From: Sheila Hershow [shershow@dezenhall.com]
Sent: Wednesday, January 16, 2008 12:13 PM
To: Faraji, Mary-Frances
Subject: RE: Sidney Wolfe
Add sending the ACC and AHA statements to editorial boards to my list of tactics.

From: Faraji, Mary-Frances [mailto:mary-frances.faraji@spcorp.com]
Sent: Wednesday, January 16, 2008 7:07 AM
To: Sheila Hershow
Subject: RE: Sidney Wolfe

Think this isn't the end... also fearing negative editorials in Post, Times, etc. Let's propose counter-strategy on today's call.

Thx,
MF

-----Original Message-----
From: Sheila Hershow [mailto:shershow@dezenhall.com]
Sent: Wednesday, January 16, 2008 7:06 AM
To: Faraji, Mary-Frances
Subject: RE: Sidney Wolfe

You predicted this, but at least it's just language and not an FDA petition.

From: Faraji, Mary-Frances [mailto:mary-frances.faraji@spcorp.com]
Sent: Wednesday, January 16, 2008 7:04 AM
To: Yancosek, Rosemarie; Atkins, Larry; Bova, Alice; Davies, Lee; Faraji, Mary-Frances; Garutti, Ronald; Granowitz, Craig; Hanley, Kenneth; Huber, Marty; Kay-Mugford, Patricia; Kelly, Alex; Koestler, Thomas; Kowalski, Robert; Kuntze, Carl Erik MD; Lively, Robert; Mcnicholas, Sean; Metzler, Joann; Perelman, Michael; Queisser, Lori; Russo, Ray; Sabatino, Thomas; Spiegel, Robert; Veltri, Enrico; Villarreal, PD; Weissman, Paul
Cc: Sheila Hershow
Subject: Sidney Wolfe
Importance: High

This from FDA WebView:

Wolfe Blasts Vytorin Report Delay
01/15/2008

Public Citizen Health Research Group director Sidney Wolfe says it is likely Merck/Schering-Plough "put their stockholders above their responsibility to public health" in delaying reporting results of a clinical trial showing that Vytorin (Zetia and Zocor) doesn't perform any better than Zocor alone.

Wolfe says he is not surprised that although the trial ended 4/06, the companies did not report results until 1/14 (see earlier story). "There's a $20 billion market for cholesterol-lowering drugs and companies will do whatever it takes to get as much of that market as they can," he says, "even if it means letting people continue to take prescription drugs that they know are not beneficial and that even may be harmful."

The companies said the delay was because the trial data are complicated and analyses took longer than expected, but Wolfe doesn't buy that explanation. "We wish we could say this is an isolated case but there are too many other examples of negative findings being buried in FDA's files," he says. "This year, the drug industry gave $400 million to the drug division of FDA, which funds most of the salaries of those scientists who review drugs. You would have to be living on a cloud to think that the money doesn't have an impact on FDA's drug approvals or regulation of the industry."

From: Sheila Hershow [shershow@dezenhall.com]
Sent: Thursday, January 17, 2008 10:23 PM
To: Faraji, Mary-Frances; Spiegel, Robert
Subject: FW: SP: Quotes - Final

Attachments: SP.ENHANCE.Quotes.01.17.08.xls; Coverage.zip

Here is our attempt to capture what doctors are saying about ZETIA, VYTORIN and ENHANCE in the media and Internet. We have attempted to put the comments into "good," "bad" and "neutral" categories, but because we may have misunderstood scientific nuances please understand that we may have put some comments in the wrong category.

From: Michelle Heisner
Sent: Thursday, January 17, 2008 4:58 PM
To: Sheila Hershow
Subject: SP: Quotes - Final

See attached.

From: Sheila Hershow [shershow@dezenhall.com]
Sent: Saturday, January 19, 2008 3:38 AM
To: Faraji, Mary-Frances; Yancosek, Rosemarie; Atkins, Larry; Banta, Ken; Bova, Alice; Davies, Lee; Garutti, Ronald; Granowitz, Craig; Hanley, Kenneth; Harms, Kelly; Huber, Marty; Kay-Mugford, Patricia; Kelly, Alex; Koestler, Thomas; Kowalski, Robert; Kuntze, Carl Erik MD; Lively, Robert; Martinez Wolmart, Lisa; Mcnicholas, Sean; Metzler, Joann; Perelman, Michael; Queisser, Lori; Russo, Ray; Sabatino, Thomas; Spiegel, Robert; Veltri, Enrico; Villarreal, PD; Weissman, Paul
Cc: Brown, Robyn; Romanelli, Joseph
Subject: Re: WSJ correction

Good to see the correction. First sign that some media outlets no longer believe they can get away with any incorrect slam at the study.

----- Original Message -----
From: Faraji, Mary-Frances <mary-frances.faraji@spcorp.com>
To: Yancosek, Rosemarie <rosemarie.yancosek@spcorp.com>; Atkins, Larry <larry.atkins@spcorp.com>; Banta, Ken <ken.banta@spcorp.com>; Bova, Alice <alice.bova@spcorp.com>; Davies, Lee <lee.davies@spcorp.com>; Faraji, Mary-Frances <mary-frances.faraji@spcorp.com>; Garutti, Ronald <ronald.garutti@spcorp.com>; Granowitz, Craig <craig.granowitz@spcorp.com>; Hanley, Kenneth <kenneth.hanley@spcorp.com>; Harms, Kelly <kelly.harms@spcorp.com>; Huber, Marty <marty.huber@spcorp.com>; Kay-Mugford, Patricia <Patricia.Kay-Mugford@spcorp.com>; Kelly, Alex <alex.kelly@spcorp.com>; Koestler, Thomas <thomas.koestler@spcorp.com>; Kowalski, Robert <robert.kowalski@spcorp.com>; Kuntze, Carl Erik MD <erik.kuntze@spcorp.com>; Lively, Robert <robert.lively@spcorp.com>; Martinez Wolmart, Lisa <lisa.martinez.wolmart@spcorp.com>; Mcnicholas, Sean <sean.mcnicholas@spcorp.com>; Metzler, Joann <joann.metzler@spcorp.com>; Perelman, Michael <michael.perelman@spcorp.com>; Queisser, Lori <lori.queisser@spcorp.com>; Russo, Ray <ray.russo@spcorp.com>; Sabatino, Thomas <thomas.sabatino@spcorp.com>; Spiegel, Robert <robert.spiegel@spcorp.com>; Veltri, Enrico <Enrico.Veltri@spcorp.com>; Villarreal, PD <pd.villarreal@spcorp.com>; Weissman, Paul <paul.weissman@spcorp.com>
Cc: Sheila Hershow; Brown, Robyn <robyn.brown@spcorp.com>; Romanelli, Joseph <joseph.romanelli@spcorp.com>
Sent: Fri Jan 18 20:49:41 2008
Subject: WSJ correction

Note online correction to Ron Winslow's story appearing in yesterday's WSJ -- see copy at end in bold.

MF

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Cutting Through the Confusion Over Vytorin
Despite Negative Study,
Doctors Say Drug Remains
An Option to Fight Cholesterol
By RON WINSLOW
January 17, 2008; Page D1
(See Corrections & Amplifications item below <http://online.wsj.com/article/SB120052963183895929.html?mod=yahoo_hs&ru=yahoo> .)
Patients are swamping doctors' offices wondering if they should stop taking the anticholesterol drug Vytorin, in the wake of a report questioning its ability to slow the progression of heart disease.

The message from many heart experts: Don't panic.
Despite high-profile news coverage and the widely quoted views of a prominent cardiologist, the study's findings offer only limited new information to influence whether patients should take the drug. And the study, known as Enhance, offers no clear signals that patients should stop using Vytorin.

"Enhance is not an alarming study," says Richard Milani, head of preventive cardiology at the Ochsner Clinic, New Orleans. "There were no safety issues related to the trial that people were somehow being harmed on Zetia."

The main finding was that Vytorin, which is marketed by a joint venture of Merck & Co. <http://online.wsj.com/quotes/main.html?type=djn&symbol=mrk> and Schering-Plough <http://online.wsj.com/quotes/main.html?type=djn&symbol=sgp> Corp., failed to prove more effective than a cheaper generic drug in stanching the development of disease in blood vessels in the neck.

Vytorin and its sister drug, Zetia, are widely used to help patients lower LDL, or bad cholesterol, beyond levels achieved using popular cholesterol pills called statins. Vytorin is a combination of Zetia and a statin. The statin, Zocor, is now available as a generic pill called simvastatin.

From: Faraji, Mary-Frances
Sent: Saturday, January 19, 2008 8:45 PM
To: Davies, Lee
Subject: RE: Request for Media Monitoring Support

Did you get my voice messages? Please call my cell and I'll fill you in on my conversation with Alex today...

Thx,
MF

-----Original Message-----
From: Davies, Lee
Sent: Saturday, January 19, 2008 3:43 PM
To: Faraji, Mary-Frances
Subject: RE: Request for Media Monitoring Support

Hi MF,
And what prompted this?
Lee

-----Original Message-----
From: Faraji, Mary-Frances
Sent: Saturday, January 19, 2008 02:49 PM
To: Sheila Hershow (shershow@dezenhall.com)
Cc: Kelly, Alex; Yancosek, Rosemarie; Davies, Lee
Subject: Request for Media Monitoring Support
Importance: High

Dear Sheila,

As we discussed earlier, Schering-Plough is requesting Dezenhall's media monitoring support from today (Saturday) forward covering the ENHANCE study and related corporate issues.

We need to receive a coverage report every morning at 8 a.m. and again every afternoon (2-3 p.m., unless later in the afternoon would be more inclusive and relevant). The first report should be sent tomorrow (Sunday) morning at 8 a.m., please.

Monitoring should cover all print, wire, online and broadcast/cable outlets. We also wish to see blog coverage, including Café Pharma, PharmaGossip, BrandweekNrx, Pharmalot and any others you recommend.

Search terms should include ZETIA, VYTORIN, ezetimibe, ezetimibe/simvastatin, John Kastelein, Steve Nissen, Robert Spiegel, Rick Veltri, ENHANCE and IMPROVE-IT, as well as the names of our executive management team, in relation to the current issues.

We realize that broadcast transcripts and clips take time to collect, so a brief summary noting network (or affiliate), program, program length and air time would be helpful for the morning report. If possible, please consolidate coverage into a single attached Word document (i.e., not separate attachments), included in order of prominence/importance/influence, to the degree possible. The cover message should be brief and call attention to key coverage, themes of the day or new developments in the evolving story.

We'd like the report to be sent by email to Alex Kelly, Rosemarie Yancosek, Cathy Dunn, Steve Galpin, Lee Davies and me. Rosemarie will forward to a consolidated internal distribution list, including members of the PReP Core Team and our extended ENHANCE team.

Please call my cell (908 432 2404) if you have any questions or suggestions about the monitoring request.

Many thanks in advance to you and your team for getting this under way over a holiday weekend.

Thanks,
Mary-Fran

From: Sheila Hershow [shershow@dezenhall.com]
Sent: Tuesday, February 05, 2008 4:18 PM
To: Banta, Ken; Eric Dezenhall
Cc: Kelly, Alex; Yancosek, Rosemarie
Subject: RE: Draft letter to the NYT public editor

Attachments: nyt public editor draft feb 4, 2008.doc

Here is my revised letter to the NYT's public editor. The changes were so extensive that I took off the red-lining to make it easier to read. I left out the stuff about biased sources because I don't think we make a strong enough case.

I urge you to have this examined for possible factual inaccuracies before forwarding to Merck.

From: Banta, Ken [mailto:ken.banta@spcorp.com]
Sent: Monday, February 04, 2008 9:34 PM
To: Eric Dezenhall
Cc: Kelly, Alex; Yancosek, Rosemarie; Sheila Hershow
Subject: RE: Draft letter to the NYT public editor

Just to slarify this is a letter to the public editor, not a 'letter to the editor.' I don't believe the public editor column is one where specific redress actions are addressed?

Ken

Sent from my GoodLink synchronized handheld (www.good.com)
Ken Banta
Schering-plough Corp
+1 917 776 5418

-----Original Message-----
From: Eric Dezenhall [mailto:edezenhall@dezenhall.com]
Sent: Monday, February 04, 2008 02:34 PM Eastern Standard Time
To: Banta, Ken
Cc: Kelly, Alex; Yancosek, Rosemarie; Sheila Hershow; Eric Dezenhall
Subject: RE: Draft letter to the NYT public editor

We're working on the revised letter but it won't be done by COB today. Having been at war with the NYT in similar situations, the letter needs to be crafted in a very specific way, namely:

- Staying factual, and avoiding diplomatic flourishes

- Differentiating between what is 1) wrong 2) biased and 3) where someone quoted is conflicted

- Establishing suggested redress

We're crunching on it, but we'd like to get this right based upon what we've found to be effective in the past. Please stand by.

From: Banta, Ken [mailto:ken.banta@spcorp.com]

Sent: Monday, February 04, 2008 1:00 PM
To: Yancosek, Rosemarie; Galpin, Stephen; Eric Dezenhall
Cc: Kelly, Alex; Schell, Margaret
Subject: Draft letter to the NYT public editor
Importance: High

Here is a draft of the cover note.

Eric, Steve or Rosemarie will be in touch to ask your help in completing the attachment that should go with this letter -- we need the chapter and verse of what we are claiming. They will be sending you the attachment shortly; It's already partly done but could your team round it out.

Also any improvements to the letter please give us your input.

We should aim to complete this today so it can go to Merck today for their review.

Thanks.

<<nyt public editor draft feb 2 08 clean.doc>>

Ken Banta
Schering-Plough Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033
Phone: 908-298-4770
Mobile: 917-776-5418
Fax: 908-298-5855

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This message and any attachments are solely for the intended recipient. If you are not the intended recipient, disclosure, copying, use or distribution of the information included in this message is prohibited -- Please immediately and permanently delete.

DRAFT

February 4, 2008

Clark Hoyt
Public Editor
The New York Times

Re: Recent Coverage Relating to the Enhance Clinical Trial

Dear Mr. Hoyt,

We are writing to bring to your attention a pattern of unfair and inaccurate coverage of our cholesterol-lowering medicines, ZETIA and VYTORIN (ZETIA combined with simvastatin), and the conduct and results of the ENHANCE clinical trial. The errors and omissions in the New York Times coverage have misinformed your readers, damages our companies' reputations [NOTE: use singular if Merck does not cosign] and, most importantly, done a disservice to patients at risk from high-cholesterol.

Our concerns relate to six articles by reporter Alex Berenson, including "After a Trial, Silence" on November 21, 2007, "Trial of Cholesterol Drug Gets House Scrutiny" on December 12, 2007, "Data About Zetia Risks Was Not Fully Revealed" on December 21, 2007; "Drug Has No Benefit in Trial, Makers Say" on January 14, 2008, "Study Reveals Doubt on Drug for Cholesterol" on January 15, 2008 and "Cholesterol As a Danger Has Skeptics" on January 17, 2008, and a related January 16, 2008 editorial, "Cholesterol Drug Bombs."

This coverage raises serious issues of journalistic integrity, including easily avoidable inaccuracies, a failure to provide context,, a lack of science literacy, and some critical omissions.

The false impression created by Mr. Berenson's series and the related editorial is that Vytorin and Zetia are medicines that were proven to be useless and possibly unsafe by the Enhance trial, and, as the editorial states, our companies "had been cynically sitting on the results for more than a year" after first attempting to manipulate the findings by changing the study's primary goal. In fact, none of this is true. The Food and Drug Administration held a January 25, 2008 news conference to address these very points in an effort to redress the confusion, even panic, caused in patients by coverage like Mr. Berenson's. The NYT chose not to report on that press conference.

Here are the chief flaws in Mr. Berenson's coverage and the January 16th editorial:

The NYT Misrepresented the Purpose, Conduct and Results of the ENHANCE trial

On 11/21/2007, Berenson reported that "[c]ardiologists have been awaiting the results of the trial, called Enhance, to learn how well Zetia and Vytorin work. If they are not as effective as other cholesterol medicines, patients taking them may be putting themselves at unnecessary risk of heart attacks." Here and elsewhere in his series he mischaracterizes the importance of the Enhance trial while downplaying abundant evidence of the safety and efficacy of the two medicines. Most falsely and egregiously, on 1/14/07 he reports that the Enhance trial of Zetia "failed to show that the drug has any medical benefit."

In fact, both Zetia and Vytorin have been proven to achieve the health benefit of lowering LDL-cholesterol, so-called "bad" cholesterol. Studies have shown that Zetia and Vytorin do a better job lowering LDL-cholesterol than statins alone without raising any additional safety concerns, and the Enhance study reaffirmed this despite Berenson's 12/21/07 speculation that the as-yet unreleased results would "contain important information about Zetia's liver risks." Lowering LDL-cholesterol has been the primary target of therapy for cardiac health for more than 20 years. The National Cholesterol Education Panel has set goals for LDL-cholesterol in high-risk patients. The American Heart Association has said that "high cholesterol levels are a very important risk factor for coronary heart disease.

At the January 25, 2008 press conference (http://www.fda.gov/bbs/transcripts/), FDA officials said that elevated LDL-cholesterol is a very well established risk factor for heart disease, and lowering LDL-cholesterol is the agency's basis for approving medicines even when there has not yet been a clinical trial proving the medicine reduces heart attacks or strokes.

Mr. Berenson is wrong in reporting here and elsewhere that the Enhance trial was intended to show that Vytorin prevents heart attacks or strokes. Such conclusions can only be reached through a clinical outcomes trial. A Vytorin outcomes trial involving more than 10,000 patients is currently under way and expected to be concluded in 2011. As Mr. Berenson fails to point out, it took a similar amount of time for most of the statins to complete their outcomes studies. For example, on 12/21/07 he reports that Lipitor has been proven to reduce heart attacks or strokes, but Lipitor had been sold for more than seven years as a cholesterol-lowering medicine before its outcomes data was accepted by FDA. Another statin, Crestor, was approved the year before Vytorin and the year after Zetia and has not yet produced outcomes data. The prescribing information for our medicines clearly states that they have not yet been proven to reduce heart attacks or strokes. This does not, however, mean that there is no medical benefit from taking these medicines which have been proven to be as safe and more effective than competing treatments in lowering LDL-cholesterol.

As FDA officials stated, the Enhance study was too short and too small to provide any conclusions about cardiovascular risks. The ENHANCE trial was an imaging study conducted in 720 patients suffering from Heterozygous Familial Hypercholesterolemia, a rare condition that affects approximately 0.2% of the population. This patient group has extremely high cholesterol levels and the great majority had been treated with aggressive cholesterol-lowering therapy before the trial began. Therefore, finding a difference in the thickness of artery walls between study patients on Vytorin and patients on simvastatin alone by examining 40,000 ultrasound images was a very challenging goal but not a measurement of which medicine is more effective in preventing heart attacks or strokes. That is why the American College of Cardiologists, AHA and FDA have issued

statements urging physicians not to make clinical decisions based on the ENHANCE imaging study alone.

What Mr. Berenson incorrectly reported on 11/21/07 is that the Enhance study was intended "to end those questions" about whether reducing cholesterol through non-statins "may not protect the cardiovascular system as much as reducing it through a statin." He writes that measuring the growth of plaque is "an important measure of the effectiveness of cholesterol-lowering medicines" (11/21/07), but he falsely reports that (1/14/08) "patients taking Vytorin actually had more growth in fatty plaques in their carodtid arteries than those on Zocor [simvastatin]." In fact, there was no statistically significant difference between the two patient groups and a reporter covering medical research should be expected to understand the concept of statistical significance. The editorial writer goes even further in mischaracterizing this finding, stating "the plaques grew almost twice as fast in patients taking the Vytorin." However, as FDA stated during the news conference:

> "You should understand that we consider LDL lowering as a well validated surrogate for approval. The intimal-medial thickness or the thickness of the plaque is a much less well-validated surrogate that we use in a much more limited way from a regulatory perspective. So we don't want to go too far down the path of making decisions about the overall benefit of these products based on this one study of this endpoint. We really would like to see the data from the outcome study."

In writing his articles, Mr. Berenson mostly quotes medical experts who are adherents of hypotheses that reduction in arterial plaque is a strong marker for improved cardiovascular outcomes. Yet the more established medical science is in agreement with FDA that lowering LDL-cholesterol is the more direct and clearer marker for better cardiovascular health.

Having mischaracterized the significance and findings of the Enhance study, Mr. Berenson and the editorial writer falsely accuse our companies of trying to manipulate the Enhance findings, conceal some of the results and delay the release of negative results, so that sales of Vytorin and Zetia would not drop. On 11/21/07 he reported that Merck and Schering-Plough "had changed the trial's 'primary endpoint' – the main medical result being measured. The companies now say that they will use only partial results to assess the trial's success in deterring the formation of plaque that can cause artery blockages and lead to heart attacks." On 1/16/08 the NYT editorial on Enhance's supposedly "very disturbing" finding falsely states: "The two companies that reap billions from the drug [Zetia] had been cynically sitting on the results for more than a year." In fact, none of this is true.

In fact, the results of the ENHANCE trial were not known to anyone at Schering-Plough or Merck until December 31, 2007, when the study was unblinded to a small group of scientists. Before that date no one at either company knew whether the Vytorin or the simvastatin patient group had done better or worse or, as it turned out, just about the same in terms of measurements of the thickening of the artery walls. On January 14, 2008 the companies announced that there was no statistically significant difference between the treatment groups on this primary endpoint. All the delays in this study occurred because the difficulties of reading 40,000 single-frame digital ultrasound images of artery walls were greater than was expected when the study began in 2002. It was essential to make sure the ultrasound image readings were as accurate as possible before the study was unblinded, so that there could be no possibility that the results were biased by investigators knowing which medicine a given patient was on. The study's patients who went through six ultrasound scans each, the scientific community and the public were entitled to the most meticulous reading of these ultrasound images. The full findings of the ENHANCE study have been provided to FDA and will be presented at the ACC conference at the end of March and published in a medical journal.

At the time the Enhance study was started in 2002, the technology of using single-frame digital ultrasound images to measure the thickness of artery walls was new. When it

became clear that some of the still blinded ultrasound images were difficult to read, missing or presented changes from one patient to another that were biologically implausible, the company asked an independent panel of expert biostaticians to recommend the best way to interpret the images. Although they recommended that the study only look at images taken from the common carotid, our companies decided not to change the study's primary endpoint.

At the January 25 news conference, FDA said that our companies had never requested approval to change the study's endpoint, but such actions are sometimes warranted:

> "There are circumstances, however, where it's legitimate and valid for a company to have seen trends in the data that's still blinded that lead them to make decisions to change the primary endpoint. So it's not our of the ordinary or illegal so to speak to make changes in your primary endpoint or the size of your study or how you plan to analyze the data if that's done before you've unblinded the data and you haven't done it in a way that might introduce bias into the analysis."

Even more troubling than the NYT's unwarranted accusations against our companies is the editorial writer's decision to provide bad medical advice to your readers, counseling them that "with no evidence of effective, it seems clear that Zetia and Vytorin should be used sparingly, in cases where all other cholesterol drugs have failed." In contrast, the American College of Cardiologists, AHA and FDA have issued statements urging physicians not to make clinical decisions based on the Enhance imaging study alone.

We urge you to fully investigate the NYT's coverage of this important topic and report your findings in the Public Editor's column.

Sincerely

Merck

Schering-Plough