NBER WORKING PAPER SERIES

WHAT'S THE "INTEREST" IN FDA DRUG ADVISORY COMMITTEE CONFLICTS OF INTEREST?

Joseph Golec
John Vernon

Working Paper 14932
http://www.nber.org/papers/w14932

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
April 2009

John Vernon thanks FDA for financial support and access to data. The views expressed herein are those of the author(s) and do not necessarily reflect the views of the National Bureau of Economic Research.

What's the "Interest" in FDA Drug Advisory Committee Conflicts of Interest?
Joseph Golec and John Vernon
NBER Working Paper No. 14932
April 2009
JEL No. G14,G38,I11,I18,I28

ABSTRACT

Food and Drug Administration (FDA) drug advisory committee members sometimes have financial interests tied to drug companies. Congress and the public have become concerned that these financial interests lead to conflicts of interest. They conclude that the conflicts bias committee recommendations, and lead to unsafe or ineffective drugs being approved for public consumption, or, conversely, delays in approval of safe and effective drugs. Our paper provides empirical evidence, based on an event study methodology, that advisory committee meetings lead to weak or statistically insignificant effects on stock prices and hence equity values of regulated companies assumed to be affected by the particular matters coming before committee meetings.

Joseph Golec
Department of Finance
2100 Hillside Road
Storrs, CT 06269
Joseph.Golec@business.uconn.edu

John Vernon
University of North Carolina at Chapel Hill
Department of Health Policy & Management
1101C McGavran-Greenberg Hall
Chapel Hill, NC 27599-7411
and NBER
vernon@email.unc.edu

I. Introduction

Food and Drug Administration (FDA) advisory committee members sometimes have financial interests tied to companies whose products are evaluated by their committees. Congress, public interest groups, and the press have become increasingly concerned about these financial interests.[1] They worry that the advice offered by advisory committee members may be biased; thus undermining the integrity of the processes that FDA uses to solicit outside advice to inform regulatory decisions. Our paper provides financial market evidence of weak or statistically insignificant effects of advisory committee actions on stock market values, an accepted measure of the value of a company (and a measure of the potential direct benefits to committee members holding stocks in these companies as well as potential indirect benefits to committee members with other financial ties to these companies).

Our analysis distinguishes between two types of meetings and finds evidence suggesting different stock price effects. Product-specific meetings may deal with such things as approval or labeling of an individual product. Meetings on general topics address regulatory issues affecting many firms, as many as the entire pharmaceutical industry. We find no evidence of effects of general topic meetings on stock prices. We do find, however, evidence of some statistically significant but mostly weak negative effects of product specific advisory committee meetings on stock prices of affected firms.

[1] See for example, Congressional Record, H4247 (daily ed. June 8, 2005) (statement of Rep. Stupak); Steinbrook, R., "Financial Conflicts of Interest and the Food and Drug Administration's Advisory Committees," New Engl. J. Med., 353: 116-117 (July 14, 2005); Lurie, P., et al., "Financial Conflicts of Interest Disclosure and Voting Patterns at Food and Drug Administration Drug Advisory Committee Meetings," JAMA, 295: 1921-1928 (Apr. 26, 2006); Saul S. "Panel backs drug amid conflict concerns," New York Times, September 10, 2005:C3.

In the rest of the paper we discuss the institutional and legal background of conflicts of interest and FDA's advisory committees, measurement of the effects of advisory committee meetings, a description of the results, and then our conclusions.

II. **Background**

FDA advisory committees play a vital role in furthering FDA's mission to protect and promote public health. Through advisory committees, FDA obtains independent, expert advice on issues relating to human drugs, animal drugs, biological products (such as vaccines and blood products), medical devices, and food. In general, drug advisory committees include consumer representatives, a patient representative, industry representatives (who do not vote) and at least two technically qualified experts who specialize in the drug or disease.

FDA advisory committees have been subject to increased scrutiny. In particular, members of the public, Congress, and consumer groups have focused attention on advisory committee members' potential conflicts of interest and how FDA reviews and grants waivers of conflict of interest.

Federal law[2] requires that individuals invited to attend an FDA advisory committee meeting as a special government employee (SGE) or regular government employee (RGE) report to the agency all financial interests relevant to the topics to be discussed at the advisory committee meeting. Individuals are required to report personal financial interests, such as stock in a regulated company and consulting fees received from a regulated company. In addition, individuals must report financial interests imputed to them through their spouse, minor children, employer, prospective employer, general partner, and organizations in which they serve as an officer, director, trustee, or

[2] Ethics in Government Act of 1978, 5 U.S.C. app., Title I (P.L. 95-521, 92 Stat. 1824)

general partner. The law considers a financial interest to be a potential conflict of interest if the discussions and potential outcomes of the advisory committee meeting will have a direct and predictable effect on the financial interest.[3]

If an individual has a potential conflict of interest, he or she may not participate in the meeting unless the agency determines that the criteria for a waiver of conflict of interest are met and such waiver is granted. Under current law and FDA policy, FDA grants a waiver only if it is necessary to afford the advisory committee essential expertise, the aggregate amount of potentially conflicting personal financial interests is $50,000 or less, and granting the waiver would be consistent with the statutory cap on the number of waivers that may be issued for the year.[4]

Individuals with substantial or closely related financial interests are either excluded from the committee meetings or not allowed to vote. Those with moderate to small or more remote financial interests sometimes are given waivers and allowed to participate because of their unique expertise. For example, a committee member could hold $25,000 worth of a drug stock or have earned a $10,000 consulting fee from a drug company and still be selected for the committee and allowed to vote. As of March 1, 2009, FDA operated 48 advisory committees and panels (16 for drugs), and, collectively, these committees had 592 members.

For the above mentioned reasons, Congress, the public, and regulators have been understandably concerned that some advisory committee members' financial interests are

[3] 18 U.S.C. 208; 21 U.S.C. 379d-1 (added by the Food and Drug Amendments Act of 2007, Pub. Law No.110-85, sec. 701)

[4] *See* Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees, August 2008, accessed at: http://www.fda.gov/oc/advisory/GuidancePolicyRegs/ACWaiverCriteriaFINALGuidance080408.pdf

conflicts of interest that could lead to bias. They worry that FDA's decisions to grant conflict of interest waivers to some experts with financial interests undermines the objectivity of the advisory committees' recommendations[5]. A widely cited study of FDA drug advisory committee members' conflicts of interest found that 73 percent of advisory meetings involved at least one member with a conflict (Lurie et al., 2006). The researchers found well over 60 percent of the conflicts consisted of members owning drug company stocks or receiving consulting fees from drug companies. They further found that conflicted members typically voted in favor of drug approvals more frequently than non-conflicted members.[6]

In that study, a member was defined to be conflicted if he had any financial interest in *a potentially affected* drug firm, not just the firm whose drug was up for approval. For example, a member who had a financial interest in a firm that makes a competing product to the subject drug was considered to be conflicted, as was a member who had a financial interest in the subject drug firm. An assumption underlying this definition is that financial benefits generated from any drug firm make or identify a committee member more favorably predisposed to the drug industry in general, and more likely to vote in favor of drug approvals. This assumption is common in the Congressional record, the popular press, and the academic press. FDA has previously articulated flaws with this study. An FDA paper published by the Center for Medicine in the Public Interest (also described in *Biotechnology Law Report* 25:5 (2006) describes flaws in the methodology used in the Lurie et al. paper (2006). Specifically, the FDA paper stated the following:

[5] Congressional Record H4245 (daily ed. June 8, 2005) (statement of Rep. Hinchey).
[6] Lurie, P., et al., "Financial Conflicts of Interest Disclosure and Voting Patterns at Food and Drug Administration Drug Advisory Committee Meetings," JAMA, 295: 1921-1928 (Apr. 26, 2006).

"Rather than asking whether having a financial tie to any pharmaceutical company tends to increase votes in support of a drug (a notion inconsistent with conventional interpretations of conflict of interest), we ask whether having a financial interest tends to increase votes in favor of that interest."

The FDA study's re-interpretation of the Lurie et al. results suggests that committee members with a financial interest in a particular company were less likely to vote in favor of that pharmaceutical company's interests than members without any financial ties. The paper also determined that committee members with financial ties to competing firms (for whom a vote of "yes" on a particular drug could be interpreted as a vote against the financial interest of the firm with which the member has financial ties) were more likely to vote against the financial interest of the companies with which they have financial ties compared to committee members with no financial ties. Finally, the FDA study reiterates the Lurie et al. finding that if all members of the advisory committees had been excluded from voting, not a single outcome of the 76 advisory committee meetings would have been altered.

III. Measuring the Effects of Advisory Committee Meetings

Previous studies on conflicted advisory committee members have focused on member qualifications and meeting outcomes. In this paper, we use stock returns to measure the effects of committee meetings on firms' financial interests. As described above, the legal standard for identifying conflicts of interest is whether the particular matter (i.e., advisory committee meeting topic) in which the federal employee participates would have a direct and predictable effect on the federal employee's financial interests. Thus, the existence of measurable stock price effects suggests such effects are direct and predictable, and the absence of measurable stock price effects would raise questions about the directness and predictability of such effects. In the absence of

measurable stock price effects, companies--and the interests of committee members in such companies--may still gain, but only insofar as the effects of the committees' deliberations were either anticipated by the market so that there is no "surprise" or so small that no effect was measurable. In the finance literature, use of stock prices to evaluate effects of events on market value is called an "event study."[7]

Our tests avoid having us decide which new drugs merit approval. They rely on the assumption that stock prices are set efficiently; a widely held view in the finance literature. The idea is that all publicly available information relevant to valuing a company's stock is reflected in its price. This view seems appropriate here because information on potential new drugs attracts a great deal of attention from investors and Wall Street investment firms hire many drug industry experts to assist them in valuing drug stocks.[8] If a stock is priced too high (low) given what investors know about its prospects, investors sell (buy) the shares, thus forcing down (up) its price until it returns to its proper price. Thus, drug companies' stock prices should reflect all publicly available information about the likelihood of a new drug being recommended for approval by an advisory committee.

The relative rarity of event studies in the medical literature suggests further explanation is merited.[9] Simply stated, the result of an event study is the portion of a stock's return caused by an information surprise. An example of a surprise is when traders expect an advisory committee to recommend approval of a drug but instead they

[7] Brown, S., Warner, J., "Measuring Stock Price Performance," J. Financial Economics, 8: 205-232 (Sept. 1980).

[8] Steinbrook, R, "Wall Street and Clinical Trials," New Engl. J. Med, 353: 1091-1093 (Sept. 15, 2005).

[9] Oberholzer-Gee, F, Inamndar S, "Merck's Recall of Rofecoxib – a Strategic Perspective," New Engl. J. Med, 351: 2147-2149 (Nov. 18, 2004).

recommend against approval. The surprise or "abnormal" portion of the associated drug stock's return is computed by subtracting the company's normal (expected) return from what the stock actually earned over the days surrounding the announcement of rejection. Stock return data is obtained from The Center for Research in Security Prices (CRSP), the most common source used in the finance literature. The appendix provides the more technical details of the event study method.

Our sample of events covers most of the FDA advisory committee meetings that occurred in 2006. Some meetings involved companies that are privately held or whose stocks are solely traded on foreign exchanges. The CRSP data base does not contain stock returns for these firms; hence, we could not include these companies in our study. Nevertheless, the sample is likely to represent the exploitable effects of the events reasonably well because CRSP covers the foreign pharmaceutical firms whose stocks are traded in the U.S., and because most of the excluded firms are privately held. Advisory committee members are unlikely to own shares of private companies because private stock is not available for purchase on stock exchanges.

We examined 24 out of the 31 drug advisory committee meetings held during 2006. Ten meetings were product-specific (drug-specific) meetings, and the remaining 14 were general topic meetings.[10] Each meeting provides a vote announcement, which is defined as an event. The FDA provided the names of the firms potentially affected by the questions voted on at each meeting. We dropped four product-specific meetings and another three general topic meetings because they did not involve a publicly-traded firm.

[10] Regulations of the Office of Government Ethics refer to particular matters involving specific parties (5 CFR 2640.102(l)) and particular matters of general applicability (5 CFR 2640.102(m)). For simplicity, we use product specific and general topic meetings to refer to these two types of particular matters.

Two product-specific meetings actually considered two separate drugs, each sponsored by a different company; hence, these two meetings provide four product-specific events.

We ran an event study to measure the abnormal return for each of the 12 individual firms potentially impacted by the 10 product-specific meetings. As is common for event studies, we also formed an equally-weighted stock portfolio of all 12 stocks' abnormal return to measure an overall average impact of the committee announcements for the group. We performed the same analysis for each general topic meeting, since each meeting's announcement impacted several firms, and then formed a portfolio of all firms impacted by general meeting announcements to measure an overall average impact for all of the groups combined.

Figure 1 illustrates the basic structure of the data used to measure an abnormal return for each company. The day that the results of the voting are announced is labeled day 0; that is the event day. One could simply compute the abnormal stock return on that day to measure the effect of any surprise announcement on a particular company's stock, but the typical event study reports the cumulative abnormal stock returns (CARs) for the event day plus some trading days around the event. For example, the trade day that occurs 3 days before the event is labeled -3 in the figure. The reason most event studies include the surrounding days' abnormal returns is that some information leakage could occur just before the event, or it could take some time following the event for the information to be fully digested by the traders. In 2006, FDA generally posted on its website briefing materials for members of its advisory committee at least 24 hours prior to the start of the advisory committee.

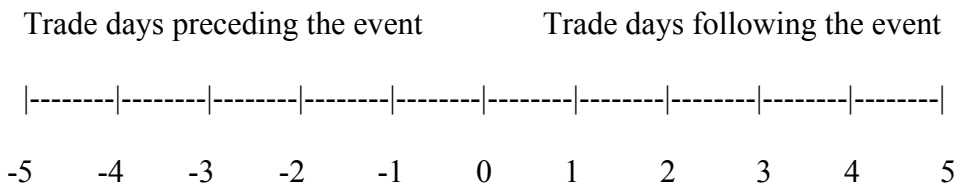

Figure 1. The Time-Line of Return Data Used to Compute Cumulative Abnormal Returns

Using a "window" of days around the event is particularly appropriate for FDA meeting announcements. Furthermore, some meetings take place over two days and information leaks on the progress of the voting could occur on the first day. To account for potential information leaks or lags, we report CARs for one day before and one day after the meeting announcement day (three trading days), five days before and five days after the meeting announcement day (11 trading days), and 21 days before and 21 day after the meeting announcement day (43 trading days). The three event windows in the tables of results are designated by (-1, 1), (-5, 5), and (-21, 21).

We report results for three different windows for a number of reasons. First, results for different windows illustrate the robustness of the results. Second, some meetings cover two days. We set the event day as the second of the two days because announcements from the meetings are more likely to come on the final day, but information leakage is possible on the preceding day. Therefore, the three-day event period is the shortest time period that reasonably covers the event's effects while minimizing the chance that some other confounding event occurs during the event period. Third, the (-5, 5) window allows a greater coverage of leak or lag effects, but increases the chance that the firms involved are affected by some other event that is then

mistakenly attributed to the FDA meeting. Nevertheless, the chance of this occurring for many firms during the window is small. Finally, the (-21, 21) window can provide evidence about whether information is impounded in the affected stocks well before the meeting is even held. This could indicate early leakage of information before any public news source is able to obtain and report on the information. Of course, this longer period is also more likely to contain confounding events.

IV. Description of Results

We present the separate event results in tables below. Each entry in the table is either a cumulative abnormal return (CAR) over a particular event window or its associated t-statistic. The CAR measures the stock or portfolio return after adjusting for the risk of the stock or portfolio of stocks. The t-statistic can be used to test the hypothesis that a CAR is statistically different from zero. For our purposes, we employ a two-tailed test, and take a t-statistic with a magnitude greater than 2 to indicate a statistically significant CAR at the 5 percent level.

As shown in Table 1, the CARs for companies affected by general topic meetings are consistent with what we would ordinarily expect to have happened by chance alone.[11] Company names are withheld for privacy reasons. Some firms were named in several meetings but many firms appear only once; hence, the results are not driven by a few firms who appear over and over again.

[11] To illustrate the questions put before advisory committees meeting to address general topic, we provide a an example. On February 9, 2006, the Cellular, Tissue and Gene Therapies Advisory Committee discussed issues surrounding potency measurements for cellular and gene transfer products. One question asked of the committee was: In the context of Cellular and Gene Therapy products, what assay design schemes would be necessary to successfully validate biological assays and allow accurate quantification and interpretation of the results obtained? In contrast, for the product-specific meeting held by the Anti-infective Drugs Advisory Committee on March 6, 2006 a question posed was: Do data from the pivotal study provide substantial evidence of safety and efficacy of [the drug] daptomycin in the treatment of *staphylococcus aureus bacteremia*?

Our hypothesis for the effects of general topic meetings is that they should be small overall because of the general nature of the topics and therefore the more unpredictable the effects of committee recommendations on a firm's profitability. At the bottom of the table we report the CARs for a combined portfolio of all of the firms in all 14 events. We find that the overall effects for the 14 meetings combined are very small; over the (-1, 1), (-5, 5), and (-21, 21) windows, the CARs are -0.09, 0.48 and -2.41 percent, respectively. None of these CARs is statistically significant.

We recognize that combining all of the meetings' effects could mask a relatively large effect for a few meetings, or that large positive effects of some meetings could offset large negative effects of other meetings. To consider this possibility, we measure and report the effect for each meeting. The CARs measuring the effect of a meeting is designated as "Portfolio" under the company number column. Given the 14 events (meetings) and three windows per event, there are 42 CARs to consider. We find that none of the 42 CARs for the portfolios are statistically significant. Furthermore, the point estimates of the CARs over the three-day event period are all very small – less than one percent except for two cases which are less than two percent. And the signs of the CARs are about evenly distributed between positive (22) and negative (20) CARs.

Finally, we considered the possibility that these portfolio-level results masked some large effects of the meeting announcements on individual companies. There are a total of 279 company-level CARs, but only 5 are statistically significant. If we assume that we could observe up to five percent statistically significant CARs by chance (approximately 14 in this case), the 5 statistically significant CARs can easily be attributed to chance. Furthermore, there are three statistically significant negative CARs

and two statistically significant positive CARs. Therefore, our evidence supports our hypothesis that the announcements of votes from general topic meetings should hold few large surprises, and therefore, have no substantial overall impact on the companies' stock prices.

Table 2 reports results for the company-specific meeting events using a similar format. Our hypothesis is that occasionally there will be statistically significant effects of company-specific meeting announcements on the stocks of companies whose drug products are under consideration by the committee. We find that the overall effects on the 12 companies involved in company-specific events are larger in magnitude than those observed for the general topic meeting effects. The CARs for the portfolio of the 12 companies over the (-1, 1), (-5, 5), and (-21, 21) windows are -2.48, -11.15, and -5.91 percent, respectively. The (-1, 1) and (-5, 5) window CARs are statistically significant. We report a total of 36 company-specific CARs for the 12 companies and find that 5 are statistically significant. More than ten percent of the CARs are statistically significant, which indicates that the results are unlikely to be due to chance. Furthermore, four of the five statistically significant CARs are negative.

The empirical results in Tables 1 and 2 support our hypotheses. There appear to be very few surprises in the general topic meetings but a statistically significant number of surprises (mostly negative) in the product-specific announcements. The results are based upon one year of meetings; hence, they are not conclusive. An open question is why the surprises tend to be negative rather than positive for the meetings with product specific topics.

VI. Conclusion

Overall, this study implies that advisory committee meetings provide little additional information about a drug product's expected sales and therefore rarely move stock prices. The study finds that FDA advisory committee meetings involving general topics have no statistically significant impact on stock prices. Some FDA meetings involving company-specific topics produce statistically significant but usually small negative stock price effects. Assuming that drug stocks are priced reasonably efficiently, these results show that investors are not surprised by the voting results announced at general topic meetings, but that such surprises sometimes occur at the product specific meetings and these surprises are negative. We suggest that the reason for this difference is that the general topics may have intrinsically less predictable effects on stock prices.

Appendix: Event Study Details

We computed all event-study results using Eventus software, the CRSP returns data set, and the market model. The market model is used as part of a common method to compute an abnormal return. The model defines the return one can expect from a stock on a particular trading day, given the stock's risk (beta) and the market return for the day. A stock's beta is a measure of its risk relative to the stock market as a whole. By definition, the market beta has a value of 1. A stock that is twice (half) as risky as the stock market has a beta of 2 (0.5). On days when the stock market increases (decreases) by, say, 2%, a stock with a beta of 2 should increase (decrease) by 4%.

The market model parameters (beta and alpha) for each firm are estimated with daily returns from a period preceding the event, in this case, starting 46 trading days before the event and going backward in time at least 63 trading days (three months) and up to 255 trading days (one year) if a company has 255 days available in the CRSP data set. The market model is

$$R_{it} = \alpha_i + \beta_i R_{mt} + \varepsilon_{it} \qquad (1)$$

where R_{it} is firm i's daily stock return on day t, R_{mt} is the market return on day t represented by the CRSP equal-weighted index return, α_i and β_i are the market model parameters measured by ordinary least squares coefficients for firm i, and ε_{it} in the error term for firm i at time t. Here we use up to one year of a firm's daily stock returns to gauge its risk. The returns come from a time period before the event windows so that the event itself does not influence the risk measure.

The normal or expected return on a particular day t, for stock i is measured as:

$$E[R_{it}] = \hat{\alpha}_i + \hat{\beta}_i R_{mt} . \quad (2)$$

The coefficients in (1) are estimated over the 255 trading days before the event window. They are used to calculate, A_{it}, the risk-adjusted (abnormal) return on a particular day t for firm i as,

$$A_{it} = R_{it} - E[R_{it}] = R_{it} - \hat{\alpha}_i - \hat{\beta}_i R_{mt} .$$

We compound these abnormal returns over the days of the event window to find the cumulative abnormal return (CAR) for a single firm.

When more than one firm is potentially affected by an event, in addition to reporting the individual firm CARs, we also report an average CAR for the portfolio of firms potentially affected by the event. We test these CARs for an overall event effect. This portfolio average CAR is computed by averaging the abnormal returns for the firms on each event day in the window, and then compounding these average returns over the event window.

CARs are measured over three event windows and their statistical significance is tested with a t-statistic. The CAR t-statistic is computed using the time-series standard deviation of the returns for either an individual stock or the portfolio of stocks potentially impacted by the given event. We report results for there event windows: a short window of (-1, 1), a medium window of (-5, 5), and a long window of (-21, 21).

Table 1. Cumulative Abnormal Returns (CARs) for Various Windows Around the Announcements of Votes from General Topic Advisory Committee Meetings

Event (Meeting) Dates	Company Number	Short Event Window (-1, 1)		Medium Event Window (-5, 5)		Long Event Window (-21, 21)	
		CAR	T-stat	CAR	T-stat	CAR	T-stat
1. February 10, 2006	1-1	-1.11	-0.393	13.15	2.424*	-10.47	-0.980
	1-2	-2.80	-0.427	-8.35	-0.662	2.95	0.119
	1-3	-1.45	-0.221	4.68	0.372	-21.22	-0.853
	1-4	11.78	1.930	13.77	1.178	14.65	0.633
	Portfolio	1.60	0.596	5.81	1.127	-3.52	-0.345
2. February 17, 2006	2-1	0.54	0.247	6.56	1.572	-0.05	-0.005
	2-2	0.44	0.155	1.59	0.292	6.62	0.616
	2-3	-1.41	-0.482	-3.00	-0.536	-7.34	-0.665
	2-4	-1.27	-0.727	0.72	0.213	-6.68	-1.006
	2-5	-0.59	-0.307	-1.53	-0.419	2.87	0.397
	2-6	-0.52	-0.199	8.72	1.739	-3.61	-0.361
	2-7	-1.01	-0.351	1.41	0.257	-0.03	-0.004
	2-8	-2.35	-1.239	-4.51	-1.242	-8.35	-1.162
	Portfolio	-0.77	-0.727	1.24	0.614	-2.07	-0.517
3. March 10, 2006	3-1	-2.71	-0.467	5.28	0.478	-23.43	-1.071
	3-2	3.16	1.609	4.43	1.177	0.78	0.105
	3-3	-1.25	-0.431	-1.26	-0.226	-4.40	-0.399
	3-4	-0.79	-0.459	0.84	0.256	-1.78	-0.272
	3-5	0.03	0.007	2.10	0.216	-9.37	-0.489
	3-6	-2.13	-0.486	2.28	0.272	8.61	0.520
	3-7	-3.78	-0.272	-5.77	-0.217	-10.45	-0.200
	3-8	-0.24	-0.022	-5.32	-0.254	12.73	0.309
	3-9	0.41	0.166	0.28	0.057	-27.96	-3.011*
	Portfolio	-0.81	-0.324	0.32	0.066	-6.14	-0.649
4. March 13, 2006	4-1	1.04	0.698	4.93	1.729	-1.94	-0.346
	4-2	0.32	0.213	0.60	0.212	7.89	1.405
	4-3	0.03	0.015	2.73	0.718	-5.52	-0.737
	4-4	1.14	0.593	3.69	1.005	-0.05	-0.007
	Portfolio	0.63	0.579	2.99	1.433	0.09	0.023

5. March 14, 2006	5-1	-0.06	-0.022	-1.23	-0.242	-11.41	-1.130
	5-2	0.10	0.038	-3.38	-0.668	-7.90	-0.787
	5-3	-1.20	-0.807	0.26	0.092	7.97	1.418
	5-4	-1.34	-0.549	1.29	0.275	-8.33	-0.899
	5-5	-1.21	-0.699	-1.07	-0.322	-4.86	-0.744
	5-6	0.92	0.213	6.53	0.792	18.91	1.161
	5-7	-1.28	-0.648	1.11	0.294	-6.49	-0.869
	5-8	-0.06	-0.033	2.24	0.611	-1.58	-0.218
	5-9	0.37	0.138	0.01	0.002	-9.78	-0.965
	5-10	0.55	0.105	-5.95	-0.591	-3.88	-0.194
	5-11	0.87	0.574	2.56	0.886	1.88	0.331
	Portfolio	-0.21	-0.200	0.22	0.106	-2.32	-0.574
6. March 28, 2006	6-1	-2.72	-1.032	-2.56	-0.507	-17.68	-1.772
	6-2	-1.77	-1.183	-3.34	-1.165	0.95	0.166
	6-3	6.26	0.630	10.44	0.548	41.09	1.091
	6-4	-3.69	-1.115	-6.38	-1.006	-3.50	-0.280
	Portfolio	-0.48	-0.171	-0.46	-0.086	5.21	0.490
7. April 26, 2006	7-1	-2.08	-0.819	-4.29	-0.881	9.00	0.935
	7-2	2.82	1.735	0.16	0.053	-0.60	-0.095
	7-3	2.31	1.108	1.37	0.345	0.60	0.074
	7-4	0.37	0.145	0.58	0.119	-5.46	-0.566
	7-5	0.73	0.482	0.70	0.241	3.94	0.674
	7-6	0.47	0.173	-2.23	-0.428	-6.60	-0.643
	7-7	-0.20	-0.091	2.49	0.578	2.65	0.309
	7-8	2.01	0.371	24.19	2.322*	26.21	1.271
	7-9	-0.75	-0.060	0.13	0.005	24.96	0.524
	7-10	-4.79	-1.587	-7.52	-1.299	-12.86	-1.123
	7-11	0.18	0.111	-2.00	-0.652	-4.86	-0.803
	7-12	-0.23	-0.058	14.22	-1.840	-8.85	-0.580
	7-13	0.01	0.001	-5.24	-0.384	-18.31	-0.680
	7-14	1.83	0.618	-1.76	-0.309	-21.52	-1.906
	7-15	-0.82	-0.386	-2.94	-0.726	-20.12	-2.507*
	7-16	2.65	1.007	5.87	1.165	-14.51	-1.460
	7-17	-1.20	-0.549	5.01	1.200	-10.06	-1.220
	7-18	2.80	1.385	4.29	1.105	1.72	0.229
	7-19	2.32	0.475	3.88	0.416	-0.17	-0.012
	7-20	0.08	0.034	2.32	0.520	-0.06	-0.016
	7-21	-1.94	-0.499	-0.18	-0.024	3.61	0.244
	7-22	-8.09	-3.145*	-7.68	-1.559	-3.01	-0.317
	7-23	-1.13	-0.312	-3.57	-0.512	-5.12	-0.372
	7-24	-1.09	-0.687	-0.28	-0.095	0.72	0.120

	7-25	-0.85	-0.428	1.87	0.490	3.26	0.433
	Portfolio	-0.18	-0.178	0.04	0.019	-2.22	-0.567
8. August 25, 2006	8-1	-0.33	-0.162	-2.14	-0.547	2.65	0.342
	8-2	4.25	1.349	3.50	0.581	-8.30	-0.696
	8-3	1.87	0.808	-0.10	-0.024	1.00	0.115
	Portfolio	1.93	1.270	0.42	0.145	-1.55	-0.270
9. September 7, 2006	9-1	-0.69	-0.350	-3.17	-0.848	-3.32	-0.453
	9-2	-0.50	-0.327	-1.24	-0.424	3.82	0.666
	Portfolio	-0.59	-0.449	-2.20	-0.872	0.25	0.050
10. September 19, 2006	10-1	1.50	0.854	2.79	0.828	8.47	1.275
	10-2	-0.62	-0.352	0.62	0.185	5.03	0.760
	Portfolio	0.44	0.329	1.70	0.666	6.75	1.332
11. September 25, 2006	11-1	-0.61	-0.214	-2.65	-0.484	-13.92	-1.284
	11-2	2.57	0.523	8.34	0.887	8.24	0.448
	11-3	1.41	0.859	3.70	1.173	1.18	0.189
	11-4	-0.94	-0.324	-4.42	-0.799	-0.94	-0.090
	11-5	2.31	0.765	-3.72	-0.645	-7.62	-0.668
	11-6	-0.95	-0.450	-0.36	-0.089	-7.27	-0.908
	11-7	-0.36	-0.100	-0.77	-0.111	-1.04	-0.076
	11-8	0.42	0.265	2.28	0.753	0.79	0.133
	Portfolio	0.48	0.402	0.30	0.130	-2.57	-0.567
12. October 6, 2006	12-1	-0.16	-0.059	-2.83	-0.548	-0.33	-0.032
	12-2	-1.72	-1.166	-1.15	-0.408	5.64	1.016
	12-3	0.70	0.319	-2.34	-0.559	-7.18	-0.865
	12-4	2.49	0.720	11.46	1.734	18.13	1.388
	12-5	0.02	0.004	-9.40	-0.866	-38.61	-1.800
	Portfolio	0.27	0.165	-0.85	-0.277	-4.47	-0.735
13. December 6, 2006	13-1	-4.31	-0.423	-7.78	-0.401	-36.92	-0.959
	13-2	4.36	1.189	-3.43	-0.487	-2.54	-0.183
	Portfolio	0.03	0.005	-5.61	-0.548	-19.73	-0.976

14. December 7, 2006	14-1	0.34	0.187	5.31	1.516	-3.67	-0.531
	14-2	-0.76	-0.382	1.49	0.387	-1.52	-0.202
	14-3	-0.37	-0.264	-0.42	-0.155	-4.49	-0.849
	14-4	0.78	0.345	2.66	0.614	9.36	1.094
	14-5	1.55	0.458	4.95	0.762	5.74	0.450
	14-6	-0.45	-0.285	-0.72	-0.235	-10.43	-1.740
	Portfolio	0.18	0.152	2.21	0.969	-0.83	-0.185
All Events	Portfolio	-0.09	-0.184	0.48	0.534	-2.31	-1.287

* Denotes that the CAR is statistically different from zero at least at the 5 percent level.

Table 2. Cumulative Abnormal Returns (CARs) for Various Windows Around the Announcements of Votes from Product -Specific Advisory Committee Meetings

Event (Meeting) Dates	Company Number	Short Event Window (-1, 1)		Medium Event Window (-5, 5)		Long Event Window (-21, 21)	
		CAR	T-stat	CAR	T-stat	CAR	T-stat
March 8, 2006	1	7.02	1.274	3.84	0.082	-1.84	-0.230
March 13, 2006	2	0.03	0.015	2.73	0.718	-5.52	-0.737
March 14, 2006	3	0.87	0.574	2.56	0.886	1.88	0.331
March 22, 2006	4	1.15	0.404	-33.18	-6.085*	-20.98	-1.949
May 17, 2006	5	1.63	1.052	0.26	0.084	-5.86	-0.982
June 2, 2006	6	2.56	1.304	4.59	1.224	6.64	0.891
September 7, 2006	7	0.60	0.257	2.27	0.511	8.15	0.931
September 7, 2006	8	-38.49	-3.987*	-96.30	-5.235*	-22.80	-0.621
September 12, 2006	9	-7.38	-1.041	-15.83	-1.168	12.75	0.477
September 12, 2006	10	-1.54	-0.437	-2.10	-0.312	-13.32	-1.024
September 21, 2006	11	-0.47	-0.190	0.60	0.126	-12.68	-1.356
October 19, 2006	12	4.20	2.038*	-3.30	-0.836	-17.47	-2.239*
	Portfolio	-2.48	-2.013*	-11.15	-4.718*	-5.92	-1.266

* Denotes that the CAR is statistically different from zero at least at the 5 percent level. The meeting on September 7th is unusual because the clinical studies relied upon by the sponsor to support approval of the drug and indication under discussion were submitted under Section 505(b)(2) of the Food, Drug and Cosmetic Act. (21 U.S.C. section 355(b)(2)). This section of the Act allows the FDA, in certain circumstances, to base approvals of new drugs entirely or partially on studies not conducted by the applicant and for which the applicant has not obtained a right of reference or use. The advisory committee meeting was an unusual circumstance and was not typical of FDA advisory committee meetings involving specific drug products.