

Conspiracy of Silence: How the FDA Allows Drug Companies to Abuse the Accelerated Approval Process

Staff Summary of Responses by the
Food and Drug Administration and
the Securities and Exchange Commission
to Correspondence from
Rep. Edward J. Markey (D-MA)
Senior Member, Energy and Commerce Committee
U.S. House of Representatives

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I. Executive Summary

In 1992, the Food and Drug Administration (FDA) established a process that amounted to a trade-off between its mission to ensure drug safety and effectiveness and the need to speed promising new drugs to market to increase treatment options for life-threatening illnesses. Called “accelerated approval,” this process allows FDA to approve a drug on an expedited basis using promising but limited information about its safety and effectiveness, but only on the condition that the company agrees to conduct further studies to confirm the safety and effectiveness of the product. Under the law, drug companies are required to do additional studies to confirm that the drug is safe, effective and works for its approved indication.

It now appears that the system of accelerated approval is broken and failing to ensure patient safety.

Based on information provided to Rep. Markey by the FDA and the Securities and Exchange Commission (SEC) in response to his inquiries, it is apparent that:

- **The Majority of Companies Benefiting From Accelerated Approval Are Failing to Complete the Postmarketing Studies Required by Law on a Timely Basis**

Although some companies do complete their required studies without any intervention from the FDA, the FDA has allowed many companies to stall or forgo completion of their required post-marketing confirmatory studies. According to FDA data:

- **50% (21/42)** of outstanding accelerated approval confirmatory studies have not been started although the drug is being marketed to consumers. Companies have been selling these products to the public for an average of **1 year and 10 months** and up to **6 years and 9 months** without even initiating the required studies.
- **46% (42/91)** of the study commitments that have been made since 1992 are not complete.
- **7% (3/42)** of outstanding accelerated approval confirmatory studies have been initiated but are behind schedule.
- **42% (18/42)** of outstanding accelerated approval confirmatory studies are proceeding according to or ahead of schedule.

- **The Public is often Left in the Dark as to the Risks Associated with Taking Accelerated Approval Drugs**

Under the current system, the FDA does not differentiate between conventional, standard approval and conditional, “accelerated” approval on the product’s label. In order for a patient or physician to learn whether the FDA has required further research on the product, the person must visit the FDA website and conduct a search. The website has proven difficult to navigate and specific information is difficult for a consumer to find.

- **FDA Provided Different Data to Rep. Markey and to the Public**

A number of discrepancies including missing information, inconsistencies in drug approval dates and status of studies were revealed when comparing the FDA data provided to Rep. Markey on March 30, 2005 with the data that is publicly available on the Postmarketing Study Commitments Database on the FDA website.

- **26.7% (36/135)** of the postmarketing study commitments reported had discrepancies between the information reported by the FDA in a March 30, 2005 letter to Rep. Markey and the information reported on the FDA Postmarketing Study Commitments database on the FDA website
- **60.0% (81/135)** of the postmarketing study commitments reported were provided by either the FDA website or the FDA letter to Rep. Markey, but not by both sources (ie. the information provided to Rep. Markey did not include any company commitments for Biogen, Corxia Corporation, ImClone Systems Inc., Ortho McNeil, Protherics, Seragen and the information available on the FDA website did not include commitments for drugs such as Casodex, Crixivan, Eloxatin, Epivir, Priftin, Rescriptor, etc.)
- **48.1% (65/135)** of the postmarketing study commitments reported had incomplete or missing information (from either the FDA website or the FDA letter to Rep. Markey) that was generally reported for other products (ie. the date the product was approved, the date the annual report was submitted or the projected date of completion).

Rep. Markey's staff has requested that the FDA identify the correct information and explain these discrepancies. The FDA has not yet provided a response. FDA's failure to appropriately track and monitor post-marketing study commitments has also been commented on by the Inspector General and Congress in the past. These latest discrepancies may be symptomatic of FDA's ongoing failure to appropriately track and monitor post-marketing study commitments.

- **Drug Company Shareholders May Not Know About a Company's Post-Marketing Study Commitments, or Other Risks Associated with the Consequences of a Failure to Conduct Required Studies**

Twenty-five publicly-traded companies whose securities are registered with the Securities and Exchange Commission have made post-marketing study commitments. According to information provided by the SEC:

- **68% (17/25)** of public companies have not disclosed any of their post-marketing study commitments to their shareholders in their filings with the SEC.
- **20% (5/25)** of public companies have disclosed all of their post-marketing study commitments to their shareholders in their filings with the SEC.

- **12% (3/25)** of public companies have selectively disclosed to their shareholders in their filings with the SEC some of their study commitments and not others.
- **80% (20/25)** of public companies have failed to disclose at least one of their post-marketing study commitments to their shareholders in their filings with the SEC.
- **32% (8/25)** of public companies have disclosed at least one of their post-marketing study commitments to their shareholders in their filings with the SEC.
- **38% (3/8)** of public companies that have disclosed post-marketing study commitments did so prior to Rep. Markey's letter requesting information from the SEC about this matter.
- **63% (5/8)** of public companies that have disclosed post-marketing study commitments did so only after Rep. Markey's letter requesting information from the SEC about this matter.

While the SEC reaches no conclusion about whether the failure to disclose this information constitutes a violation of any federal securities law, it notes that such laws do require disclosure of all material information and prohibit the omission of any material information. Since the failure of a company to carry out a post-marketing study on an accelerated approval drug, or the reporting of adverse results in a study can lead to action by the FDA to withdraw the drug from the market, the widespread failure to disclose this information raises potential shareholder protection issues.

- **The FDA Continues to Shirk Regulatory and Enforcement Responsibilities**

Under law, if a company does not conduct the study with due diligence, the FDA has the authority to withdraw the product from the market through an expedited process. However, the FDA has not withdrawn any products approved through the accelerated approval process on the basis of a failure of the sponsor to conduct the required post-marketing study.

II. Introduction

In December 2004, the Food and Drug Administration (FDA) announced that AstraZeneca's cancer product, Iressa –which had been approved through the FDA's accelerated approval process – was not an effective treatment for most cancer patients.¹ In the wake of this announcement Rep. Markey initiated a series of letters regarding the accelerated approval process, pharmaceutical companies' compliance with post-marketing study requirements, companies' disclosure of post-marketing study commitments to their shareholders and the FDA's actions to enforce company compliance.

The data which is the subject of this staff analysis can be found in the March 30, 2005 FDA Response to Rep. Markey (Appendix B) sent in response to Rep. Markey's letter to the FDA dated December 20, 2004 (Appendix A), and in the March 23, 2005 SEC response to Rep. Markey (Appendix D) sent in response to Rep. Markey's letter to the SEC dated February 17, 2005 (Appendix C) and the April 27, 2005 SEC response letter (Appendix E) sent in response to a phone call involving the Markey and SEC staff, which took place on March 31, 2005.

III. Background on the Accelerated Approval Process

Accelerated approval is an expedited approval process set up by the FDA to allow severely ill patients early access to promising new treatments. In December 1992, the FDA published new regulations (21 CFR 314, subpart H and 601 subpart E) to provide for an accelerated review process for products that treat serious and life-threatening illnesses and that provide meaningful therapeutic benefits over existing therapies.² In 1997, Congress passed the FDA Modernization Act which incorporated this approach into law in Section 112 of FDAMA (Section 506 of the act; 21 U.S.C. 356). According to the FDA website:

Under the accelerated approval process, FDA may approve products based on a surrogate marker or other clinical effect that is reasonably likely to predict clinical benefit, provided that the applicant conducts postmarketing studies to verify and describe the clinical benefit when there is uncertainty about the relation between the data submitted and clinical benefit or ultimate outcome. The accelerated approval process allows the product to enter the market sooner but with less complete clinical efficacy information than the standard review process requires. When using the accelerated approval process, FDA may require postmarketing studies to gather complete efficacy information and can withdraw marketing

¹ FDA Statement on Iressa. Rockville, Md.: Food and Drug Administration, December 17, 2004. (Accessed, December 20, 2005, at <http://www.fda.gov/bbs/topics/news/2004/new01145.html>) The FDA revised this statement and the original statement is no longer available at this address.

² Report to Congress Reports on Postmarketing Studies [FDAMA 130]. Rockville, Md.: Food and Drug Administration, April 4, 2002 (Accessed, May 25, 2005, <http://www.fda.gov/cber/fdama/pstmrktfdama130.htm>)

approval if the studies are not completed with due diligence or if the studies fail to verify clinical benefit of the product.³

In other words, the FDA approves a drug or biologic on the basis of promising but limited information about the safety and effectiveness on the condition that the company agrees to conduct further studies to confirm the safety and effectiveness of the drug after the drug enters the market. In order to be considered under accelerated approval, the product has to be designed to treat a serious or life-threatening disease for which there is no other treatment on the market. However, once the product is approved, the drug or biologic may be prescribed to anyone.

Accelerated approval is extremely important because it provides severely ill patients with new, early treatment options. If patients have no other option, it can often make sense for them to take a gamble on a drug that could potentially save their lives but also could potentially have negative side effects, or simply not work. Pharmaceutical companies have a legal obligation to follow up on the promise of the drug and confirm that the drug is safe and actually works.

The FDA and pharmaceutical companies also have a clear moral and ethical obligation to give patients an honest and complete assessment of the safety and effectiveness of pharmaceutical products. Patients trust that the FDA will do everything in its power to enforce a company's commitment to undertake follow-up studies. Making available the results from such follow up studies can be important as new drugs appear on the market to treat the same conditions. It is not in the best interest of either patient protection or shareholder protection for companies to neglect completion of studies that prove that their products both work and are safe or that the products have serious side-effects or are not as effective as originally hoped.

IV. The Importance of Post-marketing Studies: Iressa

The importance of post-marketing studies is highlighted by the recent case of Iressa. In May, 2003, Iressa, which is manufactured by AstraZeneca, was approved under the accelerated approval process for treatment of non-small cell lung cancer in individuals who have failed to respond to two or more courses of chemotherapy. Iressa showed promise in early studies. According to the FDA, "Iressa was approved because the data from clinical studies showed that it caused significant shrinkage in tumors in about 10% of patients, and this was thought likely to increase patients' overall survival time."⁴ The FDA approved Iressa, provided that AstraZeneca continue research on the drug to confirm the early results. Complying with the FDA's mandate, AstraZeneca

³ Report to Congress Reports on Postmarketing Studies [FDAMA 130]. Rockville, Md.: Food and Drug Administration, April 4, 2002 (Accessed, May 25, 2005, <http://www.fda.gov/cber/fdama/pstmrktfdama130.htm>)

⁴ FDA Statement on Iressa. Rockville, Md.: Food and Drug Administration, December 17, 2004. (Accessed, December 20, 2004, at <http://www.fda.gov/bbs/topics/news/2004/new01145.html>) The FDA revised this statement and the original statement is no longer available.

conducted a study in approximately 1700 patients to determine whether the drug would in fact prolong survival in comparison to patients taking placebo.⁵

On December 17, 2004, the FDA released a statement to inform the public that the post-marketing studies “comparing Iressa (gefitinib) with placebo in patients with non-small cell lung cancer who had failed other courses of cancer therapy showed no survival benefit from taking Iressa.”⁶ According to the *Boston Globe*, the median survival on the drug was 5.6 months, compared with 5.1 months on the placebo, a statistically meaningless difference.⁷ In other words, for most patients, Iressa doesn’t work.

In this announcement, the FDA assured patients that alternative therapies were available and instructed them to contact their physicians as soon as possible. Although Iressa is still available to consumers who have no other available options, this trial provided critical information to both physicians and patients who are trying to determine the best course of treatment for this horrible disease. If AstraZeneca had not conducted this important trial, patients and doctors may have continued to spend \$1,800⁸ a month for a drug that is ineffective for most patients when there are alternative treatments available.

AstraZeneca fulfilled its obligation to do a post-marketing study and found that Iressa was not effective. The company promptly reported this information to the FDA, which resulted in the Agency’s subsequent warning to doctors and the public.⁹ However, evidence contained in the FDA’s response to Rep. Markey’s letter indicates that many other companies break the rules and fail to conduct with due diligence the studies they promised to complete when they received approval.

V. Many Companies Fail to Complete Post-Marketing Studies

Although some companies do complete their required studies without any intervention from the FDA, the FDA has allowed many companies to stall or forgo completion of their required post-marketing confirmatory studies. Since 1992, 28 companies have made 91 postmarketing study commitments for 42 different

⁵ FDA Statement on Iressa. (Accessed, December 20, 2005, at <http://www.fda.gov/bbs/topics/news/2004/new01145.html>) The FDA revised this statement and the original statement is no longer available.

⁶ FDA Statement on Iressa. (Accessed, December 20, 2005, at <http://www.fda.gov/bbs/topics/news/2004/new01145.html>) The FDA revised this statement and the original statement is no longer available.

⁷ Raja Mishra, “Smart drug for lung cancer may be pulled from market” *Boston Globe* 5 April 2005: (accessed May 25, 2005, at http://www.boston.com/news/globe/health_science/articles/2005/04/05/smart_drug_for_lung_cancer_may_be_pulled_from_market/)

⁸ Mishra (accessed May 25, 2005, at http://www.boston.com/news/globe/health_science/articles/2005/04/05/smart_drug_for_lung_cancer_may_be_pulled_from_market/)

⁹ FDA Statement on Iressa. (Accessed, December 20, 2005, at <http://www.fda.gov/bbs/topics/news/2004/new01145.html>) The FDA revised this statement and the original statement is no longer available.

pharmaceutical products under the accelerated approval system. As of March 9, 2005, **46% (42/91)** of the study commitments that were made were not complete.¹⁰

Further, according to FDA data, the majority of these outstanding required confirmatory studies are not proceeding according to schedule.¹¹

- **50% (21/42)** of outstanding accelerated approval confirmatory studies have not been started, even though the drug is being marketed to consumers. Companies have been selling these products to the public for an average of **1 year and 10 months** and up to **6 years and 9 months** without even initiating the required studies.
- **7% (3/42)** of outstanding accelerated approval confirmatory studies have been initiated but are behind schedule.
- **43% (18/42)** of outstanding accelerated approval confirmatory studies are proceeding according to or ahead of schedule.

There are currently 16 pharmaceutical products that have outstanding confirmatory studies:¹²

1.	Alimta	Eli Lilly	Approved on 8/14/2004
2.	Arimidex	Astrazeneca	Approved on 9/5/2002
3.	Celebrex	GD Searle	Approved on 12/23/1999 ¹³
4.	Depocyt	Skyepharma	Approved on 4/1/1999
5.	Ethyol	Medimmune	Approved on 03/15/1996
6.	Gleevec	Novartis	Approved on 12/20/2002
7.	Iressa	Astrazeneca	Approved on 5/5/2003
8.	Luveris	Serono	Approved on 10/8/2004
9.	Mylotarg	Wyeth	Approved on 5/17/2000
10.	Proamatine	Shire	Approved on 9/6/1996
11.	Remodulin	United Therapeutics	Approved on 5/21/2002
12.	Sulfamylon	Mylan	Approved on 6/5/1998
13.	Synercid	King	Approved on 09/21/1999
14.	Truvada	Gilead	Approved on 8/2/2004

¹⁰ According to worksheets provided by the FDA (Appendices C, D, E, F& G). The data provided on the FDA Postmarketing Studies Commitments Database is not the same as the data provided to Rep. Markey. Please see appendix N for a side-by-side comparison of the data. Further, the FDA annual report to Congress “Report on the Performance of Drug and Biologics Firms in Conducting Postmarketing Commitment Studies; Availability” published in the Federal Register on February 8, 2005, includes all postmarketing study commitments made by companies regardless of whether they were required by the FDA as a condition of approval, not just those commitments required as a condition of accelerated approval.

¹¹ According to worksheets provided by the FDA (Appendices C, D, E & F).

¹² According to worksheets provided by the FDA (Appendices C, D, E & F).

¹³ The approval dates for ongoing studies were not included in the worksheets provided by the FDA (Appendices C, D, E & F). The approval dates for Celebrex, Ethyol, Mylotarg, Synercid and Viread were found in the Postmarketing Studies Commitments Database. Rockville, Md.: Food and Drug Administration, April 29, 2005. (Accessed May 30, 2005 at <http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm>)

15.	Velcade	Millennium	Approved on 5/13/2003
16.	Viread	Gilead	Approved on 10/26/2001

There are Seven Companies¹⁴ with Pending Studies (Outstanding accelerated approval confirmatory studies that have not been started, even though the drug is being marketed to consumers) for eight different products (as of March 9, 2005):¹⁵

1.	Astrazeneca	4 Pending Studies for Arimidex	Approved on 9/5/2002
		3 Pending Studies for Iressa	Approved on 5/5/2003
2.	Eli Lilly	2 Pending Studies for Alimta	Approved on 8/14/2004
3.	Gilead	2 Pending Studies for Truvada	Approved on 8/2/2004
4.	Millennium	4 Pending Studies for Velcade	Approved on 5/13/2003
5.	Mylan	1 Pending Study for Sulfamylon	Approved on 6/5/1998
6.	Novartis	3 Pending Studies for Gleevec	1 Approved on 12/20/2002 and 2 Approved on 5/20/2003
7.	Serono	2 Pending Studies for Luveris	Approved on 10/8/2004

There are Three Companies¹⁶ with Delayed Studies (Outstanding accelerated approval studies that have been initiated but are behind schedule) for three different products (as of March 9, 2005):¹⁷

1.	Shire	1 Delayed Study for Proamatine	Approved on 9/6/1996
2.	Skyepharma	1 Delayed Study for Depocyt	Approved on 4/1/1999
3.	United Therapeutics	1 Delayed Study for Remodulin	Approved on 5/21/2002

Although the information provided to Rep. Markey did not include explanations as to why the studies were delayed, the FDA Postmarketing Studies Commitments Database did include explanations. For example, Genzyme Biosurgery's study of Carticel SM Service, Autologous Cultured Chondrocytes was delayed "because the original study did not meet its endpoints" and Protherics study of CroFab, Crotalidae Polyvalent Immune Fab (Ovine) is delayed "because of low level of interest on the part of investigators."¹⁸

VI. FDA Fails to Inform Patients and Healthcare Professionals of the Existence of a Post-marketing Study Commitment

¹⁴ According to the FDA Postmarketing Studies Commitments Database, seven companies have pending studies: Astrazeneca has 2, Biogen Idec has 1, Genzyme has 2, King has 1, Mylan has 1, Ortho McNeil has 3 and Serono has 1. (See Appendix N or the FDA website <http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm>)

¹⁵ See Appendix D: FDA Worksheet "Pending Studies as of 3/9/05"

¹⁶ According to the FDA Postmarketing Studies Commitments Database, seven companies have delayed studies: Genzyme has 2, Gilead has 1, Biogen has 1, Protherics has 1, Shire has 1, Skyepharma has 1, United Therapeutics has 1. (See Appendix N or the FDA website <http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm>)

¹⁷ See Appendix E: FDA Worksheet "Delayed Studies as of 3/9/05"

¹⁸ Postmarketing Studies Commitments Database. Rockville, Md.: Food and Drug Administration, April 29, 2005. (Accessed May 19, 2005 at <http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm>)

In order to make decisions about the best course of treatment, it is important for healthcare professionals and patients to know that drugs approved under accelerated approval require further research to confirm their safety and efficacy. However, under the current system, the FDA does not differentiate between traditional approval and conditional approvals that are made through the accelerated approval process and require further research for the purposes of labeling.

Although the FDA does make information about post-marketing studies public through the FDA website and through annual notices in the Federal Register, the Agency does not make any effort to ensure that doctors or patients know which products were given full approval and which drugs were only given conditional approval.

Rep. Markey's letter requested information regarding ways in which consumers can find out whether a drug he/she is taking was approved using the accelerated approval process and whether the company has committed to completing further studies to confirm the safety or effectiveness of the product. The FDA's response was that,

Consumers who wish to identify products that were approved under accelerated approval may access the CDER New Drug and Biologic Approval Reports webpage at: <http://www.fda.gov/cder/rdmt/default.htm> for this information. The page is updated quarterly. It is also possible to search FDA's Post-marketing Commitments website at: <http://www.fda.gov/cder/pmc> and identify those PMC's that are required under accelerated approval. The website can be used to follow the process of these confirmatory studies; the website is updated quarterly in January, April, July and October of every year.¹⁹

In other words, in order for a physician or patient to determine whether the product they are using has research ongoing to confirm its safety and effectiveness, they must visit the FDA website.

Generally important information that the FDA wants to communicate to a patient or a physician about a product is included on the product's label. According to the FDA, "The FDA approved label is the official description of a drug product which includes indication (what the drug is used for); who should take it; adverse events (side effects); instructions for uses in pregnancy, children, and other populations; and safety information for the patient. Labels are often found inside drug product packaging."²⁰ However, information about post-approval study requirements made at the time of the approval of the product is not included in the label. If physicians or patients want to know whether the safety and efficacy of the product was confirmed prior to approval or whether the company is still in the process of conducting confirmatory studies, they have to search the FDA website.

¹⁹ See Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 4

²⁰ Drugs @ FDA Glossary of Terms. Rockville, Md.: Food and Drug Administration, September 10, 2004. (Accessed May 25, 2005 at, <http://www.fda.gov/cder/drugsatfda/Glossary.htm#label>)

In short, current labeling rules provide information regarding the safety and effectiveness of an accelerated approval drug (where the confirmatory studies are still incomplete) that appears to be just as complete as the information on fully-approved drugs (where all of the studies were completed and the clinical benefit was confirmed prior to approval.) This is misleading to consumers and doctors alike. The FDA should at least inform the patient and medical communities of the fact that studies that are necessary to confirm the safety and effectiveness of the drug are not complete.

VI. FDA Provided Different Data to Rep. Markey and to the Public

In the FDA's March 30, 2005 response to Rep. Markey's December 20, 2005 letter, the FDA stated that they had provided the full list of accelerated approval PMCs for pending, ongoing, delayed and terminated studies.²¹ However, the letter also stated that "It is also possible to search FDA's Post-marketing Commitments website at: <http://www.fda.gov/cder/pmc> and identify those PMC's that are required under accelerated approval."²²

In comparing the data in the worksheets provided to Rep. Markey on March 30, 2005 with the data that is publicly available on the Postmarketing Study Commitments Database on the FDA website,²³ staff identified significant discrepancies in the data.²⁴ Discrepancies include missing information, inconsistencies in drug approval dates and status of studies.

- **27% (36/135)** of the postmarketing study commitments reported had discrepancies between the information reported by the FDA in a March 30, 2005 letter to Rep. Markey and the information reported on the FDA Postmarketing Study Commitments database on the FDA website (ie. there was discrepancy in the date that the final report was submitted, the date the drug was approved, or the status of the trial.) (Highlighted in yellow in Appendix N)
- **60% (81/135)** of the postmarketing study commitments reported were provided by either the FDA website or the FDA letter to Rep. Markey, but not by both sources. (ie. the information provided to Rep. Markey did not include any company commitments for Biogen, Corxia Corporation, ImClone Systems Inc., Ortho McNeil, Protherics, Seragen and the information available on the FDA website did not include commitments for drugs such as Casodex, Crixivan, Eloxatin, Epivir, Priftin, Rescriptor, Viread etc.) (Highlighted in red in Appendix N)
- **48% (65/135)** of the postmarketing study commitments reported had incomplete or missing information (from either the FDA website or the FDA

²¹ See Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 5-6

²² See Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 4

²³ Postmarketing Studies Commitments Database. Rockville, Md.: Food and Drug Administration, April 29, 2005. (Accessed May 19, 2005 at <http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm>)

²⁴ See Appendix N: Rep. Markey Staff Summary of Discrepancies in FDA Data

letter to Rep. Markey) that was generally reported for other products (ie. the date the product was approved, the date the annual report was submitted or the projected date of completion. (Highlighted in blue in Appendix N)

For a side-by-side comparison of the data provided to Rep. Markey in the March 30, 2005 letter and the data in the Postmarketing Studies Commitments Database, please see Appendix N: “Rep. Markey Staff Summary of Discrepancies in FDA Data.”

The FDA website states that, “The site includes postmarketing study commitments made with the Center for Biologics Evaluation and Research (CBER) and with the Center for Drug Evaluation and Research (CDER). The postmarketing study commitments on this Web site are those that have been reviewed for accuracy.”²⁵

Further there was a discrepancy in the total number of postmarketing study commitments cited by the letter text (Appendix B) and provided in the FDA worksheets (Appendices C, D, E, F &G). The March 30, 2005 letter to Rep. Markey states that 80 commitments have been made,²⁶ but the worksheets provided by the FDA that outlined the study commitments listed 91.²⁷

On May 20, 2005, Rep. Markey’s staff requested that the FDA identify the correct information and explain these discrepancies.²⁸ The FDA has not yet provided a response.

Some of the discrepancies may be explained because one data set was up-to-date as of March 9, 2005 and the other was up-to-date as of April 29, 2005. The FDA also indicated in a conversation with Rep. Markey’s staff that some other discrepancies may be explained by the fact that the FDA failed to provide Rep. Markey with information on postmarketing study commitments made for biologics. However, these explanations do not appear to explain all of the differences in the data sets.

The FDA’s failure to appropriately track and monitor post-marketing study commitments has been commented on in previous reports. For example, in 1996, the Office of the Inspector General (OIG) of the Department of Health and Human Services (HHS) conducted an investigation of “the effectiveness of the Food and Drug Administration’s (FDA) monitoring of postmarketing studies for prescription drugs.”²⁹ The OIG found that the FDA did not have a comprehensive tracking system for postmarketing study commitments and ensuring compliance with these commitments. In the report, the OIG recommended that the FDA “establish standards, procedures, or guidelines for carrying out monitoring and tracking

²⁵ “Postmarketing Study Commitments: Frequently Asked Questions (FAQ)” Rockville, Md.: Food and Drug Administration, April 29, 2005. (Accessed May 26, 2005, at <http://www.fda.gov/cder/pmc/pmcfqa.htm>)

²⁶ See Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 5-6

²⁷ See Appendices C, D, E, F &G

²⁸ See Appendix L: Rep. Markey Staff Letter to FDA, May 20, 2005

²⁹ “Postmarketing Studies Of Prescription Drugs” Department of Health and Human Services: Office of Inspector General. May 1996. (Accessed May 26, 2005 at <http://oig.hhs.gov/oei/reports/oei-03-94-00760.pdf>)

objectives; and establish accountability for monitoring tracking and bringing commitments to closure.”³⁰ The FDA agreed to make changes and began work on a new tracking/compliance system.

In 1997, Congress passed the Food and Drug Administration Modernization Act (FDAMA), and added a provision that requires companies to report to FDA annually on the progress of postmarketing study commitments. Following enactment of FDAMA, FDA initiated a number of steps to implement the provisions of Section 130 on postmarketing studies. The FDA began requiring annual postmarketing study progress reports in May 2001. They also claimed to have developed data tracking systems to improve its monitoring and processing of annual status reports and study final reports. According to the FDA report to Congress, “The databases were implemented in July, 2000 at CBER and July 2001 at CDER. The databases will be updated as submissions are received and reviews are completed. The databases will be used to provide information to a public FDA Web site on postmarketing studies.”³¹

Thus it would appear that these latest discrepancies in FDA data may be symptomatic of FDA’s ongoing failure to appropriately track and monitor post-marketing study commitments.

VIII. Companies Fail to Inform Shareholders of Postmarketing Study Commitments

Not only does the FDA make it difficult for the public to learn about post-marketing study commitments, companies often fail to inform their shareholders about their post-marketing commitments and the status of those commitments.

According to the SEC,

...the federal securities laws are premised on the idea that a company must disclose information that a reasonable investor would think is significant, in the context of all available information, in assessing an investment in the company. Materiality generally turns on questions of financial impact to the company... Companies have strong incentives to make prudent judgments about materiality. Investors can sue a company... when... the company’s disclosure contains material misstatements or material omissions.³²

³⁰ “Postmarketing Studies Of Prescription Drugs” Department of Health and Human Services: Office of Inspector General. May 1996. (Accessed May 26, 2005 at <http://oig.hhs.gov/oei/reports/oei-03-94-00760.pdf>)

³¹ Report to Congress Reports on Postmarketing Studies [FDAMA 130]. Rockville, Md.: Food and Drug Administration, April 4, 2002 (Accessed, May 25, 2005, <http://www.fda.gov/cber/fdama/pstmrktfdama130.htm>)

³² Appendix I: SEC Response to Rep. Markey Letter, March 23, 2005, page 3

In response to Rep. Markey's inquiries, the SEC reviewed all of the companies that, according to the FDA, had, at some point, a post-marketing study commitment. According to the SEC, "For each public company, [the SEC] examined the company's annual reports for each of the last three years to determine whether the company provided disclosures regarding its post-marketing studies or obligations. Also, if the commitments were scheduled to commence prior to the periods these reports covered, [the SEC] examined the annual reports pertaining to the appropriate prior periods."³³

Since the inception of the accelerated approval program, twenty-eight companies have received accelerated approval with the requirement that they conduct further post-marketing studies. Twenty-five of these companies are public companies that are required to comply with SEC disclosure requirements. According to information provided by the SEC,³⁴

- **68% (17/25)** of public companies have not disclosed any of their post-marketing study commitments to their shareholders in their filings with the SEC.
- **20% (5/25)** of public companies have disclosed all of their post-marketing study commitments to their shareholders in their filings with the SEC.
- **12% (3/25)** of companies have selectively disclosed to their shareholders in their filings with the SEC some of their study commitments and not others.
- **80% (20/25)** of public companies have failed to disclose at least one of their post-marketing study commitments to their shareholders in their filings with the SEC.
- **32% (8/25)** of public companies have disclosed at least one of their post-marketing study commitments to their shareholders in their filings with the SEC.

According to the SEC,

...a pharmaceutical or biotechnology company would be required to disclose information regarding the status of a particular post-marketing study commitment if the information is material, that is, if investors would find that information to be significant in assessing an investment in that company. Whether investors might consider such information to be significant to a company would depend upon the company's business and its current or future results of operations. Numerous events, conditions or factors comprise the total mix of information available about the company, its financial condition and its prospects may enter into the determination as to whether any one piece of information would be material to investors.³⁵

³³ Appendix J: SEC Follow-Up Letter, April 27, 2005

³⁴ Appendix K: SEC "Attachment B," April 27, 2005, "Disclosure of post-marketing studies or obligations."

³⁵ Appendix I: SEC Response to Rep. Markey Letter, March 23, 2005, page 3

Therefore, while some post-marketing study commitments may be material to shareholders and require disclosure under law, others may not. In providing information to Rep. Markey regarding post-marketing disclosures, the SEC did not evaluate the materiality of individual post-marketing study commitments made by specific companies.

The SEC informed Rep. Markey, however, that **68% (17/25)** of public companies that are required to conduct postmarketing studies have not disclosed any of their post-marketing studies.³⁶ Those companies are:

- | | |
|-----------------------------------|--|
| 1. Abbott Laboratories | Abbott Park, IL |
| 2. Aventis | Bridgewater, NJ |
| 3. Bayer | Research Triangle Park, NC |
| 4. Eli Lilly | Indianapolis, IN |
| 5. GD Searle³⁷ | Pfizer Headquarters: New York, NY |
| 6. GlaxoSmithKline | Research Triangle Park, NC |
| 7. King | Bristol, TN |
| 8. Merck | Whitehouse Station, NJ |
| 9. Mylan | Canonsburg, PA |
| 10. Novartis | Cambridge, MA |
| 11. Pharmacia³⁸ | Pfizer Headquarters: New York, NY |
| 12. Sanofi | New York, NY |
| 13. Schering | Kenilworth, NJ |
| 14. Serono | Rockland, MA |
| 15. Shire | Wayne, PA |
| 16. Skyepharma | New York, NY |
| 17. Wyeth | Collegeville, PA |

Of the 20 public companies that have not disclosed at least one of the postmarketing study commitments, **50% (10/20)** have post-marketing study commitments that have not been fulfilled. The companies with outstanding, undisclosed commitments are:

- | | |
|----------------------------------|--|
| 1. Astrazeneca | Wilmington, DE |
| 2. Eli Lilly | Indianapolis, IN |
| 3. GD Searle³⁹ | Pfizer Headquarters in New York, NY |
| 4. King | Bristol, TN |
| 5. Mylan | Canonsburg, PA |
| 6. Novartis | Cambridge, MA |
| 7. Serono | Rockland, MA |
| 8. Shire | Wayne, PA |
| 9. Skyepharma | New York, NY |
| 10. Wyeth | Collegeville, PA |

³⁶ See Appendix K: SEC “Attachment B,” April 27, 2005, “Disclosure of post-marketing studies or obligations.”

³⁷ Became **Pharmacia** in April 2000 and was acquired by **Pfizer** April 16, 2003

³⁸ Acquired by **Pfizer** April 16, 2003

³⁹ **GD Searle** made the original study commitment. GD Searle was acquired by Pfizer on April 16, 2003.

Public companies have made 38 different post-marketing study commitments for 16 different products that they have not yet fulfilled. Of these ongoing commitments, **55% (21/38)** have not been disclosed in filings submitted to the SEC.

The 16 products produced by public companies that are the subject of the 38 unfulfilled postmarketing study commitments are as follows:

Ten drugs approved through accelerated approval have undisclosed, unfulfilled commitments:

- | | |
|-----------------------|----------------------------------|
| 1. Alimta | Eli Lilly |
| 2. Arimidex | Astrazeneca |
| 3. Celebrex | GD Searle/ Pharmacia Corp |
| 4. Depocyt | Skyepharma |
| 5. Gleevec | Novartis |
| 6. Luveris | Serono |
| 7. Mylotarg | Wyeth |
| 8. Proamatine | Shire |
| 9. Synercid | King |
| 10. Sulfamylon | Mylan |

Six drugs approved through accelerated approval have disclosed, unfulfilled commitments:

- | | |
|---------------------|----------------------------|
| 1. Ethyol | Medimmune |
| 2. Iressa | Astrazeneca |
| 3. Remodulin | United Therapeutics |
| 4. Truvada | Gilead |
| 5. Viread | Gilead |
| 6. Velcade | Milennium |

Of the ten companies that have outstanding, undisclosed studies, **50% (5/10)** of these companies have post-marketing study commitments that involve studies that are pending. (This means that the drug has been approved and is being marketed to consumers. However, the company has not started the study that is required under law to confirm the safety or effectiveness of the drug.) The companies with pending study commitments are:

- | | | |
|-----------------------|---------------------------------------|---|
| 1. Astrazeneca | 4 pending studies for Arimidex | approved on 9/5/2002 |
| 2. Eli Lilly | 2 pending studies for Alimta | approved on 8/14/2004 |
| 3. Mylan | 1 pending study for Sulfamylon | approved on 6/5/1998 |
| 4. Novartis | 3 pending studies for Gleevec | 2 approved on 5/20/2003
and 1 approved on 12/20/2002 |
| 5. Serono | 2 pending studies for Luveris | approved on 10/8/2004 |

Of the ten companies that have outstanding, undisclosed studies, **20% (2/10)** of these companies have post-marketing study commitments that have studies that are delayed. The companies with delayed studies commitments are:

- | | | |
|----------------------|---------------------------------------|----------------------|
| 1. Shire | 1 delayed study for Proamatine | approved on 9/6/1996 |
| 2. Skyepharma | 1 delayed study for Depocyt | approved on 4/1/1999 |

It is important to note that the SEC did not assess the materiality of these commitments, so the mere fact that a post-marketing study commitment was not disclosed in a companies' SEC filings does not necessarily mean that the company has omitted material information or made a material misstatement to investors.

However, in examining company statements about the aforementioned drugs, it appears that they significantly contribute to the financial success of the companies. For example:

- **Shire's Proamatine:** According to Shire's Fiscal Year 2004 annual report submitted to the SEC, for the year ending December 31, 2003, total sales for Proamatine were **\$49.3 million** representing 4.9% of Shire's total sales.⁴⁰
- **Skyepharma's DepoCyt:** In the SkyePharma April 27, 2005 presentation "Making Good Drugs Better: 2004 Full Year Results," the company claimed that, "2004 global in-market sales [for DepoCyt] doubled to **\$8 million**" which represents approximately 6.8% of total sales.⁴¹
- **Novartis' Gleevec:** According to the 2004 "Investor Relations Release," sales for Gleevec totaled **\$1.634 billion** in full year 2004. That represented approximately 8.8% of total sales in full year 2004. The report also described the drugs as a "blockbuster" drug.⁴²

Although the SEC did not assess the materiality of these commitments, the failure to disclose these study commitments does raise serious questions about the companies' willingness to be open and forthcoming with their shareholders about potential risks which might be associated with drugs the company is marketing to the public, as well as regulatory risks associated with the possibility that the drug may be withdrawn from sale by the FDA if either a post-marketing study commitment is not met, or if the study's results prove negative.

The fact that the FDA believed that it was important for the company to conduct a post-marketing study to confirm the safety or efficacy of a product means that there is still a risk that the study could reveal significant safety concerns (as in the case of

⁴⁰ Annual Report Pursuant To Section 13 Or 15(D) of The Securities Exchange Act of 1934 for The Fiscal Year Ended December 31, 2004. Shire Pharmaceuticals. March 15, 2005. (Accessed May 25, 2005 at <http://www.shire.com/shirepharma/uploads/reports/10K2004.pdf>)

⁴¹ "Making Good Drugs Better: 2004 Full Year Results." SkyePharma. April 27, 2005, (Accessed May 25, 2005 at http://media.corporate-ir.net/media_files/nsd/skye/presentations/2004FinalResults2.ppt#16)

⁴² "Investor Relations Release: Novartis delivers record results with strong double-digit net sales and earnings growth in 2004." Novartis. January 20, 2005. (Accessed May 26, 2005 at http://www.novartis.com/downloads_new/investors/full_year_2004_results_release.pdf)

Tysabri⁴³) or show that the product does not work (as in the case of Iressa⁴⁴). If the study reveals negative results, then the company may be forced to significantly limit the number of people that they market to or in the worst case scenario, the company could be forced to withdraw the drug from the market. If the companies' revenues or earnings could be significantly affected by sales of the drug in question, then the fact that the safety or efficacy of the drug has not been confirmed increases the risk for the shareholders.

Further, if a company does not conduct the study with due diligence, then the company runs the risk of the FDA withdrawing the drug from the market. Therefore, from a shareholder perspective, it therefore would appear to be important to know about both the existence of a post-marketing study commitment and the status of the studies undertaken pursuant to this commitment.

XI. Rep. Markey's Inquiry Appears to Have Spurred Company Disclosures

More than half of all of the companies that disclosed their post-marketing study commitments did so only after Rep. Markey made a public inquiry to the SEC regarding post-marketing study commitments on February 17, 2005.⁴⁵

- **37.5% (3/8)** of companies that have disclosed post-marketing study commitments did so prior to Rep. Markey's inquiry.
- **62.5% (5/8)** of companies that have disclosed post-marketing study commitments did so only after Rep. Markey's inquiry.

Of the companies that have disclosed their post-marketing study commitments, only **Agouron Pharmaceuticals**⁴⁶ **Alza Corp** and **Bristol Myers Squibb** disclosed their studies to their shareholders prior to Rep. Markey's inquiry to the SEC regarding post-marketing study disclosures on February 17, 2005. All of the other post-marketing commitment disclosures came after the Markey inquiry.

Disclosures prior to Rep. Markey's inquiry:⁴⁷

⁴³ FDA Public Health Advisory: Suspended Marketing of Tysabri (natalizumab) Rockville, Md.: Food and Drug Administration, March 3, 2005 (Accessed May 25, 2005 at <http://www.fda.gov/cder/drug/advisory/natalizumab.htm>)

⁴⁴ FDA Statement on Iressa. (Accessed, December 20, 2005, at <http://www.fda.gov/bbs/topics/news/2004/new01145.html>) The FDA revised this statement and the original statement is no longer available.

⁴⁵ See Appendix K: SEC "Attachment B," April 27, 2005, "Disclosure of post-marketing studies or obligations."

⁴⁶ **Agouron Pharmaceuticals** was acquired by **Warner-Lambert** in May 1999, which merged with **Pfizer** in June 2000,

⁴⁷ See Appendix K: SEC "Attachment B," April 27, 2005, "Disclosure of post-marketing studies or obligations."

1. **Agouron Pharmaceuticals** disclosed post-marketing study commitments for Viracept on August 21, 1997, August 4, 1998, and October 28, 1998. Viracept was approved on March 14, 1997.
2. **Alza** disclosed post-marketing study commitments for Doxil on March 29, 2000 and March 29, 2001. Doxil was approved on June 28, 1999.
3. **Bristol-Myers Squibb** disclosed post-marketing study commitments for Zerit on March 28, 1996. Zerit was approved on June 24, 1994.

Disclosures after Rep. Markey's inquiry:⁴⁸

1. **Astrazeneca** disclosed post-marketing study commitments for Iressa on February 25, 2005.
2. **United Therapeutics** disclosed post-marketing study commitments for Remodulin on February 25, 2005. Remodulin was approved on 5/21/2002.
3. **Millennium** disclosed post-marketing study commitments for Velcade on March 9, 2005. Velcade was approved on 5/13/2003.
4. **Medimmune** disclosed post-marketing study commitments for Ethyol on March 9, 2005.
5. **Gilead** disclosed post-marketing study commitments for Truvada on March 14, 2005.

This data suggests that only a few companies routinely disclose post-marketing study commitments, while others have done so only after Congressional oversight and subsequent public attention was focused on this issue, and still others have never disclosed to their shareholders that drugs their companies were marketing to the public were approved only on the basis of a commitment by the company to undertake post-marketing studies.

X. FDA Fails to Enforce Post-Marketing Study Commitments

Under the current FDA accelerated approval system, approval is conditioned upon the sponsor's willingness to perform post-marketing studies to verify the drug's clinical benefit. If the company does not conduct the study with due diligence, the FDA has the authority to withdraw the product from the market through an expedited process. The statute governing this process is Section 506 of the Food and Drug Administration Modernization Act of 1997 (21 U.S.C. 356), which states:

“The Secretary may withdraw approval of a fast track product using expedited procedures (as prescribed by the Secretary in regulations which shall include an opportunity for an informal hearing) if-

(A) the sponsor fails to conduct any required post-approval study of the fast track drug with due diligence;

(B) a post-approval study of the fast track product fails to verify clinical benefit of the product;

⁴⁸ See Appendix K: SEC “Attachment B,” April 27, 2005, “Disclosure of post-marketing studies or obligations.”

- (C) *other evidence demonstrates that the fast track product is not safe or effective under the conditions of use; or*
- (D) *the sponsor disseminates false or misleading promotional materials with respect to the product.*”

According to the FDA, “Completion of post-marketing confirmatory studies is part of the required process established by FDA regulations for accelerated approval.”⁴⁹ The FDA claimed that “Assuring completion of these studies in a timely manner is part of [the Center for Drug Evaluation and Research’s Office of New Drugs] routine responsibilities, as is prompt and careful review of the studies as they are planned and submitted.”⁵⁰ According to the FDA’s April 4, 2002, “Report to Congress: Reports on Postmarketing Studies [FDAMA 130],” the FDA’s “enforcement authorities have worked well when clinical benefit has not been adequately demonstrated or when patient safety has been at risk. It is our intent to diligently monitor industry and FDA performance concerning the conduct of postmarketing studies.”⁵¹

However, the FDA also confirmed that “To date, there have not been any withdrawals of the products approved under accelerated approval related to a failure of the sponsor to conduct the required post-marketing confirmatory trial.”⁵²

The FDA justified this inaction by claiming that, “When warranted, there have been public discussions of delays in conversion of applications approved under accelerated approval to full approval.”⁵³ However, it appears that many companies may need more than a public discussion to motivate them to complete their studies.

If the FDA has never acted to ensure that companies complete studies that are necessary to confirm that products are safe and effective, then FDA is failing to protect the public health.

XI. Under the Current System Bad Actors Have Few Incentives to Complete Post-Marketing Confirmatory Studies

According to the FDA, “Completion of post-marketing confirmatory studies is part of the required process established by FDA regulations for accelerated approval; thus, incentives are not provided for fulfilling regulatory requirements. Companies face the possibility of product withdrawal if confirmatory studies are not completed with due diligence or fail to demonstrate clinical benefit.”⁵⁴

⁴⁹ Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 4

⁵⁰ Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 2-3

⁵¹ Report to Congress Reports on Postmarketing Studies [FDAMA 130]. Rockville, Md.: Food and Drug Administration, April 4, 2002 (Accessed, May 25, 2005, <http://www.fda.gov/cber/fdama/pstmrktfdama130.htm>)

⁵² Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 3

⁵³ Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 3

⁵⁴ Appendix B: FDA Response to Rep. Markey Letter, March 30, 2005, page 4

However, if the FDA never penalizes companies who fail to conduct the required confirmatory studies, there would appear to be little regulatory incentive in place for drug companies to complete these studies. Moreover, if shareholders are not informed, and therefore are not aware, of the conditional nature of accelerated approval, there would appear to be little likelihood of any market pressure from shareholders on the company by discounting shares of the stocks of those companies that fail to comply with their study commitments. Under the current system, the completion of the study does not provide the company with any additional benefit except for the peace of mind that they have confirmed the safety and efficacy of the drug, however, the same study carries a financial burden and, depending on the outcome, a potential risk to the future profitability of the product.

From a financial perspective post-marketing confirmatory studies are very expensive and completion of the study does nothing to increase profits. Once the company gets approval (even if it is through the accelerated approval process) the company generally has access to the entire market with no strings attached. Companies do not have to include any additional statements on the label for drugs approved under accelerated approval that informs the consumer that the company is required to do more research on the drug to confirm that it is safe and effective.

Under the current system there are few benefits and numerous risks associated with conducting post-marketing studies, so it is to companies' advantage to delay their completion indefinitely.

XII. Post-Marketing Studies: From Recommendation to Requirement

When a mandate is not enforced, then it is often viewed as a recommendation rather than a requirement. Unfortunately, it seems that some companies need more than a recommendation to act in the best interest of the public health.

When shareholders learn that companies have not been disclosing post-marketing study commitments or the status of those studies, they may begin to ask questions. In an efficient market, shareholders would put pressure on companies to disclose the existence of post-marketing study commitments and complete them, and if companies fail to do so with due diligence, shareholders would hold them accountable, either by forcing changes in corporate governance or by selling shares in the company.

However, it is not the responsibility of those who have invested in drug company stocks to protect public health – they are, quite naturally, focused on the companies' financial and operational performance and its future prospects for growth. The FDA is the agency that is tasked with protecting the public health and acting in best interest of the patient community.

The FDA's failure to take action to ensure that companies complete required post-marketing confirmatory studies may stem, in part, from the FDA's limited desire to enforce its own regulations. While the FDA has authority to act, at a practical level it may

find it very difficult to withdraw a drug from the market, even if there is significant evidence of a safety concern. Patients who suffer from a serious or life-threatening disease are reluctant to have the government withdraw from the market a drug that they may believe works for them, especially if the reason for withdrawal is not based on evidence that the drug is dangerous or ineffective but rather because the company has violated an agreement with the government.

In the FDA's April 4, 2002, "Report to Congress," the FDA stated that "If non-compliance is a problem, FDA intends to provide information to Congress in support of a request for additional legal authorities."⁵⁵ In light of the apparent failure of companies to complete postmarketing studies in a timely manner, Rep. Markey asked the FDA, "what additional enforcement authorities do you think would be effective in ensuring that companies comply with the requirements to complete post-marketing studies?"⁵⁶ The FDA did not answer the question in its response to Rep. Markey and did not include any recommendations for more appropriate enforcement mechanisms.

Although the FDA should not be forced to take promising drugs away from patients simply because companies refuse to conduct the required studies, if companies fail to uphold their post-marketing study commitments, then in the interest of public health, the FDA needs to have some alternate means of enforcement. For example, there should be significant fines levied on companies that do not conduct their studies with due diligence or there should be enhanced penalties associated with any harm that occurs to a consumer because a post-marketing study was never undertaken or not completed in a timely manner. This would shift the risk-reward analysis in favor of doing the promised studies. Clearly an empty threat to withdraw a drug from the market is not sufficient to convince companies that they need to complete their agreed upon post-marketing studies.

The FDA needs to start enforcing the completion of these studies. If the FDA believes that the current enforcement mechanisms are inappropriate the agency should make recommendations as to the appropriate means of enforcement. The public deserves to know whether drugs that were given accelerated approval are safe and whether they actually work, and that is what post-marketing confirmatory studies are supposed to help determine.

XIII. Conclusion

Accelerated approval is an important drug review mechanism that is designed to help desperate patients with life-threatening illnesses have increased access to new, promising treatments. However, the current system is broken.

- The majority of required post-marketing confirmatory studies are not proceeding according to schedule.

⁵⁵ Report to Congress Reports on Postmarketing Studies [FDAMA 130]. Rockville, Md.: Food and Drug Administration, April 4, 2002 (Accessed, May 25, 2005, <http://www.fda.gov/cber/fdama/pstmrktfdama130.htm>)

⁵⁶ Appendix A: Rep. Markey Letter to the FDA, December 20, 2004, page 4

- Consumers are being misled by a system which does not require companies to inform consumers that an accelerated approval drug requires further study to confirm safety and efficacy. The FDA needs to adjust its labeling requirements so that the consumer is made aware that an accelerated approval drug is subject to further study to address questions about safety and/or efficacy.
- Companies do not routinely disclose post-marketing study commitments, and therefore shareholders are often left in the dark as to the risks associated with the uncertainty of the drug's future.
- The FDA continues to shirk its duty to enforce compliance.

Accelerated approval was supposed to be a system of “approval today, proof tomorrow;” not “approval today, no further proof needed.” If the FDA does not enforce company compliance with conducting post-marketing study commitments, then the public will never know if the products that they believe are safe and effective are no better than sugar pills or may be even dangerous to their health.