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

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

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

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

We also have some concerns about the agreement's use of the word targeted surveillance with respect to the scope of the Sentinel program. When CU first advocated for Sentinel, it was envisioned as a first-alert system rather than a follow-up safety system. We hope that the use of the word targeted does not represent a narrowing of the scope of the program.

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

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

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

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

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

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

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

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

But the Alliance is a nonprofit organization of 180 members both individuals and corporate, and consumer groups, patient groups, that focuses on strengthening the FDA through appropriations. And I know this activity is all about user fees but I think it is very important for maybe not those on the dais but everybody else who is interested in this topic. User fees deserve a great deal of attention in the policies that are being done. But there also is an important responsibility to make sure that if you have got initiatives that you want funded or you want FDA to focus on new initiatives, we really have to make sure that FDA is adequately funded through appropriations.

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

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

Thank you.

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

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

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

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

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

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

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

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

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

Thank you for the opportunity. Thanks.

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

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

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

I have seen a lot in Congress lately.

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

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

MR. FREY: Any other comments from the room?

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

MR. FREY: Great, set him up.

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

included in today's discussion as a public comment.

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

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

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

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

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

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

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

DR. MULLIN: I've asked Jane, who

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

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

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

consumer advertisements.

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

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

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

Although some talked about it as an

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

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

safety surveillance.

There is one other thing. That was the MedWatch, the concern about MedWatch data. It is true that the current AERS system, which we call the legacy AERS system because we are hoping to make it legacy very soon, does allow the reporting of information that is not very standardized and it is not very easy to analyze.

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

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

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

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

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

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

If there is nothing else, we will

wrap things up. Safe travels home.

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