Transcript of FDA Press Conference on Chantix

FTS HHS FDA

Moderator: Susan Cruzan
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Coordinator: Welcome and thank you all for standing by. Your lines have been placed in listen-only mode.

To ask a question during the question and answer portion, please press star 1 on your touch-tone phone.

Today's conference is being recorded. If you have any objections you may disconnect at this time. Now I'd like to turn the conference over to Ms. Susan Cruzan. Ma'am, you may begin.

Susan Cruzan: Thank you. Good afternoon and welcome. My name is Susan Cruzan with the Food & Drug Administration's Office of Public Affairs.

This is an FDA teleconference for credentialed media to discuss a US Food & Drug Administration, public health advisory, announcing new safety warnings for the smoking cessation drug Chantix.

With me today are several officials from FDA's Center for Drug Evaluation and Research. Dr. Curtis Rosebraugh who is the Deputy Director of the Office of Drug Evaluation II in the Center for Drug

Evaluation and Research with the Food and Drug Administration, Dr. Bob Rappaport, Director, Division of Anesthesia, Analgesia and Rheumatology Products also in (CDER) with FDA, and Dr. Celia Winchell, Team Leader with the Division of Anesthesia, Analgesia and Rheumatology as well.

Dr. Rappaport will make brief remarks. We'll then move into a question and answer segment. And Dr. Rosebraugh and Dr. Winchell and Dr. Rappaport will be available to answer questions.

Reporters will be in a listen-only mode until we open up the call questions.

I just want to remind you that the news release announcing a public health advisory and healthcare professional seat has been sent to reporters on our media list and is posted on FDA's Web site at www.fda.gov.

At this time I will turn the call over to Dr. Rappaport. Thank you.

Dr. Bob Rappaport: Thank you Susan. We appreciate your joining us today for this discussion. We first issued an early communication on some of the problems that we were seeing with Chantix Varenicline for the treatment of nicotine addiction to get people to stop smoking back in November of last year.

At that time it was considered an early communication because we were just beginning the process of reviewing a large number of reports to sort through and figure out which were really attributable to the drug and which were possibly attributable to other causes.

As we've continued to review those cases over the last couple months, we've become increasingly concerned as we've seen that there are a number of compelling cases that truly look as if they are the result of the exposure to the drug and not to other causes.

And these cases involve as noted in our public health advisory cases of abnormal behaviors, of changes in mood and even cases of suicidal ideation and suicide. So clearly these are very concerning findings for this product which is being widely used.

Now I should note that we're being extremely cautious as we go through this review process because we also feel that this is an extremely important drug and a very effective drug for the treatment of - for - to allow patients to quit smoking.

So we don't want to - we want to provide fair balance in our evaluation as we go through this process.

The language that we have approved as of yesterday in the label is pretty much - I think is outlined in the alert and notes report of behavioral and mood changes that are apparently caused by the drug itself.

The one piece that you might've noted in our public release documents today that is not in the label is another finding that we have noted as we've been going through this process of patients having behavioral and mood changes after stopping the drug, so what appears to be a withdrawal syndrome.

We are not yet absolutely sure that that is related to stopping the drug. But it is - does appear to be that that is a strong possibility. And we continue to review those cases and further cases to try to better understand that problem.

So at this time we're continuing with the review process which will continue over the next few months as we try to really pin down as much as we are able to what extent these problems are being seen with Chantix and to what extent there are other related problems associated with the drug.

As we move forward with this, we do think that the most important messages that should be out there for patients and for prescribers is that should a person who's taking Chantix experiencing - experience early symptoms, changes in behavior, changes in mood, unusual thoughts, that they should discuss with their healthcare providers as soon as possible whether they should continue on the drug or not.

So at this time I'm going to turn it back to Susan.

Susan Cruzan: Thank you Dr. Rappaport. We can open up the lines for questions now.

Coordinator: At this time if you would like to ask a question, please press star I on your touch-tone phone. You may withdraw your request by pressing star 2 . Again, at this time if you would like to ask a question, please press star 1. One moment please.

Our first question comes from Kim Dixon with Reuters. Your line is open.

Kim Dixon: Hi there. How are you - how many cases have there been of suicide and suicide ideation? And these are just adverse event reports that are coming in? That's one I guess.

And are you asking the company to do any kind of additional post marketing surveillance to nail this down?

Dr. Bob Rappaport: Well I'll start by turning this over to Dr. Winchell to answer first.

Dr. Celia Winchell: And I'll ask (unintelligible) we had 420 suicide (unintelligible) cases.

Kim Dixon: I'm sorry, you're breaking up. I don't know if anyone else is having that problem.

(*Technical issues*)

Susan Cruzan: Yes, operator, we do have some feedback.

Coordinator: Thank you. One moment.

This is the operator. If you could try answering the question again at this time.

Dr. Celia Winchell: (Unintelligible).

Kim Dixon: Yes, it's not any better. I don't know if anyone else is having this problem but I'm hearing lots of static. I can't hear what anyone is saying.

Woman: Okay, let's try it again.

Woman: Operator? We still have feedback.

Kim Dixon: It’s not feedback. It’s that - it’s like spotty like I can hear you for a - it’s like a bad cell phone connection.

Woman: (Unintelligible).

Coordinator: I might ask if anyone close to the microphones has Blackberrys that are on could you please turn your Blackberry cell phones off?

Woman: (Unintelligible).

Woman: Okay, is that better? Kim is that better?

Kim Dixon: No. But maybe you should try somebody else. Maybe - I mean I’d like my questions answered obviously but - hello?

Coordinator: Please continue to stand by. I believe the speaker line is calling and for a better connection.

Woman: Caused by the drug itself.

Woman: (Sarah)?

Coordinator: Okay you have reconnected. Thank you. Would you like to continue with Kim Dixon with Reuters?

Woman: Yes (unintelligible).

Coordinator: Yes, unfortunately we are still hearing, it’s kind of an in and out from your line ma‘am.

Woman: All right. Well (unintelligible).

Kim Dixon: Okay, well I haven't heard anything that you said.

Dr. Rappaport was completely clear. So I'm not sure what the problem was as was Susan before that.

Woman: (Unintelligible).

Kim Dixon: Should I redial in operator?

Coordinator: Kim, you're fine. Your line is fine.

Kim Dixon: Okay.

Coordinator: Susan, I just wonder if you could perhaps maybe try adjusting the phone. Perhaps there is a connection on it that is (unintelligible).

Okay, and they have disconnected again.

Kim Dixon: All right.

Coordinator: Wait a moment. Thank you all for your patience.

Woman: Are you there?
Coordinator: Okay your phone is still doing the same thing.

Susan Cruzan: (Sarah)? Yes, we were okay until we opened it up for callers. Can you hear me?

Kim Dixon: I can hear you Susan. You're fine now.

Susan Cruzan: Okay. Kim, can we try - can you - can we try another reporter and then come back to you?

Kim Dixon: Sure.

Coordinator: Okay, thank you. One moment.

Susan Cruzan: Okay, thank you (Sarah). Hold on. I'm going to put it back on speaker.

Can you hear us?

Coordinator: Okay, we can hear you.

Susan Cruzan: Okay, let's try it again.

Coordinator: Okay. Shannon Pettypiece, Bloomberg News, your line is open.

Shannon Pettypiece: Hi. Let's try me. And I obviously have the same question she had. I was wondering the number of cases you've gotten and - you know, of reports you've gotten, especially of suicide.

And then, the company suggests that these behaviors may be an actual result of nicotine withdrawal. So if you could give any explanation for why the FDA suspects it might be something more than that, more than just the natural feelings you get when you stop smoking?

Susan Cruzan: Can you close the line while we answer please?

(*end technical issues*)

Coordinator: The line is closed.

Dr. Celia Winchell: Okay can we try that? Let's try that.

Coordinator: Sounds good.

Dr. Celia Winchell: All right, this is Celia Winchell. With that caveat that these are crude counts from our adverse event database which means that as we review them case by case, occasionally we find duplicates or cases that were miscoded.

The total number of cases that involve suicidal thinking or suicidal behavior that we have at this time in our database is 491 of which 420 are from the United States.

Of these we have 37 that that involve completed suicide. But because that's a small number we've been able to look at those. And it appears that those are 34 unique cases in the United States.

In addition there are five foreign cases of completed suicide in our database.

Dr. Bob Rappaport: There was a second part to that question. We have actually seen cases where the mood changes, the changes in behavior have occurred while the patient was still smoking. So that's why we feel this is at least at times, at least some of these cases are related to the drug itself.

Susan Cruzan: (Sarah), can we take the next caller?

Coordinator: Thank you. Our next question comes from Bennett Cunningham, CBS News. Your line is open.

Bennett Cunningham: Good afternoon. I had two quick questions. I wanted to find out -- this is a request. Why isn't the FDA forcing Pfizer to restructure its label now?

And how does what you're doing today differ from what Pfizer did two weeks ago with updating its label?

Dr. Bob Rappaport: We - I'm sorry, would you repeat that question?

Coordinator: One moment please.

Bennett Cunningham: Sure, real quick. I wanted to find out number one, this is a request. Can the FDA and why hasn't the FDA mandated these new warning type label or, you know, on Pfizer, on this Pfizer product?

And number two, what's the difference between what Pfizer did two weeks ago and what you're requesting now?

Dr. Bob Rappaport: Okay. I'm going to start from the second part of your question.

Bennett Cunningham: Okay.

Dr. Bob Rappaport: What Pfizer announced two weeks ago is essentially what we worked through with the company prior to that in terms of developing this new label.

So although they announced it at the time that they submitted to us and as the particular type of submission that it was, it became effective immediately, so that is the same process and the same ultimate end and the same label that we were working with them on over the past weeks.

Now in terms of the first part of your question, the FDA is able to incorporate new warnings into labels by working with the sponsors whether - and we generally do not mandate those types of changes into labels, although there may be some changes that have been - that are under the new law that was recently passed that will give us different authority in how we manage that. Those issues are still being discussed.

Coordinator: Our next question from Todd Zwillich with WebMD. Your line is open.

Todd Zwillich: Hi. Two questions. Well I'm still not clear on the question from the gentleman from CBS which is the changes that Pfizer has already made. Are they parallel to what you're asking them to do today, meaning, have they already done it?

And B, my second question is what are the denominators? Can you give us an idea of a denominator with 420 US cases of suicidality. What is the denominator in terms of, you know, number of prescriptions or number of people who've used it? Thank you.

Dr. Bob Rappaport: The change to the label (unintelligible).

Woman: (Unintelligible).

Dr. Bob Rappaport: Fine. Yes, thank you. The changes to the label are the same changes that Pfizer incorporated into their label and announced in their press release a couple weeks ago. And Dr. Winchell will answer the other question.

Dr. Celia Winchell: Well Pfizer's press release a couple weeks ago did say 5 million. They estimate about 5 million patients have taken Chantix. So that's probably the denominator.

Coordinator: Our next question from Kim Dixon with Reuters. Your line is open.

Kim Dixon: Hi. One just clarification on those numbers. You said on the number of suicides first - I think you said 37 completed cases. And then you said 34 in US and five foreign. That equals 39. So did I hear something wrong?

Dr. Celia Winchell: Right. I'm sorry, I said that in the wrong order. The total number of reports that we have in the database is 42 which breaks out to 37 US and five foreign. But of those 37 I found three duplicates so that that makes 34. So your total cases should be 39.

Coordinator: Our next question from Carl Stark, Philadelphia Inquirer Newspaper. Your line is open.

Carl Stark: Yes, I wondered if you could talk about the trials that were done for this drug. And where there hints of any of this in the trials and how large they were, how large the trials, how many people were treated?

Dr. Bob Rappaport: Dr. Winchell will answer that question.

Dr. Celia Winchell: Sure. We had nearly 4000 people treated with Varenicline in the trials, a smaller number of people treated with placebo and with a comparator drug also used for smoking cessation.

And no, we did not see this in the clinical trial.

Susan Cruzan: Thank you. Can we have another question please?

Coordinator: Matt Perrone, Associated Press, your line is open.

Matt Perrone: Yes, thanks guys.

Are there any other FDA approved drugs for smoking cessation? And I'm wondering if you can give us an idea how - whether they're labeling includes, you know, some of these warnings about, you know, risk of erratic behavior, suicidality, et cetera?

Dr. Celia Winchell: The other drugs approved for smoking cessation include various forms of nicotine replacement such as gum, patches, lozenges. Those don't carry this type of warning in their labeling.

And part of the process of our safety review will be to probe for whether our database shows any indication of these problems with those products.

And then in addition, there's one other product approved for smoking cessation. And that's (Uproprion). It's also an antidepressant. So the label for that does carry warnings about suicide because that's part of the class labeling for antidepressants.

Susan Cruzan: Thank you. Can we have the next question please?

Coordinator: Christine Cox, South Bend Indiana Tribune, your line is open.

Christine Cox: Can you talk about any depressive history in these people that, you know, had these suicidal thoughts or committed suicide? Were they depressed?

Dr. Bob Rappaport: We've seen cases, patients who had history of depression. And we've seen cases of people who had no history of depression.

These events are occurring sporadically and at times in people who had no history of psychiatric disease or changes in behavior in the past.

Coordinator: (Lynn Peterson), Trend Medicine, your line is open.

(Lynn Peterson): Just recently yesterday I think it was you issued a warning about the suicidality with epilepsy drugs. And you did not do a phone call with reporters over that. And that covered a whole range of drugs. Yet you're arguing it with Chantix. And could you please put that in perspective?

Dr. Bob Rappaport: Well the - I can't speak to the reasons why they chose not to do a press conference related to the epilepsy drug.

But in - with our drug, the concern is that there are many patients out there who are taking this drug who - for whom these kinds of serious outcomes could be prevented simply by being aware of the problem

and the potential for serious changes in mood and behavior.

And if patients and their caretakers and their healthcare providers are aware of these findings, they can catch them early and intervene and hopefully prevent the more serious outcomes.

Coordinator: Janet St. James, WFAA TV in Dallas, Texas, your line is open.

Janet St. James: What is the threshold for ruling on more serious FDA action including but not limited to a possible black box warning or other regulatory action taken by the FDA?

Dr. Bob Rappaport: I'm going to ask Dr. Rosebraugh to...

Dr. Rosebraugh: Yes, this is Dr. Rosebraugh. We as Dr. Rappaport said, we're in the midst of doing a thorough evaluation on this. And we of course will take action as appropriate.

I think we - this is an evolving issue. And as we get into it more and more, we're finding more and more things and we just need to get that sorted out.

Coordinator: Mike Huckman, CNBC, your line is open.

Mike Huckman: Hi. We need to know two things please. How many total adverse event reports have you received in connection with Chantix?

And then secondly, was there any discussion about (Askan) or (unintelligible) at Pfizer at least temporarily pull the drug off the market and/or stop advertising it? Thank you.

Dr. Bob Rappaport: Yes. It's pretty garbled. I think that I'm going to do the second one. And I'll let Dr. Winchell do the first one.

Dr. Celia Winchell: As Dr. Rappaport pointed out, this actually is a very important drug. And, you know, although we are getting these reports, there's also a lot of anecdotal reports out there where this drug has worked when no other drug would.

Smoking itself has very serious consequences. And so I think it's important to try to manage the risk associated with the drug, also realizing that it has a lot of benefits for some folks.

And then the first one you were asking about the number of total adverse events.

Dr. Bob Rappaport: Before we get to that though, the other part of your question I think was also -- this is Dr. Rappaport -- regarding advertising.

And the company voluntarily changed their advertising as soon as they submitted the changes to the label. So I'm sure you've noted that their direct to consumer TV ads have changed dramatically.

And Dr. Winchell, do you have a comment?

Dr. Celia Winchell: I'm not sure I can tell you how many total cases have been reported to our adverse event database involving this drug because of course there are many, many different types of complaints that people call in. I have information on the ones specific to the topic that we're discussing today.

Do you have those numbers Mike that we had given earlier?

(Sarah)?

Coordinator: Do you want me to go back to the previous questioner?

Dr. Celia Winchell: Yes. I wanted to find out if he had the numbers that we gave for the issues we're talking about today.

Coordinator: Thank you. One moment.

Mr. Huckman, your line has reopened sir.

Mike Huckman: Yes I've got the numbers. Thank you very much.

Dr. Celia Winchell: Mike, do you have the numbers that we gave for the issue for (unintelligible)?

Mike Huckman: Yes I do. Thanks a lot.

Dr. Celia Winchell: Okay, we'll take the next caller please.

Coordinator: Peggy Peck, MedPage Today, your line is open.

Peggy Peck: Yes. Thank you very much for taking our questions. I'm looking back at when this drug was approved. And it did receive a priority review and it was approved from the statements released at the time because of a significant potential benefit to public health, yet there' been a number of drugs - a growing number it appears to me of these priority reviews

that then run into problems.

So I'm wondering is it time for you to review sort of fast tracking drugs?

And on follow-up, this drug is my understanding, does affect or target a specific receptor in the brain. And that is different than any drugs currently approved for smoking cessation. And perhaps is that the difficulty that you're seeing here? Thank you.

Dr. Rosebraugh: Yes. This is Dr. Rosebraugh. I'm going to take your first question.

We do priority reviews particularly when we think there is a public health benefit.

When this drug came in, it went head to head against an existing drug and proved superior to it. And once again, smoking itself carries some serious risk.

The other thing I would add is sometimes people get priority reviews a little bit confused. We had the same amount of data so we are reviewing the same amount of data. We tried to put more manpower on it so that we can get it out faster.

So it's not that we are curtailing any safety information, it's the same amount of information. We just put more people on it and do it faster.

Now to get on to your question about targeting a receptor, I'll let Dr. Winchell…

Dr. Celia Winchell: Yes. Actually the Varenicline acts as a sub unit of the same

receptor were nicotine acts. So it's not unique in that sense because nicotine also acts at the same site in the brain. That's kind of how it works is that it gets in the way of nicotine and provides a little bit of the activation to that receptor that nicotine would provide which tends to keep the patient from experiencing cravings for cigarettes or urge to smoke.

And in addition when somebody smokes the Varenicline gets in the way. So they don't experience that reward from smoking. And that helps them break the smoking habit.

What we're seeing though is in some cases, a minority of cases, where having an unexpected result of the action at this receptor, something we didn't see in clinical trials.

Susan Cruzan: Thank you. We have time for one more question.

Coordinator: Kim Dixon, Reuters, your line is open.

Kim Dixon: Thanks. I'm going to get my actual question in. You talked about causality in the beginning of the call. And you said Dr. Rappaport, apparently some of these were - actually apparently some of these were caused by the drug itself.

But this language - that language -- and I think that you said that those would be reflected in a label and that's in one of the alerts and I printed out a bunch of the alerts -- but is there something about causality in the label?

Because I looked up the Chantix labeling information if this is what

Pfizer did two weeks ago, it doesn't appear to be the same thing.

Dr. Bob Rappaport: I think that you're - were using the term apparently differently because I think what I meant to say is that it's certainly possible that these are related.

We have no definitive evidence that there is a causal relationship here. It's just that they are strongly appearing to be related.

And as we go further with our review, we may reach a level where we believe that there is clear causality. But we have not gotten there yet.

Susan Cruzan: (Sarah), we will take one more call.

Coordinator: Thank you. Jennifer Corbett, Dow Jones, your line is open.

Jennifer Corbett: Yes. Hi. Thanks for taking my question. I'm sorry you've probably gone over this repeatedly. But I wanted to know if you could clarify the actual number of completed suicides. First I hear 37, then I heard 39?

Woman: Thirty-nine in US and foreign cases.

Thirty-nine total cases.

Dr. Bob Rappaport: In the world.

Susan Cruzan: That will conclude our call today. Thank you very much.

I do have to note that the information on the media advisory for the replay was not correct. The number for the replay is 888-566-0452.

Again, 888-566-0452. And for international callers, it’s 203-369-3048.

Thank you all for joining us today. Have a great evening.

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