies

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1 it considers, and its reasons for selecting a
2 specific contractor.

3 We know the FDA will be soliciting
4 public comment for the contractor's statement
5 of work, a very good idea. We urge that
6 Agency responses to the public comments also
7 be part of the public record.

8 And secondly and most importantly,
9 we strongly urge the FDA to adopt
10 comprehensive scientific integrity policies,
11 based on the core values articulated by the
12 White House through its Office of Science and
13 Technology policy. The Obama administration
14 through OSTP urged federal agencies to ensure
15 a culture of scientific integrity, noting that
16 scientific progress depends upon honest
17 investigation, open discussion, refined
18 understanding, and a firm commitment to
19 evidence.

20 I have closed down the place, I
21 guess. These policies should protect
22 scientists to express dissenting views or

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1 raise concerns about manipulation or
2 censorship of scientific data from retaliation
3 by supervisors. They also must respect the
4 rights of scientists to publicly express their
5 views, even when those views disagree with the
6 Agency's position, provided that the
7 scientists make clear they are speaking for
8 themselves and not the FDA. And I have
9 submitted for the record, our Union of
10 Concerned Scientists proposed best practices
11 for scientific integrity policies.

12 Although as stakeholders we are
13 meeting in different groups, we all are
14 patients and consumers. Public interest
15 advocates, healthcare professionals, drug
16 industry reps are not immune from health
17 crises. We all rely on drugs and medical
18 devices when we become ill or injured.
19 Presumably, all of us should want the same
20 thing; effective drugs that reach the public
21 through an efficient process that minimizes
22 delays without compromising patient safety in

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1 any way.

2 We look forward to working with you
3 and Congress in the coming months to ensure
4 that PDUFA V supports the FDA's efforts to
5 protect the public from unsafe drugs while
6 facilitating innovation. And thanks very much
7 for listening.

8 MR. FREY: Thank you, Celia.

9 Next we have Diana Zuckerman.
10 Diana does not have slides, so we don't need
11 to worry about the AV issue.

12 Diana is President of the National
13 Research Center for Women and Families.

14 DR. ZUCKERMAN: I'll just wait
15 until that noise stops. Hopefully it won't
16 take long.

17 (Pause.)

18 DR. ZUCKERMAN: My blank screen. I
19 am Dr. Diana Zuckerman. I am President of the
20 National Research Center for Women and
21 Families, which is a think tank that uses
22 research to improve the health of adults and

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1 children. And I am also speaking on behalf of
2 our Cancer Prevention and Treatment Fund,
3 which analyzes research results that can
4 improve the prevention, diagnosis, and
5 treatment of cancer. Thanks for the
6 opportunity to speak on this panel.

7 Celia mentioned her perspective as
8 a journalist. Mine is as a scientist. I am
9 trained in epidemiology and public health at
10 Yale Medical School. I was on the faculty at
11 Vassar and at Yale and a longitudinal
12 researcher at Harvard before moving to
13 Washington, D.C. to work on Capitol Hill. I
14 also worked at HHS at the Institute of
15 Medicine and now as the head of a nonprofit
16 think tank.

17 I am very glad to be on this
18 consumer panel and I strongly agree with the
19 recommendations of my colleagues and we are
20 all part of the patient consumer and public
21 health coalition. I should mention however
22 that our organization is not really a consumer

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1 organization. It is a think tank but we align
2 ourselves with views of the consumer groups
3 and other public health groups and scientific
4 integrity groups because we all share the view
5 and our mutual interest in better research and
6 better healthcare.

7 My perspective is also influenced
8 by being a fellow at the University of
9 Pennsylvania Center for Bioethics and on the
10 Board of Reagan-Udall Foundation and the Board
11 of the Alliance for a Stronger FDA.

12 And I consider myself one of FDA's
13 biggest fans because I have tremendous respect
14 for the Agency and a great respect for the
15 importance of the work that you all do. But I
16 am unfortunately not a great fan of the
17 process or the outcome of this PDUFA
18 negotiation.

19 I think one of the issues is that
20 as patients and consumers we have been
21 obviously excluded from the process. Now we
22 are included in the process but we are still

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1 not at the table. And the issue is should we
2 be at the table and why should we be at the
3 table. We don't pay the fees but we do pay
4 for the medications directly when our own
5 money is used and indirectly through paying
6 for insurance coverage. And of course as
7 taxpayers, we are all paying for the
8 appropriations which are also used to support
9 the FDA and all the important work that you
10 do.

11 So we are going to continue to
12 advocate that Congress increase funding for
13 the FDA and that user fees and appropriations
14 be combined in ways that strengthen the Agency
15 in all the work that they do, not just
16 speeding the process of getting products to
17 market.

18 User fees obviously help the FDA do
19 its job and I think that everyone in this room
20 agrees that we want drugs to get to the market
21 as quickly as possible, as long as they are
22 safe and as long as they are effective. But

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1 what we don't always agree on is how to prove
2 that a product is safe and effective and what
3 is proper evidence of that.

4 So in terms of our agreements and
5 disagreements, I want to reiterate what has
6 been said that we have the concern about the
7 tone and the focus of the negotiations so far
8 in the proposal so far.

9 I think it is a really good idea
10 for the FDA to meet with industry
11 representatives early in the process, early in
12 the approval process. We have no disagreement
13 with that. We think that this can make the
14 process more efficient and we think that it is
15 in nobody's best interest for companies to
16 work to get a product approved without a clear
17 understanding of what the expectations and
18 needs are of the FDA. So, it is fine for any
19 improvements of that sort. I can support
20 that. But these kinds of meetings are going
21 to be very resource-intensive. And we do care
22 and we are concerned that so much focus is on

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1 these meetings and it is going to use so much
2 staff time that it is unclear whether user
3 fees will be adequate to do all the other
4 important work and particularly to focus on
5 safety and effectiveness.

6 We outlined in a letter in August,
7 a letter that the coalition sent to HHS
8 Secretary Sebelius our main concern that most
9 of the recommendations are aimed at industry's
10 goals of reducing barriers to new drug
11 approvals, rather than protecting and
12 promoting the health of patients. Performance
13 goals should be on all kinds of performance
14 and that should include safety and
15 effectiveness, ways of protecting patients
16 from the risks, not just speeding them to
17 market.

18 What we find is that the proposed
19 recommendations are really quite specific in
20 terms of commitments to industry but
21 surprisingly vague on safety commitments. For
22 example, the proposal section on the

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1 enhancement and modernization of FDA drug
2 safety system is only two and a half pages out
3 of a total of 34 pages of this document and we
4 think that shows a lack of focus and a lack of
5 specificity on safety and effectiveness.

6 Where it states that the FDA will
7 "continue to use user fees to enhance and
8 modernize the current U.S. drug safety
9 system," that's nice but what does that mean?

10 Will any of the increases in user fees be
11 used to improve drug safety or will the
12 amounts remain the same as in PDUFA IV? Are
13 there any new monies from user fees that will
14 be slated to increase the staff of the Office
15 of Surveillance and Epidemiology, for example?

16 If the FDA is increasing the number of staff
17 to expedite drug development, won't that put
18 even more pressure on an already smaller OSE
19 staff?

20 I want to spend a couple of minutes
21 talking about REMS and the Sentinel research.

22 The proposal specifies that user fees will

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1 provide support for enhancing REMS and
2 Sentinel. And that's great but it says almost
3 nothing about how that will be accomplished
4 and whether the goals will be to enhance
5 safety or whether there are other goals in
6 those changes. For example, the REMS section
7 focused on reducing the burden on industry, on
8 healthcare professionals and on patients but
9 it doesn't talk about the importance of
10 ensuring safety. And this is especially
11 worrisome to us because in the Federal
12 Register notice of this meeting, it refers to
13 REMS as a strategy design to get drugs on the
14 market "drugs that could not otherwise be
15 approved because of the risks that would
16 outweigh the benefits." So if that is the
17 purpose of REMS, to get drugs on the market
18 that would otherwise not be approved, then
19 there should be a lot more attention to the
20 safety aspects of this as well.

21 The statements about meetings that
22 the FDA must have with industry are very

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1 specific. The statements on the Sentinel
2 research, in contrast, is extremely vague. We
3 are strong supporters of Sentinel research but
4 we are concerned about whether Sentinel data
5 will be reviewed and acted upon in a timely
6 manner. And Kate has already mentioned
7 concern that we have about looking only at
8 expected risks rather than having an open mind
9 looking at the research results and trying to
10 figure out what it means. So while we can
11 understand that industry is particularly
12 concern that blockbuster drugs might be found
13 to have unexpected risks and they want to make
14 sure that those risks are absolutely clearly
15 conclusively present before warning anybody
16 about a drug, the other side of that is that
17 Sentinel is supposed to be an early warning
18 system. And if we wait until all the data are
19 absolutely conclusive, and if we focus only on
20 expected risks, it won't be an early warning
21 system. It will be a later warning system.

22 So, we want to have more public

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1 discussion and I understand there will be
2 more, but we are concerned that up until now
3 there has been very little public discussion
4 about how Sentinel is being used, what
5 limitations are being put on that and by whom.

6 My colleagues have talked about
7 conflicts of interest. I just want to add a
8 couple of words about that. Having attended
9 many advisory committee meetings for the FDA,
10 I have seen firsthand the importance of having
11 people who are very knowledgeable about a
12 topic but there is all kinds of knowledge that
13 contributes to the effectiveness of an
14 advisory committee. And when you have really
15 good statisticians and when you have really
16 good epidemiologists and public health
17 experts, that contributes greatly, even if
18 they aren't purely expert on the exact illness
19 that is going to be treated. It is very
20 important to have that kind of scientific
21 staff and at many advisory committee meetings,
22 those scientists are not really listened to.

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1 Our center did a review of advisory
2 committee meetings and we directly quoted from
3 many of them. And you have advisory committee
4 members saying things like well I wouldn't
5 want my mother to take this drug and I have a
6 lot of concerns about whether it is really
7 safe. And then a few minutes later, they are
8 voting to recommend approval. So we really do
9 need experts who are looking at the science
10 and not just looking at the fact that patients
11 need new drugs. Because yes, patients need
12 new drugs but only effective and safe drugs
13 and drugs that are, for the most part, at
14 least contribute something that other drugs on
15 the market don't contribute.

16 I would also like to mention the
17 AHRQ has been mentioned in terms of work that
18 they have done. I have almost never seen
19 experts from AHRQ ever speaking at an FDA
20 advisory committee meeting. I have almost
21 never seen academic researchers who do work on
22 comparative effectiveness research or the off-

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1 label uses or effectiveness issues. I have
2 almost never seen them at advisory committee
3 panels in any way shape, or form, or as
4 speakers. And that is another source of
5 expertise that could be greatly helpful, not
6 just people with conflicts of interest.

7 I also want to say that it is these
8 advisory committees tend to move towards
9 consensus and people with conflicts of
10 interest do tend to speak a lot more and kind
11 of take over the conversation in ways that I
12 think are not helping a more objective
13 scientific process. So I think it is fine to
14 have them there to speak and share their
15 expertise but not to take over the discussion
16 at these meetings.

17 I want to talk a little bit about
18 the section on enhancing benefit risk
19 assessment, which will develop a five-year
20 plan to implement a benefit-risk assessment.
21 It states that FDA will facilitate "a balanced
22 consideration of benefits and risks." Well

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1 again, what does that mean? We thought that
2 FDA has been doing that. We hope and assume
3 that they are doing that, but judging from the
4 discussions at FDA advisory committee
5 meetings, it often seems that those
6 discussions focus more on the potential of
7 helping just one or two patients, rather than
8 being concerned about the risks to many
9 patients. And because of that, I am not
10 absolutely confident that this balanced
11 consideration is going to be balanced, truly
12 balanced. And so we would like to know more
13 about that, considering the large number of
14 patients who have taken drugs that we know
15 have harmed them, such as Vioxx and Avastin
16 and Ketek, just for a few examples.

17 A couple of words about meta-
18 analysis. That is something that I did early
19 in my career while I was still an academic.
20 And I agree that there are a lot of meta-
21 analyses out there that are biased in terms of
22 the studies they are including in the

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1 analysis. And so I support the efforts that
2 FDA is making to improve their expertise on
3 that score.

4 I want to say just a couple of
5 words about biomarkers and surrogate endpoints
6 because the proposal talks about that as yet
7 another way to get drugs to market faster and
8 we understand the need and importance and
9 particularly for certain kinds of new drugs.
10 But on the other hand, there has been a
11 growing body of evidence that biomarkers are
12 not always clear evidence that patients are
13 being helped.

14 So for example we know that drugs
15 that are extremely effective at lowering
16 glucose levels are not necessarily the best,
17 safest drugs for the treatment of diabetes.
18 And that drugs that are great at reducing
19 cholesterol levels are not always the best of
20 the cholesterol lowering drugs for saving
21 people's lives.

22 So despite the tremendous pressure

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1 to replace meaningful outcome measures with
2 biomarkers and surrogate end points in order
3 to shorten the time needed to complete
4 clinical trials, I really urge the FDA to be
5 very cautious on that score.

6 In terms of patient-reported
7 outcomes, obviously patients should be
8 evaluated objectively to determine the risks
9 and benefits of medications but the reason why
10 we have double-blind clinical trials is that
11 because patients and doctors can be biased in
12 terms of their understanding of how a drug is
13 affecting them. When the Women's Health
14 Initiative Trial was ended, for example, years
15 ago, many women were very upset about being
16 taken off their hormone drugs thinking that it
17 had really helped them tremendously and many
18 of those women found that they had in fact
19 been on placebo. So while it is very
20 important to hear from patients about their
21 experiences, that also always has to be
22 balanced with scientific evidence.

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1 So just a couple of more things I
2 wanted to mention. We do agree with the idea
3 of increasing accountability for the use of
4 user fees and we particularly like to see how
5 it is used to improve safety and effectiveness
6 issues, not just speed.

7 In terms of the recommendations
8 that are missing, you have heard a few of
9 those. Others have talked about direct-to-
10 consumer advertising, which clearly need to be
11 reviewed better but also recent research shown
12 that ads to physicians are also lacking some
13 of the components that the FDA requires and
14 yet they are not in those ads. So clearly,
15 the FDA needs more staff to review all ads,
16 those for physicians and also those for
17 patients.

18 And I just want to use the example
19 that recently Kentucky -- Well, not that
20 recently. A couple years ago, Kentucky Fried
21 Chicken's ad was taken off the air when they
22 were referring to Kentucky Fried Chicken

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1 basically as a healthy food for your family
2 because it was healthier than Big Macs. That
3 was a somewhat misleading ad because although
4 a particular portion of Kentucky Fried Chicken
5 had fewer calories, it had other things that
6 weren't so healthy. And yet at the same time,
7 the FDA has had ads for Seroquel and other
8 atypical antipsychotics that really are
9 misleading in terms of presenting these drugs
10 as if they were antidepressants when they are
11 a typical antipsychotic.

12 So the FTC, which regulates
13 Kentucky Fried Chicken ads has a very
14 different standard of misleading. And yet, I
15 think most consumers would know that Kentucky
16 Fried Chicken is not a health food but most
17 consumers know almost nothing about Seroquel.

18 When they see an ad they are going to believe
19 whatever is in it. So for that reason, those
20 standards need to be higher.

21 So in conclusion, in today's
22 budgetary climate user fees are necessary and

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1 especially because the FDA has been
2 underfunded for years. We understand that it
3 is very difficult for FDA to struggle to
4 manage the expanded demands with inadequate
5 appropriations and those demands are growing
6 and the fees are not growing enough. And the
7 appropriations are, of course, at risk of
8 being reduced.

9 So the bottom line is that user
10 fees should not be considered a payment by
11 companies for the FDA approval or for FDA's
12 services. It is a fee for participation, just
13 like an entrance fee to the Grand Canyon. You
14 pay to go. You can't get in without it but
15 that doesn't mean you can do whatever you want
16 when you get there.

17 Thanks very much for the
18 opportunity to speak on this panel.

19 MR. FREY: All right. Thank you,
20 Diana. A number of our folks have been taking
21 notes throughout this panel. So in the
22 afternoon comment period, we will look at

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1 addressing some of the issues you raised as
2 appropriate. Hopefully you can stay for that
3 session.

4 Next up is the healthcare
5 professional panel. If those folks can make
6 their way up to the head table, we will get
7 going with that.

8 Our first speaker on this panel
9 will be Marcie Bough, the Senior Director of
10 Government Affairs Association.

11 DR. BOUGH: Thank you. I
12 appreciate the opportunity to be here. Again,
13 my name is Marcie Bough. I am Senior Director
14 of Government Affairs for the American
15 Pharmacists Association or APhA. APhA is the
16 largest and oldest national professional
17 society for pharmacists. And we represent
18 over 62,000 members working in all practice
19 settings.

20 Consistent with our previous
21 comments to FDA on PDUFA reauthorization, APhA
22 supports the PDUFA program in its ability to

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1 support FDA drug review process and supports
2 the recommendations within PDUFA V agreement
3 that has been presented here today. We see
4 this recommendation as powerful and necessary
5 improvements to the program.

6 Generally, APhA supports revisions
7 outlined in the draft related to enhanced drug
8 application and review model, modifications to
9 the user fee schedule for the drug review
10 process, and to ensure FDA can meet PDUFA
11 performance goals, extend a time frame for
12 which FDA must approve or reject drug new
13 applications, development of a five-year plan
14 to improve FDA's drug risk-benefit process and
15 analysis, enhancement to post-market
16 surveillance and adverse event tracking
17 activities, through programs such as the
18 Sentinel initiative, and enhancements for
19 managing drug application of biomarkers and
20 pharmacogenomic details.

21 In addition related to risk
22 evaluation and mitigation strategies or REMS,

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1 we support the outlined strategy and time
2 frame for FDA to continue to discuss and
3 gather public input on improving REMS
4 programs, improved REM standardization and
5 integration into existing technologies and
6 workflows within healthcare settings, earlier
7 consideration, communication, and discussion
8 of REMS and the drug review process between
9 manufacturers and FDA, development of guidance
10 on assessing the REMS program effectiveness,
11 impact on patient access, and burden on the
12 healthcare system, and development of guidance
13 on how to apply statutory criteria for when a
14 REMS would be required.

15 Furthermore, APhA commends FDA for
16 its repeated effort for engaging stakeholders
17 and the public in the development of the
18 proposed PDUFA reauthorization
19 recommendations. We believe that the dialogue
20 between FDA and stakeholders at the same time
21 that FDA was in discussions with the industry
22 has greatly improved in the reauthorization

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1 process, is reflected in the proposal and
2 exceeds the minimum requirements for gathering
3 public input. Importantly through the
4 process, stakeholders have had ample
5 opportunity to discuss priority issues with
6 FDA related to PDUFA and other issues of
7 interest that were outside the scope of PDUFA
8 program.

9 APhA greatly appreciates the time
10 that FDA listened to and discussed improving
11 REMS programs, while recognizing the need to
12 improve standardization and to address
13 implementation challenges for physicians,
14 pharmacists, other prescribers and
15 wholesalers.

16 My remaining comments provide
17 additional information on the proposed
18 revisions related to pharmacogenomics, post-
19 market safety surveillance and REMS. Related
20 to pharmacogenomics, we recommend that
21 activities outlined in the proposal also
22 address the need to increase healthcare

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1 provider awareness and patient awareness of
2 pharmacogenomic-related medical activity and
3 how applicable medication labeling and dosing
4 can be implemented into practice.

5 As a resource for such activities,
6 APhA recently released a white paper on how
7 pharmacists can integrate pharmacogenomics
8 into practice using medication therapy
9 management while working with prescribers and
10 labs to improve patient care. The paper
11 highlights HHS's personalized healthcare
12 initiative, FDA's work on pharmacogenomics and
13 personalized medicine and a previous APhA
14 workshop on this topic. The document is
15 publicly available online at pharmacist.com
16 and will be submitted to the docket.

17 Related to the Sentinel initiative,
18 we encourage FDA to consider how pharmacists
19 can be involved as the initiative matures.
20 Many pharmacists and pharmaceutical scientists
21 work in practice settings through practice-
22 based research networks and post-market

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1 surveillance activities that produce valuable
2 data about the safety and effectiveness of
3 drug products that will be beneficial to
4 Sentinel.

5 Related to REMS, again APhA very
6 much supports the proposed recommendations to
7 standardized REMS as it reflects the issues
8 that APhA has been advocating to FDA on many
9 occasions. Improving REMS is a key priority
10 for APhA and we have taken a leading role with
11 regards to this by sponsoring two stakeholder
12 meetings that both generated informative white
13 papers. We appreciate that FDA observed both
14 those of those meetings.

15 Our goal is to be a resource for
16 FDA manufacturers and others helping to ensure
17 that REMS programs achieve their intended
18 outcomes, including maximizing effectiveness
19 of REMS interventions while limiting burdens
20 on the healthcare system and recognizing the
21 important role that pharmacists can play in
22 safe medication use as part of the healthcare

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1 team.

2 Again, we greatly appreciate FDA
3 listening to APhA and the other provider
4 stakeholders on input regarding REMS
5 improvements. The need for standardization
6 integration to existing workflows in health
7 systems and use of technologies limiting
8 burden and ensuring earlier REMS discussion
9 between FDA and manufacturers are again
10 reflected in the proposal which we support.
11 We also support including projects associated
12 with addressing pharmacy systems, education,
13 dispensing of patient risk-benefit information
14 and looking at practice setting activities.

15 It is critical that we continue to
16 work together on improving REMS programs,
17 given the importance that REMS have in
18 providing a mechanism to ensure patient access
19 to those drugs that would not otherwise be
20 approved or remain on the market. APhA
21 encourages FDA to use our materials and
22 resources for continued discussion and

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1 dialogue on REMS standardization and
2 improvements as outlined in the draft
3 proposal. Our 2011 REMS white paper
4 summarizes recommendations from our REMS
5 stakeholder meeting on approving program
6 design and implementation. The documents
7 publicly available on pharmacist.com will be
8 submitted for the docket and builds on our
9 previous 2009 white paper that we have used in
10 previous PDUFA discussions.

11 Finally, Table 3 and several
12 figures in our 2011 white paper summarize key
13 recommendations and highlights for you to
14 consider as we continue with REMS improvements
15 discussions. They highlight the needs to
16 standardize programs, components, and
17 processes, leverage existing technologies in
18 medical and pharmacy practice settings,
19 maximize effectiveness of programs, and
20 optimize provider patient interventions,
21 including the benefit of using pharmacist-
22 provided interventions for certain REMS

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1 programs which is determined such an
2 intervention best meets the requirements for
3 elements to assure safe use and documentation
4 of safe use activities.

5 The white paper also highlights the
6 need to evaluate adequate resources and
7 reimbursement models for implementation of REM
8 required interventions so that providers do
9 not avoid prescribing or dispensing
10 medications based on REMS requirements and we
11 need to avoid having a negative financial
12 impact on practice for providing REMS-required
13 interventions.

14 Specifically, payment models are
15 needed to ensure adequate staff and resources
16 are available to implement REMS-required
17 program activity, especially those requiring
18 elements to assure safe use. Such models
19 could range from REMS fee structures for
20 manufacturers based on market share of
21 particular REMS drug or various forms of
22 reimbursements through public and private

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1 payers, some of which fall outside the scope
2 of the PDUFA agreement.

3 And finally the white paper
4 highlights the need to establish a centralized
5 repository or clearinghouse of REMS
6 information to improve access to and awareness
7 of REMS information, facilitate communications
8 and awareness of implementation requirements,
9 utilize continuing education opportunities for
10 provider training and education and ultimately
11 limiting burden on the healthcare systems.

12 On a final REMS note, we do support
13 FDA's guidance previously released this year
14 on how medication guides will be used in the
15 REMS program. We support refocusing REMS on
16 programs with elements to assure safe use,
17 rather than the many that are MedGuide only
18 REMS.

19 In closing, we appreciate the
20 efforts that FDA has for such transparency and
21 dialogue between FDA manufacturers and the
22 stakeholders as reauthorization discussion

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1 moved forward. These efforts have improved
2 the current draft, reflect important issues
3 raised by stakeholders that are relevant to
4 PDUFA and overall should help improvement as
5 reauthorization processes and proposals move
6 through congress. Again, APhA appreciates the
7 time and effort that FDA has spent discussing
8 REMS improvements, as the aim is to align REMS
9 programs with the practical burdens and
10 concerns of healthcare providers and patients
11 while continuing to seek improvements.

12 Thank you for the opportunity to
13 present today and we look forward to
14 continuing to work with FDA manufacturers and
15 the other stakeholders as we move through the
16 program. Thanks.

17 MR. FREY: Thank you, Marcie. Next
18 on our list is Barry Dickinson. Barry is the
19 Director of Science and Biotechnology at the
20 American Medical Association.

21 DR. DICKINSON: All right, thank
22 you. I also, like many of the other speakers

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1 today, would like to commend the Agency for
2 the process that you have put in place,
3 starting with the 2010 public hearing and
4 continuing with the monthly stakeholder
5 meetings and with this hearing today for
6 giving us an opportunity to provide input into
7 the process for the draft commitment letter
8 for PDUFA V.

9 The Science and Technology Division
10 at the AMA comprises our core drug policy,
11 genetics and molecular medicine, including
12 personalized medicine activities. And the
13 council is an elected group of physicians from
14 our House of Delegates that develops reports
15 on a variety of science and public health
16 topics for our House of Delegates that
17 establish the AMA policy on a number of
18 different science-based issues. My remarks
19 are going to reflect actually the formal
20 comments that we submitted also to the docket.

21 So for those of you who may not be
22 familiar with the AMA, we are an umbrella

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1 organization. There are about 116 medical
2 specialties in our House of Delegates, 50
3 state medical societies and some territories,
4 federal physician services, and then there are
5 a number of other sections like medical
6 students, residents, and fellows, etcetera.
7 So we don't represent a specific physician
8 group or medical specialty but rather should
9 be viewed as representing the physician voice
10 in general. So as the only physician
11 organization on the panel today, I feel that
12 weight somewhat.

13 Our interest in PDUFA is based on
14 our policy statement about funding for the
15 Agency. So the AMA supports a strong and
16 adequately funded FDA to ensure safe and
17 effective medical products are made available
18 to the American public. We also are of course
19 charged with monitoring and responding
20 appropriately to legislation that affects the
21 FDA and regulations that might be proposed and
22 then, I think this statement emanates from

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1 about the late '60s, affirm our support of an
2 adequate budget for the FDA so as to favor the
3 Agency's ability to function efficiently and
4 effectively.

5 So, we don't have any policy
6 statements on what percentage of funding
7 should come from user fees or appropriations
8 but I think we all agree that a strong
9 appropriations base would be something that
10 would be something we would favor.

11 So historically, the AMA has
12 supported PDUFA from its first iteration in
13 1992. And I think with the demonstrated
14 success, at least in terms of how success has
15 been measured for review times, that support
16 has continued.

17 And notwithstanding the comments
18 from the previous panel the consumer
19 viewpoint, I think that our general
20 philosophical statement would probably be
21 viewed as a centrist position. So we believe
22 that the prescription drug user fee should be

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1 primarily used to facilitate Agency review of
2 applications, without compromising safety, and
3 improve the quality and efficiency of drug
4 development, review, and risk management for
5 newly approved products.

6 So as long as those two overarching
7 areas can be viewed as being satisfied, then
8 we would view the PDUFA program as a success.

9 And there was some comment made by
10 Dr. Mullin in her presentation this morning
11 about some of the additional requirements that
12 were placed on the Agency by FDAAA in 2007
13 that actually impacted the performance goals.

14 And so we would hope that PDUFA V doesn't
15 result in that kind of metric.

16 So our reaction to the draft
17 commitment letter and the technical proposal
18 is affected in large measure by what we asked
19 for in 2010. So I was at the public hearing
20 in 2010. We had four major requests. We
21 asked the Agency to consider changes to design
22 to improve the risk-benefit assessment of

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1 prescription drug products to further
2 incorporate pharmacogenomics into drug
3 development and clinical investigation, to
4 revisit the construct and assignment of risk
5 evaluation and mitigation strategies, and
6 enhance and modernize the current drug safety
7 system.

8 So with regard to benefit-risk
9 assessment, this has been something I think
10 virtually every speaker has addressed today.
11 I think we all appreciate assessing benefit-
12 risk balance and prescription drugs is a
13 prominent challenge. It is a challenge facing
14 not only pharmaceutical manufacturers and the
15 Agency but the prescribers and patients who
16 are seeking to make informed treatment
17 decisions for products that are on the market.

18 And so a need for a structured
19 approach toward benefit-risk assessment has
20 become increasingly apparent. But I specify
21 in the essential attributes that both
22 regulators and companies should consider

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1 across the lifecycle of a drug, the entire
2 process of drug development review and
3 approval would be strengthened and we would
4 hope also the transparency of that process
5 would be enhanced.

6 So the draft commitment letter
7 addresses this issue in part by putting in
8 place a mechanism for enhanced communication
9 between FDA and sponsors during drug
10 development and establishing a mechanism to
11 use patient-reported outcomes as study
12 endpoints. Notwithstanding again, the
13 limitations that were noted in the previous
14 panel for using patient-reported outcomes as
15 an endpoint.

16 With regard to biomarkers and
17 genetic factors, pharmacogenomics, etcetera,
18 the shift from population values to individual
19 metrics for therapeutic decision-making based
20 on biomarkers and genetic factors, I think we
21 all appreciate will only continue to expand
22 and increase in importance. I think this

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1 approach is absolutely necessary to improve,
2 as Dr. Woodcock noted in her introductory
3 remarks this morning the science of drug
4 development. It also may help address, as Dr.
5 Allen noted, this huge lag we see between the
6 time a sponsor identifies a candidate drug,
7 the preclinical phase, the clinical phase, and
8 then the eventual review of the application.
9 And it also has the potential to rescue some
10 of those candidate drugs that drop by the
11 wayside for various reasons, particularly when
12 a potentially serious adverse effect is noted.

13 If a reason for that adverse effect
14 can be delineated and based on a mutation or
15 specific genetic factor, then that can help
16 that candidate drug to potentially survive and
17 create a mechanism for avoiding use of that
18 particular drug in a patient that might be at
19 risk.

20 Throughout the entire process since
21 2007 of creating the REMS program and then the
22 Agency trying to figure out a way to implement

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1 it, we have been consistent and steadfast in
2 urging the FDA to standardize the design and
3 implementation of REMS to evaluate its
4 effectiveness as these continue to
5 proliferate, particularly those that have
6 restricted distribution or elements to assure
7 safety features. And we would like to have
8 the impact of REMS evaluated, both on patient
9 access and the burdens that these programs
10 intended to promote safe use of medications
11 might have on the healthcare system.

12 So in our view this issue is
13 directly addressed in the commitment letter.
14 I think it is Section D-1. And as long as the
15 verbiage that is in the commitment letter is
16 followed through on, we would be supportive of
17 those efforts if it does come to fruition.

18 And then finally in terms of the
19 culture of drug safety and modernizing the
20 FDA's drug safety system, the AMA supports
21 assessment of current and new methodology to
22 maximize the usefulness of tools used for

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1 collecting adverse event information at
2 various points during the product lifecycle,
3 development and validation of risk management
4 and risk communication tools, including
5 mechanisms for public communication about the
6 benefits and risks of products and, of course,
7 efforts to modernize the safety tracking
8 systems and opportunities for linked data
9 management.

10 Certainly a commitment to refine
11 and expand the use of the Sentinel initiative
12 for active post-marketing surveillance is a
13 step in the right direction. It is not the
14 only thing that needs to be accomplished
15 again, as noted by comments from the consumer
16 panel. And also we would hope that
17 standardizing the REMS program would move this
18 needle forward to a certain extent in the
19 post-market phase.

20 So I guess in summary it is fair to
21 say that the AMA supports the general approach
22 taken by the draft commitment letter for PDUFA

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1 V and is hopeful that the final agreement
2 largely reflects the current draft. Thank
3 you.

4 MR. FREY: Thank you, Barry.

5 Next we have Marissa Schlaifer.
6 Marissa is Director of Pharmacy Affairs at the
7 Academy of Managed Care Pharmacy.

8 MS. SCHLAIFER: Thank you. The
9 Academy of Managed Care Pharmacy is pleased to
10 provide comments to the Food and Drug
11 Administration on the proposed recommendations
12 for the Congressional reauthorization of the
13 Prescription Drug User Fee Act or PDUFA for
14 fiscal years 2013 through 2017.

15 AMCP is a national professional
16 association of pharmacists and other
17 healthcare professionals who serve society by
18 the application of sound medication management
19 principles and strategies to improve
20 healthcare for all. The Academy has more than
21 6,000 members who develop and provide a
22 diversified range of clinical, educational,

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1 and business management services and
2 strategies on behalf of the more than 200
3 million Americans covered by managed care
4 pharmacy benefits.

5 AMCP is a member of the alliance
6 for a stronger FDA. AMCP believes funding for
7 the FDA at a dollar level sufficient so that
8 it may fulfill its obligations to ensure
9 medication safety is absolutely necessary.
10 The Academy's preference is for this funding
11 to be provided in total by the federal
12 government. However, absent this course of
13 action, which we recognize to be unlikely, the
14 Academy supports PDUFA reauthorization. We
15 believe funding is imperative not only to
16 support the prescription drug review program
17 but also to support effective post-market risk
18 management and, as I will mention further, the
19 managing and monitoring of direct-to-consumer
20 advertising of prescription products.

21 Therefore, the Academy is
22 supportive of the post-market risk management

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1 provisions contained in PDUFA and specifically
2 I am going to mention three of the provisions
3 in the PDUFA package: biomarkers and
4 pharmacogenomics, standardizing REMS, using
5 the Sentinel Initiative to evaluate drug
6 safety issues.

7 The provisions related to
8 biomarkers and pharmacogenetics include the
9 provision for FDA staff training on approaches
10 to conducting a pharmacogenomic review of new
11 drug and greater understanding of challenges
12 when using pharmacogenetic markers. And this
13 information in addition to the importance that
14 there is in identifying and speeding up the
15 drug approval process. Managed care decision-
16 makers and healthcare professionals need
17 information on the accuracy and validity of
18 pharmacogenomic markers.

19 Important decisions are made by
20 healthcare professionals and will be,
21 especially going forward in the future, on the
22 appropriateness of use of medications and

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1 these will be needed to be made with the use
2 of pharmacogenetic markers. As we have drugs
3 with higher risk, it is going to be more
4 important to use these markers to determine
5 the benefit-risk management. And although we
6 know it is not a specific concern to the FDA,
7 this information is very important moving
8 forward, as coverage decisions need to be made
9 on the use of new medications.

10 As far as standardizing REMS, we
11 are very supportive of the provisions included
12 in the commitment package, to standardize and
13 better integrate REMS into the healthcare
14 system, to take advantage of increasing
15 prevalence of electronic medical records and
16 other IT capabilities, and especially on
17 measuring the effectiveness of current REMS
18 programs.

19 The specific provisions we wanted
20 to mention our support on guidance on how to
21 apply statutory criteria to determine whether
22 a REMS program is necessary and to ensure that

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1 the benefits outweigh the risks. It is
2 essential to ensure that REMS programs are
3 applied going forward to the most appropriate
4 medications.

5 We are supportive of the provision
6 to increase public meetings or to begin public
7 meetings to explore strategies to standardize
8 REMS and, where appropriate, with the goal of
9 reducing burden.

10 And also the public workshops on
11 methodologies for assessing the effectiveness
12 and the impact of REMS. It is very important
13 that as REMS programs exist for a certain
14 amount of time to go back and review whether
15 or not these programs are effective.

16 As Marcie mentioned, APhA held
17 several stakeholder meetings related to REMS
18 and AMCP staff participated in the APhA REMS
19 stakeholder meeting in October 2010. At that
20 time, as has already been mentioned,
21 participants discussed actions to improve
22 current REMS programs, including developing

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1 methods in which REMS can be implemented using
2 technology and systems that already exist in
3 the provider workspace.

4 As was already mentioned, in
5 addition looking at ways to standardize REMS
6 programs, the Academy feels it is very
7 important to standardize REMS programs if
8 possible but that we do recognize that there
9 may be times when unique drugs require unique
10 programs.

11 Additionally I want to mention the
12 provisions on using the Sentinel Initiative to
13 evaluate drug safety. Specifically as all
14 here are familiar, the Sentinel Initiative is
15 a long-term program designed to build and
16 implement a national electronic system for
17 monitoring the safety of FDA approved
18 products. It is federal, academic, and
19 private entities working together to develop
20 methods to obtain disparate data sources and
21 validated means for active post-market drug
22 safety surveillance. This is a program that

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1 AMCP strongly supports and is very important
2 to our membership. Our membership has
3 followed these programs with interest as the
4 program has made effective use of what managed
5 care pharmacy recognizes as our most important
6 resource, real world data on the use of
7 medications, which is much different, often,
8 than the data that we see in randomized
9 controlled trials.

10 The current program with 17 data
11 partners includes mostly health plans and our
12 members have been strongly involved in working
13 to work through this somewhat challenging
14 program and the new data the ways that data is
15 being combined, so that the medication trends
16 can be seen across the various health plans.

17 It is also important that FDA
18 communicate post-market surveillance results
19 in a timely, transparent, and appropriate
20 manner. And I think there is many provisions
21 within the package of obtaining that data. We
22 want to make sure that FDA shares that data in

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1 a timely manner, in a transparent manner, and
2 also in a manner where healthcare
3 professionals, you know, sort of challenges
4 when patients have access to the data and that
5 healthcare professionals have access and know
6 how to share it and communicate with their
7 patients about information that is being
8 shared by the FDA.

9 Finally we need to mention one of
10 the opportunities that we would have liked to
11 see PDUFA funds being directed toward, as
12 already mentioned by several speakers before,
13 in addition to funding to support effective
14 post-marketing risk management programs, the
15 Academy would have liked to see and did
16 earlier encourage FDA to include funding for
17 the management and monitoring of direct-to-
18 consumer advertising of prescription drug
19 programs.

20 AMCP supports the allocation of
21 PDUFA fees for mandatory reviews of direct-to-
22 consumer advertising and would like to see

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1 those reviews applied both to television
2 advertising and to other media.³

3 Finally, I do want to take the
4 opportunity to thank FDA staff for its efforts
5 toward keeping stakeholder organizations
6 informed throughout the PDUFA V process. We
7 did have the opportunity to participate in the
8 monthly meetings and very much appreciated the
9 information that we were able to receive and
10 to contribute during that process. So thank
11 you for the opportunity to participate in
12 those meetings and in the meeting today.

13 MR. FREY: All right, thank you,
14 Marissa.

15 The last speaker before lunch is
16 Kasey Thompson. Kasey is the Vice President
17 of the Office of Policy Planning and
18 Communications at the American Society of
19 Health-System Pharmacists.

20 DR. THOMPSON: Thank you. Good
21 afternoon, everybody. Thanks for having us
22 here today to present at this meeting and

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1 thanks to the FDA for the process you have
2 created starting in 2010 with the public
3 meeting and monthly meetings thereafter. We
4 found those very useful and a good source to
5 provide input to the process throughout.

6 A little bit about our
7 organization. We were founded in 1942. We
8 represent approximately 35,000 pharmacists who
9 practice in hospitals and integrated health
10 systems. We are a supporter of user fees but
11 believe as many others do, that appropriations
12 is the best means to fund the vital public
13 health mission of the Agency and work as a
14 part of the Alliance for a Stronger FDA to
15 work with Congress to achieve that, but
16 recognize the realities that user fees create

17 So I want to talk you a little bit
18 about risk evaluation and mitigation
19 strategies. As FDA refines its
20 recommendations for PDUFA V, ASHP urges FDA to
21 include a requirement that sponsors propose
22 REMS with elements that assure safe use to

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1 demonstrate that they have sought input from
2 healthcare providers related to elements to
3 assure safe use.

4 And again, the purpose of REMS is
5 patient safety first and foremost.
6 Standardization has to happen and FDA has done
7 some things to work to that end. But still
8 yet today, there are situations that it is not
9 clear that REMS were created for patient
10 safety. The burden is high on patients in
11 terms of accessing the drugs in many
12 circumstances and the burden is high on
13 healthcare practitioners in terms of managing
14 the processes related to various REMS that are
15 in existence.

16 To avoid miscommunication, REMS
17 should be required and validated only for
18 patient safety reasons, as I just mentioned,
19 not for marketing and promotion reasons or
20 economic reasons. We know that is not the
21 intent of the FDA but still in hospitals and
22 health systems, we have patients bringing in

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1 drugs to the hospitals that they acquired from
2 their health plans directly. Hospitals are
3 expected to ensure that those drugs are safe
4 without ever having the drug in their
5 possession, a very difficult task to achieve.

6 And then they are expected to administer the
7 drug outside the normal process of care.

8 When developing a REMS, the FDA
9 should ensure that there are no lack of access
10 to medication histories, no delays in
11 obtaining medications, no increases in
12 workload and variability in process for
13 healthcare providers, and no conflicts between
14 hospital regulatory and accreditation
15 requirements and those with health plans and
16 patient demands especially.

17 There is a different thing that
18 nobody else has mentioned. Our members in
19 hospital and health systems have noted in
20 particular that the recall process is
21 antiquated and out of date. It is not
22 effective. We support that the FDA have the

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1 authority, that it be given the authority to
2 mandate recalls.

3 We believe that there needs to be a
4 single source of FDA recalls and that would be
5 the FDA, that recall notices should include
6 clear identification of the recalled product,
7 explanation of the reason why the product is
8 being recalled, a way to report possession of
9 the recalled product, instructions on the
10 appropriate disposition or return of recalled
11 products.

12 Now related to consumer medication
13 information, something the Agency has been
14 working to improve for some time, we support
15 the concept of approving the quality,
16 consistency and simplicity of written CMI. We
17 encourage the FDA to work in collaboration
18 with stakeholders to create evidence-based
19 models and standards for CMI. We believe that
20 research must be conducted to validate these
21 models and actually use studies in pertinent
22 patient populations, not just some model that

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1 is assumed to be effective be put out there
2 and assume that it will be better than the
3 current model that exists today.

4 CMI's should be developed by
5 unbiased third-party drug publishers and not
6 via self-policing manufacturer developed
7 processors for the creation of CMI.

8 Now as others have mentioned, we
9 would like to talk a little bit about
10 promotion and dissemination of off-labeled
11 uses. We recognize there are processes in
12 place and provisions where manufactures can
13 provide information for off-label uses to
14 providers. However, we believe that the FDA
15 should permit promotion and dissemination of
16 information only if manufacturers have
17 submitted a supplemental new drug application
18 within a reasonable time period after that
19 information has begun to be distributed to
20 healthcare providers and others.

21 Direct-to-consumer advertising is
22 something that we have had concerns about for

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1 a long time and have had policy on for a long
2 time. We opposed direct-to-consumer
3 advertising of specific drug products unless
4 the following minimal criteria are met:
5 collection and assessment of post-marketing
6 surveillance data, clear presentation of
7 benefits and risks of therapy, promotion of
8 medication safety and informed decisions,
9 clear relationships between the medication and
10 the disease state, no advertising or marketing
11 to minors, inclusion of mechanisms that direct
12 consumers to medication adverse event
13 reporting systems. And again, we view these
14 as minimums. Very few programs out there
15 today in DTC achieve these.

16 Patient-reported outcomes. We
17 advocate for expanded use of validated
18 patient-reported outcomes tools in clinical
19 research and direct patient care. We support
20 the development of validated PRO tools that
21 are sensitive to differences in cultural and
22 health history. We encourage that additional

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1 research on PRO tools be done. And we
2 encourage additional education for clinicians
3 and patients about the appropriate use of
4 these tools, an area that there is a great
5 need for.

6 Now globalization of clinical
7 trials, we strongly encourage the FDA to
8 increase the oversight of foreign clinical
9 trials, given potential inconsistencies in
10 protocol implementation and concerns about
11 availability and integrity of data.

12 We advocate for standardization and
13 electronic submission of data from foreign
14 trials and we encourage the FDA and private
15 entities to conduct research and study the
16 potential impact of the globalization of
17 clinical trials, a trend that is ever
18 increasing.

19 So in summary, we would like to see
20 REMS be standardized, the burden on patients
21 and healthcare providers be decreased through
22 the REMS program and more healthcare provider

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1 engagement in the creation of REMS way in
2 advance of their being released.

3 We support mandatory recall
4 authority from a single source and believe
5 that the FDA should be given the authority to
6 do that and we believe that the system as it
7 exists today does not work.

8 Consumer medication information, we
9 would love to see the quality enhanced. We
10 would love to see a process that assures
11 evidence-based and unbiased CMI on the market
12 but we believe anything that gets created
13 needs to be validated and proven that it is
14 effective. And promotion and dissemination of
15 off-label uses, we believe that supplemental
16 new drug applications need to be required
17 before that information is released to
18 providers.

19 Thank you very much for your time.

20 We appreciate the opportunity to present to
21 you today.

22 MR. FREY: All right. Thank you

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1 very much, Kasey. Thank you to the healthcare
2 professional panel for providing your
3 comments.

4 A word about the slides that you
5 have seen today. We will add them to the
6 docket before it closes next Monday. So I
7 don't think there is anything else we have
8 before lunch. I hope everybody is hungry and
9 we will reconvene at 1:00.

10 (Whereupon, a lunch recess was taken.)

11

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1 access to safe and effective breakthrough
2 therapies.

3 If you may not know, BIO represents
4 more than 1,100 biotechnology companies,
5 academic institutions, state biotech centers
6 and related organizations across the U.S. and
7 30 other nations. And we strongly believe
8 that as a nation we need to focus on policy
9 discussions of how we can unleash the promise
10 of biotechnologies so Americans and patients
11 can realize the benefits that it has to offer.

12 And the PDUFA program is a key element of the
13 overall innovation ecosystem.

14 A fundamental part of a
15 biotechnology company's ability to innovate
16 and raise private investment is having an FDA
17 with the resources and mechanisms required to
18 effectively and consistently review and
19 approve innovative products in a timely
20 manner, based on the best available science.
21 And since 1992, Congress, FDA, the
22 biopharmaceutical industry have supported a

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1 carefully structured user fee program to help
2 fund FDA's human drug review capacities. And
3 this has contributed to the approval of more
4 than 1200 new medicines. And as we saw in
5 FDA's opening presentation, it has reduced
6 review times considerably by more than a year.

7 Also noting the opening
8 presentation, we recognize that the human drug
9 review program has been under certain stresses
10 in recent years as new regulatory requirements
11 such as REMS and increased utilization of
12 advisory committees and more foreign
13 inspections have been layered on the review
14 processes. And in the same time, the
15 scientific complexity of applications have
16 increased. And as a result, overall approval
17 times were lengthened in the early years of
18 PDUFA IV.

19 From my perspective,
20 unpredictability in the review process and
21 sub-optimal communication with sponsors and
22 decreased FDA performance not only hinders

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1 patient access to new treatments but also
2 negatively impacts the ability of
3 biotechnology companies to raise funding to
4 support clinical development in ongoing
5 innovation into key public health priorities.

6 And for that reason, we support
7 PDUFA V as under PDUFA V, industry and FDA
8 have agreed on a set of enhancements that seek
9 to reinforce FDA's review performance and
10 really get back to basics for patients. These
11 proposals as mentioned have been informed by
12 unprecedented levels of public input through
13 workshops, meetings, stakeholder outreach and
14 we really feel this has strengthened the
15 agreement considerably.

16 Underlying these PDUFA V
17 recommendations are the principles that a
18 science-based transparent and well-managed
19 review process that appropriately balances
20 benefits and risk enhances public trust and
21 patient access to new medicines.

22 I will briefly touch on some of the

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1 recommendations. First, with respect to the
2 NME review program, historically about 80
3 percent of all applications are ultimately
4 approved but less than half of products
5 submitted to FDA are approved on the first
6 submission. And sponsors and FDA can and must
7 do better for patients.

8 By strengthening scientific
9 dialogue and transparency between FDA and the
10 sponsor under the new review program for NMEs,
11 we can minimize the potential for review
12 issues that can delay patient access to needed
13 treatments and increase FDA sponsor and
14 scientific dialogue transparencies such as the
15 mid-cycle communication exchange of discipline
16 review letters and advisory committee
17 information, and importantly the late cycle
18 meeting will help to identify and resolve
19 issues earlier in the review.

20 Now this represents a significant
21 paradigm shift for FDA's review process, while
22 maintaining the highest standards for safety

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1 and efficacy. Coupled with an additional two-
2 month validation period during the review and
3 a robust third-party evaluation, we expect
4 this program will lead to fewer review cycles
5 and shorter overall approval times to ensure
6 earlier patient access.

7 Secondly, to help advance American
8 innovation and promote the development of the
9 next generation of modern medicines, FDA is
10 committed to a philosophy under PDUFA V that
11 timely and interactive communication with
12 biotechnology and life science companies
13 during drug development is a core Agency
14 activity.

15 FDA's recent report on driving
16 biomedical innovation highlights that the
17 private sector is the engine of innovation and
18 that much of the innovation begins with small
19 business. Indeed many small biotechnology
20 companies operated on the cutting edge of
21 biomedical science to develop new therapies
22 for devastating diseases, yet we must

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1 acknowledge that the scientific method does
2 not operate in a vacuum and that it is
3 critical to promote interactive scientist to
4 scientist communication between FDA and
5 sponsors.

6 In the course of drug development,
7 sponsors sometimes have simple clarifying
8 questions, the responses to which could have
9 significant impact on the development program
10 but may not rise to the level of necessitating
11 a formal meeting. To obtain timely responses
12 to such questions, sponsors currently have to
13 engage in lengthy exchanges of multiple formal
14 letters with FDA, which we believe is not an
15 efficient use of both FDA and the sponsor's
16 time. And for small biotechnology companies
17 reliance on limited venture capital, these
18 delays can create significant impediments to
19 their development programs.

20 Additionally, independent reports
21 commissioned by FDA have demonstrated that
22 enhanced communication during drug development

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1 ultimately results in higher quality
2 applications, which can enhance the efficiency
3 for FDA reviewers themselves.

4 So for these reasons, BIO fully
5 supports the PDUFA V proposal to promote
6 innovation through enhanced communication
7 between FDA and sponsors during drug
8 development. It will establish best practices
9 for this type of interactive dialogue, train
10 staff on communication practices, and provide
11 the Agency with additional staff capacity to
12 respond to sponsor inquiries in a timely
13 manner.

14 Third, the agreement also makes new
15 resources available to modernize regulatory
16 science, for example, some of the areas of
17 personalized medicine and rare disease drug
18 research. Modern approaches to drug
19 development and evaluation such as through the
20 application of new tools for rare disease drug
21 development, flexibility with regard to
22 creative study designs and new endpoints,

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1 greater utilization of biomarkers and patient-
2 reported outcome tools, will introduce new
3 efficiencies into the drug development
4 enterprise and also provide FDA with
5 additional tools to evaluate the benefits and
6 risks of pharmaceutical products.

7 These proposals will also integrate
8 more structured systematic approaches to
9 assessing benefit-risk of therapies and allow
10 FDA to conduct outreach to patients and hold
11 workshops to better understand the patient
12 perspectives on disease severity and unmet
13 medical need.

14 And fourth, PDUFA V continues
15 industry's commitment to a lifecycle approach
16 to product evaluation by strengthening FDA's
17 post-market surveillance and benefit-risk
18 management capacity. Earlier discussion of
19 REM strategies and standardized approaches to
20 REMS and further validation of the Sentinel
21 network will promote a high patient confidence
22 in the safety of drugs and biologics.

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1 Now it should be noted that while
2 the agreement reinforces industry's commitment
3 to a well-funded drug and biologics program
4 that supports sound science-based regulation
5 consistent with FDA's public health mission,
6 user fees are intended to support a limited
7 FDA activities around the drug review process
8 and were never intended to supplant a sound
9 base of appropriations.

10 User fees under PDUFA now count for
11 nearly two-thirds of the cost of human drug
12 review program. As a proud member of the
13 Alliance for a Stronger FDA, BIO urges
14 Congress to support FDA's mission and fund the
15 Agency at the Administration's full FY'12
16 requested level.

17 Additionally, it is critical for
18 PDUFA to be reauthorized well in advance of
19 PDUFA IV's expiration in September 2012 in
20 order to avoid a reduction in force at FDA.
21 Even the threat of downsizing at FDA would be
22 devastating to the Agency's public health

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1 mission and the ability to review new drugs
2 and biologics. And BIO looks forward to
3 working with Congress and FDA to fully
4 implement these enhancements under PDUFA V.

5 And finally, successful
6 implementation of PDUFA V from a practical
7 perspective will require both FDA and
8 individual companies to make changes to their
9 existing regulatory procedures and
10 communications practices. We recognize the
11 preparing for these changes is a shared
12 responsibility. For example, under the NME
13 review program both FDA medical reviewers and
14 industry regulatory professionals will need to
15 be aware of the revised review schedule, be
16 prepared for key points of interaction during
17 the review, such as the mid-cycle
18 communication and late-cycle meeting, and
19 understand their respective expectations and
20 roles.

21 The NME review program will become
22 effective on day one of PDUFA V, on October

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1 first, 2012. So to facilitate effective
2 implementation, we encourage both
3 biopharmaceutical sponsors and FDA to begin
4 internal planning and staff training on the
5 new review processes and communications
6 practices well in advance of final passage of
7 the legislation.

8 And in conclusion, thank you for
9 the opportunity to speak today and I will be
10 pleased to answer any additional questions.

11 MR. FREY: Thank you, Andrew.

12 Our last panelist of the day is
13 David Wheadon, the Senior Vice President of
14 Scientific and Regulatory Affairs, at PhRMA.

15 DR. WHEADON: First I want to thank
16 you for this opportunity to say yet again many
17 things that you have heard all morning and
18 into the afternoon. So I will try not to
19 belabor many points.

20 Certainly the Pharmaceutical
21 Research and Manufacturers of America, better
22 known as PhRMA, appreciates the opportunity to

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1 participate in this public meeting and share
2 its view that the reauthorization of PDUFA is
3 very important and should be done as
4 expeditiously as possible.

5 PhRMA represents the country's
6 leading biopharmaceutical research and
7 biotechnology companies, which are devoted to
8 inventing medicines that allow patients to
9 live longer, healthier, and more productive
10 lives. PhRMA companies are leading the way
11 and searching for new cures. PhRMA companies
12 alone have invested an estimated 49.4 billion
13 dollars in 2010 in discovering and developing
14 new medicines.

15 The PDUFA V performance goals
16 letter is a result of extensive technical
17 negotiations between industry and the FDA.
18 And it is very important that we remember and
19 understand that at that table, the most
20 important thing on the minds of everyone
21 involved in that negotiation was patients;
22 patient safety and patient benefits in terms

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1 of the promise of cures that could be brought
2 to the table.

3 PhRMA strongly supports the
4 original goals of PDUFA, which are to provide
5 patients with timely access to innovative
6 medicines, to preserve and strengthen FDA's
7 high standards for safety, efficacy, and
8 quality, and to advance the scientific basis
9 for the Agency's regulatory oversight. PhRMA
10 also strongly endorses the recommendations of
11 the PDUFA V performance goals letter. This
12 agreement, as drafted, will provide FDA with
13 the resources and tools required to carry out
14 their important role in preserving and
15 promoting public health.

16 PhRMA urges congress to act
17 expeditiously in reauthorizing PDUFA. It is
18 paramount to do so because, as pointed out
19 earlier, failure to do so could result in
20 catastrophic consequences for the Agency and
21 the important work that it does.

22 PhRMA was an original participant

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1 in the original PDUFA beginning in 1992 and we
2 look forward to continuing to be involved in
3 caring for this very important program.

4 Unfortunately during the last
5 reauthorization of PDUFA, Congress introduced
6 substantial policy changes and provisions that
7 significantly impacted the FDA's
8 responsibilities and activities. Current
9 provisions in the Food and Drug Administration
10 Amendments Act, better known as FDAAA, while
11 passed with good intention, increased the
12 Agency's regulatory burden to the detriment of
13 the efficiency and effectiveness of the drug
14 review process. As a result, the percentage
15 of missed user fee goals rose sharply in the
16 years following FDAAA, as Theresa Mullin
17 outlined for you this morning.

18 We have seen some incumbent
19 improvement in those achievements of PDUFA
20 goals in the past couple of years and PDUFA V
21 was intended or is intended to try and build
22 upon that improvement in performance in the

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1 Agency's ability to carry out its important
2 role.

3 There are a number of very
4 important initiatives included in the PDUFA V
5 technical agreement, a lot of which you have
6 heard about already this morning. I just
7 wanted to highlight a few very important
8 points contained in the agreement.

9 First, the Enhanced NME Review
10 Model. This new review program is not really
11 new but it is really an improvement upon the
12 Agency's review program focused on new
13 molecular entities in the regional BLAs, is
14 intended to increase the efficiency of the
15 process, not to short circuit, not to lower
16 the quality standards, the safety standards
17 that the Agency brings to its review, but to
18 increase the efficiency.

19 If you look at the data that the
20 FDA shared with us at the beginning of the
21 negotiations, 32 percent of priority reviews,
22 32 percent of drugs that go through priority

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1 review that ultimately get approved do not get
2 approved in the first cycle. In terms of
3 standard reviews, 62 percent of drugs that
4 ultimately get approved do not get approved in
5 the first cycle. Clearly, there is an
6 opportunity for greater efficiency and more
7 appropriate use of the FDA's very limited
8 resources. And this is indeed what the
9 Enhanced NME Review Program is intended to do.

10 The success of the new review
11 program and the Agency's ability to achieve
12 the drug review goals will be independently
13 assessed and publicly reported in 2015 and
14 2017. Beyond the Enhanced NME Review Model,
15 advancements in regulatory science have also
16 been included, which you have heard about
17 already this morning.

18 Importantly, such things as use of
19 pharmacogenomics and biomarkers to more
20 effectively and in a more targeted fashion
21 identify patients that will benefit from
22 proposed innovative new therapies and also

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1 identify patients who may not have the
2 intended effect, i.e., have side effects from
3 those therapies. Very important and also an
4 inclusion parameter within PDUFA V.

5 Standards for and validation of
6 patient-reported outcomes is also included.
7 We have heard from many of the patient and
8 consumer groups that the perspective of the
9 patient is important to be included as drugs
10 are developed and ultimately reviewed and
11 hopefully approved by the FDA. PDUFA V
12 includes tenets that will look at a more
13 robust review, evaluation, and qualification
14 of patient-reported outcomes.

15 Also important is the increasing
16 need to develop innovative medicines for rare
17 diseases. As John Jenkins is very quick to
18 point out, FDA had been relying upon a staff
19 of about one and a half to really help the
20 Agency wrestle with how you approach studying
21 and reviewing and ultimately approving drugs
22 for rare diseases. PDUFA V will augment that

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1 staff significantly to really get the Agency
2 and sponsors more aligned and focused on how
3 you refine our scientific approaches to bring
4 needed medicines to patients suffering from
5 these rare diseases.

6 And last but not least, there will
7 be a significant look at the Agency's approach
8 to benefit risk. We have heard a lot about
9 the need to have a balance between looking at
10 benefit and risk and how decisions are made
11 based on that assessment. The Agency has
12 started a very robust set of programs to have
13 an objective approach to this and PDUFA V will
14 build upon that, involving stakeholders beyond
15 industry and the FDA involving patients and
16 more importantly, involving as well other
17 regulatory agencies around the world that are
18 also looking at this issue of benefit risk and
19 how we are going to have a more collated and
20 systematic approach in objectively quantifying
21 these important parameters.

22 We have also heard a lot about the

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1 drug safety system today. Certainly REMS was
2 a component of FDAAA that has added a
3 significant amount of workload to the FDA
4 under PDUFA IV. We recognize the role and
5 important need for REMS in ensuring safe use
6 of innovative products but perhaps there is a
7 way that we could have a more standard
8 approach, looking at standardized tools that
9 allow us to use REMS efficiently and
10 effectively in appropriate populations. We
11 have also heard a lot about Sentinel and its
12 important mandated use under FDAAA.

13 PDUFA V is also looking at how we
14 can build upon the pilot data coming out of
15 Sentinel to ensure that the best science and
16 at the end of the day, the best decisions
17 driven by that science can be utilized using
18 large safety data bases that Sentinel will be
19 utilizing in driving the regulatory science of
20 efficient evaluation of safety signals and
21 allowing that data to be used to make
22 appropriate decisions around whether products

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1 continue to be made available to patients.

2 PhRMA is encouraged at the positive
3 response that we have seen across the domain
4 of stakeholders that have been involved in
5 this process, one of the most transparent
6 processes that I have seen in the over 20
7 years that I have been involved in this
8 industry in terms of this PDUFA
9 reauthorization. And we certainly ask
10 Congress to build upon this spirit of working
11 closely and collaboratively with patients'
12 best interest as the ultimate goal. And as
13 such, we ask that Congress very thoroughly yet
14 efficiently and expeditiously reauthorize
15 PDUFA in order that the FDA and our industry
16 can get about their important work of bringing
17 innovative medicines to patients as safely but
18 as thoroughly and as efficiently as possible.

19 Thank you.

20 MR. FREY: All right, thank you
21 David.

22 Are there any clarifying question

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1 for the two industry representatives?

2 (Pause.)

3 MR. FREY: All right. Thank you
4 very much, panel.

5 I would like to invite the FDA
6 panel back to the table.

7 So I think earlier this morning I
8 said we had 11 folks who had indicated a
9 desire to speak. We now have 16. So to make
10 this run smoothly for those who would like to
11 speak, we are just going to run through this
12 list. So the first up, and I apologize if I
13 mispronounce your name, is Emil Kakkis. Any
14 of the mikes. If they are not on now, they
15 are about to be on.

16 DR. KAKKIS: Thank you the
17 opportunity. I am Emil Kakkis, President of
18 EveryLife Foundation for Rare Diseases. I
19 have been in the business of developing
20 treatment for rare diseases as an academic,
21 and as a company executive, and also heading a
22 nonprofit foundation.

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1 I think the PDUFA deal has a number
2 of good things for rare diseases in there and
3 we applaud the effort of the FDA and the
4 industry has made to include rare diseases as
5 part of the equation. And so we think there
6 is certainly something good in there.

7 I do think, though that in the end
8 it falls short of being something great. I
9 think it is good but it could be great. And I
10 think that though an opportunity that happens
11 only five years, I think that something more
12 could be put into the plan.

13 Our feeling is with the chronic
14 underfunding of FDA in the past, that the
15 reviewers are under a lot of pressure to meet
16 the requirements of drug reviews. And
17 particularly in the rare disease area where
18 the disease are very complicated and require a
19 lot of time, it is extremely difficult to meet
20 those requirements to evaluate for safety and
21 efficacy.

22 We think that an increase in PDUFA

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1 fees that were somewhat larger would allow a
2 greater number of reviewers to be hired and
3 that there would greater concordance of their
4 training and specialization into the fields
5 that are being studied and that if they would
6 allow reviewers more specialization within the
7 review divisions, it would have given us the
8 ability to get reviewers to become more expert
9 in narrower subject matter and become better
10 at managing the timeline and doing great
11 reviews that assure the kind of safety and
12 efficacy everyone wants.

13 I think the reviewers also need
14 enough time to be able to do the kind of
15 academic work that it takes to keep up with
16 the field. And if they are running around
17 barely keeping up with whatever is put to them
18 in terms of review, I think it is very
19 challenging to do the kind of academic work
20 that is important in making yourself up-to-
21 date.

22 I think that if you had more

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1 specialization and more reviewers, I think we
2 would get expert reviews; we would hit the
3 timelines more readily; we would do that
4 without sacrificing or the appearance of
5 sacrificing safety and efficacy. And I think
6 in the end, I think this would be a more
7 substantial thing that could be achieved out
8 of PDUFA than what we have at the moment. I
9 think the PDUFA deal does a lot of good things
10 and I am supporting those but I would say
11 there could be more.

12 I think lately the FDA has made
13 some positive moves in the area of
14 specialization. In the cancer area, I have
15 seen some discussion of that. I have seen
16 some of the other divisions separating out.
17 We think those are great moves. We support
18 them. We think they just need to do more and
19 we would have hoped there would be perhaps
20 more money in PDUFA to be able to do the kind
21 of work that I think would help the reviewers
22 do their very difficult jobs. Thank you.

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1 MR. FREY: Thank you. Next on our
2 list is Lindsey Dawson from The AIDS
3 Institute.

4 MS. DAWSON: Good afternoon. My
5 name is Lindsey Dawson. I am a Policy
6 Associate with The AIDS Institute. Today the
7 AIDS Institute, a national nonprofit
8 organization providing leadership in HIV and
9 AIDS public policy research, advocacy, and
10 education offers its strong support for the
11 proposed recommendations of the fifth renewal
12 of PDUFA as negotiated between the FDA and the
13 pharmaceutical industry.

14 PDUFA is an important tool in
15 ensuring drug safety, timely access to
16 pharmaceuticals and fostering community
17 engagement in the drug review process.
18 PDUFA's development over time is owed to a
19 productive relationship between the federal
20 government, industry stakeholders and
21 community members, an iterative process
22 sparked much by AIDS activists almost 30 years

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1 ago.

2 The FDA's mission to protect and
3 promote public health necessitates safe
4 expedited review of and timely access to
5 drugs, particularly for rapidly progressive
6 and infectious diseases. Prior to 1992, FDA's
7 drug review process was less predictable and
8 slower than other countries, with a backlog of
9 pending applications.

10 PDUFA makes funding available
11 through user fees to accelerate the drug
12 review process, hiring more reviewers, and
13 updating systems, thereby getting drugs to
14 market more efficiently, making the reviewer
15 process more transparent, and promoting
16 innovative therapies.

17 PDUFA benefits the FDA by injecting
18 user fees to partially cover high reviewing
19 costs and subsidizing appropriated funds.
20 Industry, by providing more efficient pathways
21 to market and consumers in need of drugs as
22 soon as they are safely available. Safety has

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1 also been enhanced by increasing post-market
2 drug monitoring, including data collection on
3 adverse events.

4 PDUFA's goals are particularly
5 important to people living with HIV. We know
6 that timely access to medications is essential
7 to people living with HIV and that treatment
8 is prevention. Access to the most current
9 drugs available has been critical from the
10 early days of the AIDS crisis and remain so at
11 present, where for those who are fortunate to
12 have access to regular healthcare and
13 treatment, HIV is a manageable chronic
14 condition. Whether we now know that access to
15 treatment is not only critical to individuals
16 living with HIV, but through suppression of
17 viral load, treatment is also a public health
18 measure, making the availability of drugs a
19 critical component in battling the epidemic.
20 Because treatment is prevention and access to
21 drugs is critical for the more than 1.2
22 million Americans living with HIV, we are

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1 fully supportive of the proposals of PDUFA V.

2 In addition to providing timely
3 access to drugs, PDUFA has taken steps to
4 cultivate community involvement from a range
5 of stakeholders from patient groups to
6 advocates, to industry, and to federal
7 agencies. The AIDS Institute also applauds
8 PDUFA for incorporating risk evaluation and
9 mediation strategies and drug safety
10 monitoring, which is particularly critical to
11 drugs that are fast tracked and for
12 encouraging innovation between the FDA and
13 sponsors. An ongoing dialogue about complex
14 care and needs is a best practice begun by and
15 to this day remains important to the HIV-AIDS
16 community.

17 The AIDS Institute supports PDUFA
18 V, which is cost neutral to the federal budget
19 yet supports federal activity to promote safe
20 and timely access to drugs for individuals
21 awaiting new and innovative pharmaceuticals,
22 including people living with HIV. Thank you.

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1 MR. FREY: Thank you. Next we have
2 Kevin Nicholson from the National Association
3 of Chain Drug Stores. Is Kevin in the room?

4 All right, we will move on to
5 Roslyne Schulman. Roslyne is from the
6 American Hospital Association.

7 MS. SCHULMAN: Thank you. And I am
8 going to make just very brief comments, which
9 will be followed up by our comment letter in
10 more detail.

11 Through the PDUFA reauthorization
12 stakeholder consultation process, the AHA and
13 other stakeholders have raised concerns about
14 REMS. In particular while we understand that
15 more serious risks require a more restrictive
16 distribution of drugs, REMS are often
17 challenging and burdensome to implement in the
18 hospitals and should involve cooperation of
19 all segments of the healthcare system.

20 What adds urgency to these and
21 other concerns about the application of REMS
22 to hospitals is the looming prospect of future

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1 REMS programs for drugs that are very widely
2 used in hospital inpatient settings and other
3 newer drugs. The creation of these types of
4 REMS will undoubtedly have an even greater
5 impact on hospital practice.

6 The AHA and others have urged the
7 FDA to obtain input from hospital pharmacists
8 and other providers on REMS designs. We have
9 also advocated changes to make REMS more
10 standardized and to establish metrics to
11 evaluate the success of REMS. Further, we
12 urge the FDA should assess the growing burden
13 that REMS puts on hospitals and healthcare
14 systems.

15 We are pleased that the FDA in its
16 draft commitment letter for PDUFA V has
17 included steps to address these concerns.
18 That is, FDA proposes to explore with public
19 input strategies and initiate projects to
20 standardized REMS with a goal of reducing
21 burden on practitioners, patients, and others
22 in the healthcare setting. This will include

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1 conducting public workshops and developing
2 guidance on methods for assessing the
3 effectiveness of REMS, the impact on patient
4 access, and the burden on the healthcare
5 system.

6 The AHA supports the FDA's
7 recommendations with regard to REMS.

8 MR. FREY: All right. Thank you
9 very much.

10 Next we have Everett Neville from
11 Express Scripts.

12 MR. NEVILLE: Good afternoon.
13 Everett Neville, Express Scripts.

14 I want to speak today on the REMS
15 component of PDUFA. Express Scripts fills
16 about 40 million prescriptions a year, many of
17 these do have REMS involved and we expect to
18 have more REMS in the future. Additionally,
19 we help operationalize REMS programs with
20 PhRMA on the service side through such
21 activities as REMS hubs.

22 The REMS program has played an

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1 important role in our industry. We recognize
2 that by having these safeguards in place we
3 are able to effectively manage potential
4 safety risks and allow the use of beneficial
5 life-improving and life-sustaining therapies
6 that otherwise would likely not be made
7 available to the public. However, we also
8 think the REMS process can be improved and we
9 would suggest the following areas.

10 The evaluation and study of the
11 effectiveness of the various components of
12 REMS. Our experience and incidental evidence
13 suggest that patient and physician registries
14 requiring testing and required physician
15 training are effective. However, the
16 effectiveness of patient medication guides
17 seems to be less clear. We would encourage an
18 investigation of alternative ways to educate
19 the patient population. And for drugs with
20 serious side effects, we would encourage the
21 use of the more stringent ETASU.

22 Secondly, to ensure that REMS are

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1 well monitored, specific and coordinated,
2 clinical requirements such as patient testing
3 should only be in a REMS if it is part of the
4 required ETASU and that that ETASU is required
5 in order to obtain access, prescribe the
6 medication, or obtain the medication as a
7 patient. A communication plan or a MedGuide
8 in these cases does not seem to be sufficient.

9 Third, the coordination of REMS
10 processes such as monitoring, verifying
11 training, recording registries and patient
12 access services should be required of
13 manufacturers. Today, many of these services
14 are fragmented and in the hands of different
15 providers. This results in an increased
16 burden on patients, pharmacies, and optimal
17 delay in obtaining therapy.

18 Fourth, REMS requirements should be
19 coordinated with state pharmacy regulations.
20 Too often today many enrollment forms do not
21 contain the necessary information required to
22 dispense a medication. This results in a

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1 delay in therapy and increased burden on both
2 the pharmacy and the patient and the
3 physicians. Coordinating this with the
4 associations of state boards of pharmacy would
5 seem to address this.

6 Lastly, we encourage the
7 standardization of REMS programs for drugs
8 with similar safety profiles. While we
9 recognize that a single standardized REM
10 program is not workable, given the different
11 safety concerns among therapies, some same
12 relation of components should be possible.
13 For example, timing of pregnancy test and
14 physician training registries could be
15 standardized.

16 Thank you.

17 MR. FREY: All right, next we have
18 Theresa Morrow from the Women Against Prostate
19 Cancer, if Theresa is in the room.

20 All right, we will move on to Frank
21 Oldham, National Association of People with
22 AIDS.

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1 MR. OLDHAM: Thank you. I'm going
2 to start a little bit differently from
3 everyone else. Having been a resident of New
4 York City and a person living HIV-AIDS in New
5 York City, I lived there when Dr. Margaret
6 Hamburg was Commissioner of Health and now she
7 is the head of the FDA. And I am very proud
8 that we have an advocate for people living
9 with HIV-AIDS as the in charge of FDA at this
10 point. So it is really an honor to have this
11 opportunity and an honor to be here at this
12 time.

13 I am Frank Oldham, Junior,
14 President and CEO of the National Association
15 of People with AIDS. Founded in 1983, NAPWA
16 is the oldest national AIDS organization in
17 the United States and in the world and
18 represents an estimated 1.2 million Americans
19 living with HIV today.

20 I am one of the 1.2 million. I
21 have lived with HIV for 22 years. In those
22 years, I have seen new medications transform

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1 HIV from the death sentence into a manageable
2 chronic condition for those who are lucky
3 enough to have access to the drugs.

4 NAPWA and I personally support
5 reauthorization of PDUFA because the user fees
6 authorizes support of reliable, safe, speedy
7 process, for testing and approving the new
8 medications that people living with HIV and
9 other serious conditions need. PDUFA V
10 provides for increased industry fees to
11 provide even more support for safer and more
12 predictable review of new medications.
13 Regulators support this because it pays the
14 salaries of the scientists administrators may
15 need to provide their legislatively mandated
16 function of approving new drugs and therapies.

17 Industry supports this because it
18 helps them bring their products to patients
19 sooner.

20 Consumers and patients included in
21 the 1.2 million Americans living with HIV whom
22 NAPWA represents support this because a faster

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1 approval process gives them earlier access to
2 new drugs they need right now. Those of us
3 who live with HIV know that early access to
4 new drugs can be a matter of life and death.
5 Since 1992 when PDUFA was first enacted, the
6 average approval time for new drugs, new
7 medications decreased by more than half. The
8 same decade has seen a welcome flood of new
9 HIV antiviral medications that have changed
10 HIV from a death sentence into a serious but
11 survivable condition. Many of us are still
12 here because PDUFA works.

13 PDUFA V not only supports a faster
14 testing and review process, it also encourages
15 innovative basic medical science by providing
16 an environment in which scientific review to
17 keep pace with the basic science and a
18 predictable review process that gives
19 researchers and investors better prospects for
20 seeing promising developments through to
21 commercialization.

22 As an effective HIV preventive

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1 vaccine and a functional cure for HIV either
2 of which can save the public billions and
3 billions of dollars remain tantalizingly just
4 out of reach, we at NAPWA call the attention
5 to the important research and a need for a
6 regulatory climate that supports it.

7 PDUFA V also takes important steps
8 in requiring risk evaluation and medication
9 strategies and long-term pre- and post-
10 approval drug safety monitoring. We support
11 this. PDUFA V is one of the very real issues
12 where regulators, and industry, patients, and
13 all are asking the same thing. We hope the
14 lawmakers who represent 1.2 million Americans
15 living with HIV that NAPWA serves and indeed
16 all Americans will enact PDUFA V swiftly, as
17 it is designed when it reaches Congress.

18 Thank you.

19 MR. FREY: Thank you. Next we have
20 Rebecca O'Connor from the Parkinson's Action
21 Network.

22 MS. O'CONNOR: Good afternoon. My

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1 name is Becca O'Connor and I am the Director
2 of Government Relations with the Parkinson's
3 Action Network. We are a nonprofit that
4 advocates for better treatments and a cure for
5 the Parkinson's community. My comments will
6 be brief and will echo some of what has
7 already been said today. Partly brief because
8 I have a cold, so please excuse me.

9 PAN appreciates and applauds the
10 FDA's efforts to develop a five-year plan that
11 addresses and incorporates patient input as
12 outlined in the agreement. There is among
13 patients some fear and suspicion about the
14 FDA's approval process and this is rooted in a
15 perceived lack of transparency and opportunity
16 for meaningful patient input. So while we
17 appreciate and are encouraged by the attention
18 and focus on patient input in the proposed
19 agreement, the ultimate value of this proposed
20 plan will lie in notably missing details.

21 The long-term schedule and timeline
22 for public meetings with patient advocates

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1 leaves us and others, as others have noted
2 today to wonder how and when will patient
3 input into critical issues including burden of
4 disease be incorporated evaluated in the
5 decision-making process. Moreover, will this
6 input be taken into consideration in a timely
7 fashion? To have any real impact, meetings
8 and discussions with patient advocates as
9 contemplated in the agreement must be
10 correlated to corresponding with the timing of
11 FDA decision-making.

12 PAN also is among the groups that
13 Diane Dorman references earlier today that are
14 concerned about the conflict of interest
15 piece. And without going into great detail
16 because it has been covered, I will just say
17 that we have joined on to a sign-on letter
18 with 50 plus patient organizations
19 recommending that there be reasonable
20 amendments to the layer of evaluations for
21 experts. That is in fact a real issue within
22 our community where there are limited experts

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1 on the issue of Parkinson's.

2 In conclusion, we appreciate the
3 FDA's intent and demonstrated commitment to
4 ensuring patients have increased involvement
5 in the process and look forward to working
6 with you further as PDUFA is reauthorized.

7 MR. FREY: Thank you. Next is
8 Andrew Sperling from the National Alliance on
9 Mental Illness.

10 MR. SPERLING: Thank you. I'm
11 Andrew Sperling with NAMI, the National
12 Alliance on Mental Illness. I'm listed twice.
13 I promise I am only going to speak once.

14 NAMI is the nation's largest
15 organization representing people living with
16 serious mental illness and their families.
17 NAMI has always fought hard and wants to see
18 newer more innovative treatments for disorders
19 such as schizophrenia, bipolar disorder, and
20 major depression. We believe we need new
21 breakthrough treatments. Most of the
22 treatments for these very serious and complex

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1 disorders are largely palliative in nature.
2 And helping patients, helping consumers
3 control their systems so they can function at
4 a higher level, what we really need quite
5 frankly is breakthrough treatments that will
6 really change the trajectory of these
7 disorders.

8 While we also need that, we also
9 need incremental improvements on the
10 treatments we have now. Even marginal
11 improvements, new products that can have maybe
12 a different side effect profile or deal with,
13 for example, the negative symptoms of
14 schizophrenia with even marginal improvement
15 can vastly improve prospects for treatment
16 adherence and recovery. So we need both the
17 incremental side of the treatments we have in
18 terms of making improvements, but also
19 breakthrough treatments that can really change
20 the trajectory of the illness. And PDUFA is
21 absolutely critical to this.

22 And NAMI supports the technical

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1 agreement that is before us today. NAMI
2 supports the performance goals and the need to
3 increase drug efficiency and predictability.
4 NAMI supports the inclusion of the enhanced
5 communications with sponsors to support more
6 efficient and effective reviews. NAMI
7 supports the enhancement of the benefits risk
8 assessment. We are very pleased that there is
9 a provision in there to try and increase
10 transparency in this process. It's badly
11 needed.

12 NAMI supports the new requirement
13 for electronic submission and standardization
14 of application data. NAMI participated in one
15 of the stakeholder groups that developed this
16 technical agreement and were actually, quite
17 frankly, in some of the meetings surprised to
18 learn of the cumbersome and outdated process
19 that the FDA was operating under in terms of
20 the documents they had in boxes that filled --
21 no electronic submission. We were actually
22 stunned that that was still going on today.

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1 And we are very pleased that this is a part of
2 the agreement to have electronic submission
3 and standardization of data, application data
4 so you can look across multiple clinical
5 trials. It is very, very important.

6 Independent review. NAMI is very
7 pleased that there is enhanced independent
8 review for the performance goals going
9 forward. This needs to be independent. NAMI
10 strongly supports the provisions of agreement
11 to improve regulatory science. This is, I
12 think for NAMI, one of the most important
13 parts of this agreement.

14 Not only the improvement and the
15 development of standards for meta-analysis,
16 which would be very, very important, but
17 probably most important from NAMI's
18 perspective are the additional investments and
19 developments for pharmacogenomics and
20 biomarkers. This is very hot area of science
21 in terms of research in schizophrenia,
22 developing biomarkers associated with this

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1 very complex disorder. We are making progress
2 and if we could continue to do that and have
3 PDUFA work hand-in-hand with some of the
4 scientific research going on, to really
5 actually predict for someone with
6 schizophrenia which medication is going to
7 work for them is really a cutting edge where
8 we really need to make a lot of progress.

9 NAMI supports the advancement and
10 validation of patient-reported outcomes,
11 another part of the agreement which they could
12 move PDUFA in a very positive way.

13 NAMI supports the critical
14 improvements to enhance FDA's robust safety
15 system, improvements to REMS and Sentinel that
16 have been talked about over and over again
17 today but we do want to make clear our support
18 for that.

19 And then finally on the issue of
20 conflict of interest, I know it has been
21 talked about a lot today but NAMI did sign the
22 letter that was referenced by our colleagues

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1 from NORD and PAN and a number of other
2 organizations. We have experience with this,
3 at least in terms of the advisory committees
4 that have in recent years issued black box
5 warnings with respect to SSRIs and
6 antipsychotics and we were very discouraged to
7 see some of the leading experts and leading
8 researchers in psychiatry that were conflicted
9 out of those panels. We believe that the
10 panels need, quite frankly, the full panoply
11 of experts to make sure their deliberations
12 really get the most up-to-date information and
13 really hear from the experts in the field. So
14 we would encourage moving in this arena.

15 Thank you very much.

16 MR. FREY: Thank you, Andrew.

17 Next we have John Kamp, Coalition
18 of Healthcare Communication. I don't think I
19 see John.

20 All right, James Sykes, HealthHIV.

21 MR. SYKES: Good afternoon. I am
22 James Sykes, Advocacy Manager for HealthHIV.

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1 HealthHIV serves as the AIDS
2 education and training center national center
3 for HIV care in minority communities. Our
4 mission is to advance effective prevention
5 care and treatment and support for people at
6 risk for or living with HIV by providing
7 education, technical assistance, and health
8 services research to organizations,
9 communities, and professionals.

10 As the leading national HIV
11 nonprofit representing primary care providers,
12 community and faith-based organizations
13 involved HIV prevention, care, and treatment,
14 we thank you for the opportunity to provide
15 public comment on the proposed recommendations
16 for the reauthorization of the prescription
17 drug user fee act or PDUFA.

18 As a supporter and advocate for the
19 development of new treatments overall and for
20 HIV specifically, HealthHIV has been following
21 the PDUFA negotiations closely. We are
22 pleased that the negotiations have yielded a

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1 process that includes recommendations aimed at
2 expediting reviews of new molecular entities,
3 new drug applications, and the biologics
4 license applications. We are encouraged that
5 the PDUFA V enhancements have the potential to
6 decrease drug development time, promote
7 innovation by enhancing communication between
8 the FDA and sponsors during drug development,
9 improve the FDA's capacity to address
10 submissions involving patient-reported
11 outcomes, and facilitate development of
12 treatments for rare disorders.

13 The accelerated approval process
14 that was instituted by the FDA in 1992 allowed
15 for earlier approval of drugs that treated
16 serious diseases and filled an unmet medical
17 need. Over 100 critical products, including
18 most HIV therapies and many cancer treatments
19 were approved under the accelerated approval
20 process or programs. This past June marked
21 the 30th anniversary of HIV. June 1, 1981 was
22 the date when the CDC's Morbidity and

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1 Mortality Weekly Review, the MMWR, detailed
2 the story about five cases of Pneumocystis
3 carinii pneumonia in young gay men in Los
4 Angeles.

5 We now know that that was the
6 beginning. Those diseases were caused by
7 acquired immunodeficiency syndrome or AIDS and
8 caused by the human immunodeficiency virus.

9 It was not until 1987 that the FDA
10 approved the first drug for the treatment of
11 HIV, zidovudine or AZT. It took just over
12 three months for the FDA to approve its use.
13 Since then, 35 different drugs have been
14 approved for the treatment of HIV, the most
15 recent being Complera that was approved in
16 August of this year. It took six months for
17 Complera to receive FDA approval.

18 In the 24 years since the
19 development of AZT, the length of the approval
20 process has varied between two and a half to
21 ten months. And the length of time to
22 approval has been increasing, not decreasing

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1 since PDUFA was first enacted.

2 This new PDUFA V agreement has the
3 potential to expedite the review process and
4 provide predictability for both industry and
5 consumers.

6 I would be remiss if I did not
7 mention that from 1981 through 1987, according
8 to the CDC, approximately 47,993 people died
9 of AIDS during that period of time. Often
10 during these discussions we lose sight of the
11 fact that we are talking about drugs that save
12 people's lives. It is from this perspective
13 that HealthHIV supports the recommendations
14 proposed under PDUFA V negotiations. We
15 strongly encourage Congress to reauthorize
16 PDUFA with its enhancements before the Act
17 expires in September 2012.

18 Thank you for this opportunity.

19 MR. FREY: Thank you. Next we have
20 Thair Phillips from RetireSafe.

21 MR. PHILLIPS: Good afternoon. I'm
22 Thair Phillips, President of RetireSafe. We

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1 are a 20-year-old senior advocacy organization
2 representing about 400,000 supporters
3 nationwide. We also will give a detailed
4 statement to be submitted later.

5 I think that sometimes we get
6 involved here in some of the details and
7 complications of drug approval and we forget
8 that maybe there are some people out there,
9 especially older Americans who may not
10 understand all of the technicalities of drug
11 approval. In talking to a group of people at
12 a senior expo, I asked a small group how many
13 of them knew what a PDUFA was. And the one
14 gentleman said he that wouldn't know what a
15 PDUFA was if it jumped out the bushes and bit
16 him. And I think that when we start talking
17 about PDUFA and that whole benefit and impact
18 it has on their lives, it might bring a little
19 bit closer to home on how important this
20 process really is.

21 Here is a couple of things that
22 they do know, as I talk with older Americans.

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1 They know that medicine in America is safe
2 and they respect it to remain safe in the
3 future. They don't want to hear and be
4 confused by labels or by side effects. They
5 don't want their doctors to be confused by
6 those things. They want to make sure that the
7 medicine they get is of the proper strength
8 and that it has been manufactured and stored
9 correctly. They want to know that medicine
10 remain safe in America.

11 The second thing that they know is
12 that America has been the light of innovation
13 of the world for cures and they want it to
14 remain that way. They don't want to hear the
15 regulations got in the way of getting a quick
16 cure brought to market. They don't want to
17 know that Congress can't get their act
18 together to approve funding for the FDA so
19 that they can do their job. They don't want
20 to hear that budget cuts will underfund the
21 approval process. They don't want to hear
22 that an ounce of prevention has prevented a

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1 pound of cure or that that pound of cure now
2 is going to get in the way and is going to not
3 be able to stop a ton of expensive treatment.

4 That we really have our priorities in the
5 right order.

6 The understand that the cost of
7 heart disease and Alzheimer's and diabetes is
8 huge and has a huge impact on healthcare
9 costs, the very costs that people are trying
10 to come up with a cure for right now. And
11 they also understand that an effective cure or
12 at least an enhanced treatment for any of
13 these diseases could almost solve any of our
14 healthcare costs in a heartbeat. If we could
15 have a silver bullet for diabetes, what an
16 impact that would have.

17 Older Americans look to the FDA to
18 find the correct balance between safety and
19 timely approval. In these times of fiscal
20 accountability, we cannot be penny wise and
21 pound foolish. Money should not be the impact
22 or the controller over safety and innovation.

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1 Thank you.

2 MR. FREY: Thank you. Next we have
3 Lisa Swirsky from Consumers Union.

4 MS. SWIRSKY: Can you hear me? CU
5 is the nonprofit publisher of Consumer
6 Reports. We have a longstanding interest in
7 drug safety and efficacy through our Best Buy
8 Drugs reports, we are proud to say we bring
9 vigorous comparative effectiveness safety
10 information to about 100,000 readers and we
11 are particularly proud to say we do that for
12 free.

13 We are gratified that the FDA's
14 approach to speeding approval timeframes
15 focuses on boosting submission quality.
16 Nonetheless, we remain concerned that the
17 overall focus of the draft comment letter
18 still emphasizes the completion of approval
19 processes within set timeframes.

20 While we understand the need for
21 reasonable goals, the over focus on timeframes
22 risks overshadowing FDA's primary role

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1 ensuring timely access to safe and effective
2 drugs not just timely approval.

3 To facilitate improved quality of
4 submissions, the FDA proposes new pre-
5 submission meetings. It is important that FDA
6 meet these new obligations without diverting
7 attention to resources away from its current
8 responsibilities. We are concerned that these
9 safety initiatives such as REMS and Sentinel
10 get relatively scant attention in the proposal
11 and argue safety and efficacy should be at the
12 heart of FDA's proposals and not a secondary
13 concern.

14 With respect to the REMS process,
15 we are concerned with a draft's emphasis on
16 diminishing the burden of REMS process for
17 industry and for patients. While we support
18 efforts to make REMS more efficient, it is
19 important to remember that the overall goal of
20 REMS is provide access to higher risk drugs in
21 a way that minimizes the impact of those
22 risks. Standardization of REMS should not

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1 constrain necessary flexibility to address
2 risks in a case-specific manner.

3 We also have some concerns about
4 the agreement's use of the word targeted
5 surveillance with respect to the scope of the
6 Sentinel program. When CU first advocated for
7 Sentinel, it was envisioned as a first-alert
8 system rather than a follow-up safety system.

9 We hope that the use of the word targeted
10 does not represent a narrowing of the scope of
11 the program.

12 We also strongly disagree with some
13 of the earlier comments about the need to put
14 conflicted experts on advisory panels. We
15 fail to see why advisory panels cannot consult
16 with whatever experts necessary, including
17 those with financial ties, without having the
18 conflicted experts actually sit on the panels
19 themselves.

20 Finally, I would like to reaffirm
21 some of the disappointment expressed by some
22 earlier speakers about the things that are not

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1 addressed by the draft agreement, including
2 stronger oversight of some troubling marketing
3 practices such as direct-to-consumer
4 advertising and offering inappropriate
5 promotion of off-label use.

6 And I also want to reaffirm the
7 thanks that many other panels expressed to the
8 FDA for seeking input from a diverse range of
9 stakeholders. Thank you.

10 MR. FREY: Thank you very much.
11 Are there any other comments from the room at
12 this time? Okay, I have got two. Go ahead,
13 Nancy.

14 MS. MYERS: Thanks. Hi. My name
15 is Nancy Myers. I'm President of Catalyst
16 Health Care Consulting but I would like to put
17 a different hat on as I talk to this group.

18 One of my beloved volunteer
19 activities is working with a group called the
20 Alliance for a Stronger FDA. And you all have
21 heard it a couple times mentioned today.
22 There were a couple of panelists. We almost

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1 got everybody to mention it on the panel. And
2 the next time you hear Alliance for a Stronger
3 FDA, I expect everybody to start a wave.

4 But the Alliance is a nonprofit
5 organization of 180 members both individuals
6 and corporate, and consumer groups, patient
7 groups, that focuses on strengthening the FDA
8 through appropriations. And I know this
9 activity is all about user fees but I think it
10 is very important for maybe not those on the
11 dais but everybody else who is interested in
12 this topic. User fees deserve a great deal of
13 attention in the policies that are being done.

14 But there also is an important responsibility
15 to make sure that if you have got initiatives
16 that you want funded or you want FDA to focus
17 on new initiatives, we really have to make
18 sure that FDA is adequately funded through
19 appropriations.

20 So there is a group out there, the
21 Alliance. It is a nonprofit.
22 Strengthenfda.org is our website. But if you

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1 are interested in making sure that FDA is
2 funded well, please join our effort because
3 the next couple of years are going to be very
4 difficult to make sure federal agencies are
5 adequately funded.

6 Thank you.

7 MR. FREY: Okay, over here on my
8 left.

9 MS. SHERIDAN: Thank you. We are
10 also a member of the Alliance for a Stronger
11 FDA so thank you for that.

12 My name is Jennifer Sheridan. I am
13 the Associate Director for Federal Affairs at
14 the Alzheimer's Associations.

15 As many of you know, Alzheimer's is
16 a complicated progressive and fatal disease
17 that is currently impacting 5.4 million
18 Americans and by 2050, it will impact nearly
19 16 million Americans.

20 Insufficient understanding of the
21 basic biologies of Alzheimer's, lack of
22 biomarkers, and slow disease progression make

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1 clinical development of innovative treatments
2 a long and, in many cases, a prohibitively
3 costly endeavor.

4 I actually will echo a lot of what
5 has already been said today but the
6 Association is pleased to see the
7 recommendations that the FDA will augment the
8 Agency's capacity to address the growing
9 number and complexity of biomarker submissions
10 by increasing the number of staff available
11 for biomarker qualifications, as well as
12 training for reviewers. We are also pleased
13 to see a patient-centered process put forth to
14 discuss the risk-benefit assessment and look
15 forward to seeing additional details on how
16 that process is actually going to work.

17 Moving forward we hope to see a
18 renewed and continued focus on correcting any
19 barriers that discourage the aggressive
20 pursuit of preventive and other pre-
21 symptomatic treatments for complex diseases
22 like Alzheimer's and a renewed discussion

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1 about accelerating drug review process for
2 complex and costly diseases that have serious
3 unmet medical needs.

4 Thank you for the opportunity.
5 Thanks.

6 MR. FREY: Thank you. I think we
7 had a couple others who were interested.
8 Darby, you want to go ahead?

9 MS. HULL: Hi, I'm Darby with the
10 Consumer Federation of America. And I don't
11 want to make a full set of comments but I did
12 want to reiterate a concern that was raised on
13 an earlier panel about oversight of foreign
14 clinical trials. That was one of CFA's
15 concerns and that was one of the concerns I
16 think that the Patient Consumer Coalition had.

17 And I did have a question for the
18 FDA panel and I don't know if you are taking
19 questions or not. But if you are, I was
20 wondering if you had any thoughts regarding
21 the increase of legislation regarding
22 overregulation. I think that is a theme that

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1 I have seen a lot in Congress lately.

2 DR. MULLIN: Well, there are a lot
3 of proposals and a lot of discussion going on
4 on the Hill. And I think that we will look
5 forward to providing technical assistance when
6 we have the opportunity to do so for
7 particular legislation.

8 We think that the current standards
9 are good ones and are good protective
10 standards for safety and effectiveness. And
11 we really think it is very important to have a
12 timely process, a very rigorous and rapid
13 process to get safe and effective medicines to
14 patients as soon as possible.

15 MR. FREY: Any other comments from
16 the room?

17 MR. VALENTINE: We have one comment
18 from the webcast.

19 MR. FREY: Great, set him up.

20 MR. VALENTINE: This is from
21 William Vaughan who is a consumer advocate.
22 And he has posed a couple of questions to be

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1 included in today's discussion as a public
2 comment.

3 He states that he thinks that it is
4 important to consult patients on benefit-risk
5 but asks will patients and patient groups be
6 asked to disclose funding and any COI when
7 they appear before FDA. He asks because many
8 groups receive large amounts of money from
9 particular drug sponsors and this could just
10 institutionalize a new form of lobbying
11 pressure on the FDA.

12 So he wonders if disclosure and COI
13 rules need to apply.

14 DR. MULLIN: I think Bill's
15 question is a good one in being indicative of
16 I think some complexities that we will be
17 looking at. There were some comments, a few
18 people commented, I think Dan Perry and Becca
19 O'Connor maybe there wasn't a whole lot of
20 detail in the commitment letter about exactly
21 how we would be collecting patient input and
22 incorporating that into our process and that

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1 is because we have a lot of issues and things
2 to look at and figure out. We want to get
3 input that is rigorously collected, that is,
4 as I think Dan said, representative of the
5 patient population, and that is actually very
6 rather challenging to do, and information that
7 is really useable.

8 I know this is not just of interest
9 to FDA and to you all. The Hastings Center
10 has indicated that they think this is an
11 important issue to look at. They look at
12 ethical issues. So there are a lot of
13 important questions to look at. And raising
14 those questions and asking them is helpful to
15 us as we think through the process because we
16 want to do it right.

17 If we don't get reliable
18 information, we won't be able to use it and we
19 do want to be able to use it.

20 MR. FREY: You said he had a number
21 of questions. Was that it? Okay. All right.

22 DR. MULLIN: I've asked Jane, who

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1 led the discussions in our PDUFA IV
2 negotiations related to direct-to-consumer
3 advertising user fees. And that has come up in
4 the past. That is not something we have not
5 considered. So she can give you a recap of
6 the status of that.

7 MS. AXELRAD: Yes. In the
8 negotiations over PDUFA IV we had recommended
9 to Congress and in fact there is actually
10 language in the statute that would have
11 provided user fees for the FDA review of DTC
12 broadcast advertisements. And it was a fairly
13 elaborate program. Unfortunately, the
14 Chairman of our Appropriations Committee did
15 not believe that that program should be funded
16 by user fees and instead appropriated some
17 money for the review of broadcast ads.

18 And there is some other language in
19 the statute that deals with reviews of direct-
20 to-consumer advertisements and some
21 authorities in Title IX, I think, to determine
22 when we want to require review of direct-to-

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1 consumer advertisements.

2 So basically that program was
3 negotiated as part of the last user fee
4 reauthorization and because it didn't go
5 forward, it was not the subject of
6 negotiations this time around.

7 DR. MULLIN: I just want to make
8 one more point of clarification. I have been
9 saving my comments and began taking notes on
10 what people were saying.

11 There were a couple of folks who
12 were concerned that we were only going to be
13 using Sentinel to look at expected risks and I
14 think that the more likely scenario is that we
15 get reports of what are actually serious and
16 unexpected risks. Expected risks are going to
17 be on the label. But it is the serious and
18 unexpected risks that we hear about after the
19 drug is on the market when we are likely to
20 try to see whether that signal is confirmed by
21 going and utilizing the Sentinel capability.

22 Although some talked about it as an

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1 active surveillance system going on all the
2 time collecting and pouring information into
3 FDA, that was never actually the way we
4 thought it would get used. That would just
5 inundate FDA with a lot of false signals. But
6 structuring the query to see whether the large
7 body of healthcare data that can be collated
8 and used to explore a question about a
9 particular safety risk, which is how we are
10 envisioning trying to see how well it works
11 here, is a really effective way to use that
12 kind of information to see whether that much
13 larger population can be loaded into a common
14 data model, and what does it do. Does it
15 confirm the signal that we are concerned about
16 where we have preliminary information or does
17 it not confirm it? So that would be very
18 valuable to us and that is how we are planning
19 to use it.

20 It is an adjunct to our passive
21 surveillance system and other sources of
22 information that we have to do post-market

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1 safety surveillance.

2 There is one other thing. That was
3 the MedWatch, the concern about MedWatch data.

4 It is true that the current AERS system,
5 which we call the legacy AERS system because
6 we are hoping to make it legacy very soon,
7 does allow the reporting of information that
8 is not very standardized and it is not very
9 easy to analyze.

10 We expect to retire that system
11 within the coming year and replace it with the
12 FDA Adverse Event Reporting System, known as
13 FAERS and the data that will be collected and
14 entered in FAERS will be using an Individual
15 Case Safety Report format, ICSR data format,
16 which will be much more amenable to analysis.
17 And we expect that data to be much more useful
18 to us and address the concerns that we were
19 hearing from some of the panelists today.

20 MR. FREY: All right. The FDA
21 panel has nothing else. So I think we will
22 move to wrap up.

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1 A couple of thanks. Thanks to you
2 all for coming out today for the meeting and
3 being patient with us. Thank you to the
4 panelists for their thoughtful comments.

5 And I want to also thank a number
6 of folks who without their help this meeting
7 wouldn't have been possible. Andrea Tan, go
8 ahead and wave. James Valentine is also over
9 there. Rokhsana Safaai-Jazi, Pat Kuntze and
10 the staff of the White Oak Conference Center
11 have been hugely helpful in putting this
12 meeting on.

13 One last reminder. The FR notice
14 that announced this meeting, there is a slight
15 discrepancy in it. October 31st, as I said
16 earlier, that is the day, the deadline for
17 comments to the docket. So Halloween is the
18 day, next Monday.

19 And the *Federal Register* notice
20 includes instructions for how to submit to the
21 docket.

22 If there is nothing else, we will

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1 wrap things up. Safe travels home.

2 (Whereupon, at 2:13 p.m., the foregoing
3 proceeding was adjourned.)

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