



## ***Bayer Corporation: The Recall of Phenylpropanolamine (PPA)***

For years, the consumer care division of Bayer Corporation has successfully marketed a number of well-known brands that have earned the trust of American consumers. These brands include Bayer aspirin, Aleve analgesic, Phillips' Milk of Magnesia, One-A-Day vitamins, and Alka-Seltzer medicines. Responding to concerns raised about an ingredient found in some of its products, Bayer and several other drug manufacturers co-sponsored a study to assess the safety of this ingredient. Not only was Bayer interested in the results, the Food and Drug Administration (FDA) was interested as well.

The results of the study concluded that the ingredient carried a risk. However, Bayer and the FDA did not agree on the severity of the risk. As a result, Bayer's supply chain was not prepared when the FDA requested a voluntary recall of all products containing the ingredient. Perhaps more importantly, Bayer management had not anticipated the media's interpretation of the FDA actions. The resulting headlines would likely tarnish the reputation of one of Bayer's key brands, Alka-Seltzer. If not addressed properly by the company, the headlines also had the potential to jeopardize the images of all the Bayer brands. Please see Exhibit 1 for a historical timeline of Alka-Seltzer from its introduction in 1931 through the FDA's actions in 2000.

### **Company Overview**

Bayer Corporation is the wholly owned U.S. subsidiary of the German chemicals and pharmaceuticals giant, Bayer AG. Bayer AG's activities are divided into four business segments – Health Care, Agriculture, Polymers, and Chemicals – which comprise 15 business groups worldwide. The parent firm, based in Leverkusen, Germany, was formed in 1863 by chemical salesman Friedrich Bayer and Johann Friedrich Weskott. Bayer AG is made up of more than 350 companies in 150 countries. The majority of its sales come from Europe.

---

This case was prepared by Research Assistants Daniel Hwang, Michael Kolar, and Brendan Cox under the direction of James S. O'Rourke, Concurrent Associate Professor of Management, as the basis for class discussion rather than to illustrate either effective or ineffective handling of an administrative situation. Information was gathered from corporate as well as public sources.

Copyright ©2001. Eugene D. Fanning Center for Business Communication. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, used in a spreadsheet, or transmitted in any form by any means – electronic, mechanical, photocopying, recording, or otherwise – without permission.

In 1899, Bayer invented aspirin and changed the world forever. Western medicine finally had an inexpensive and reliable means for relieving pain and reducing fevers. Today, Bayer aspirin is a staple in most medicine chests and has been found to prevent blood clots, thereby reducing the risk of strokes and heart attacks.

Bayer Corporation invests 80 percent of its research and development dollars in health care and life sciences projects. It operates 50 sales offices and 50 manufacturing operations, while marketing some 10,000 products from nine divisions: agriculture; coatings and colorants; consumer care; diagnostics; fibers, additives, and rubber; industrial chemicals; pharmaceuticals; plastics; and polyurethanes. (Exhibit 2)<sup>1</sup> While Bayer's flagship product, aspirin, has been a strong sales performer throughout its existence, the company's robust research and development budget has enabled it to bring several other breakthrough over-the-counter (OTC) pharmaceutical products to the market.

### **Alka-Seltzer Medicines**

Alka-Seltzer is an example of a breakthrough product introduced by Bayer. The original product was developed in the late 1920s when it was discovered that the main ingredients, acetylsalicylic acid and sodium bicarbonate, helped to combat flu symptoms. Today, products marketed under the brand are available in over 50 countries worldwide. The brand was first marketed in 1931 and gained mass popularity in the 1950s through advertisements about its effervescent nature, often featuring the product's mascot, "Speedy." However, Alka-Seltzer remedies are also currently available in liqui-gel and non-effervescent tablet forms. Though it was originally marketed to provide relief of headaches, stomach problems, and heartburn, many of today's Alka-Seltzer products are specifically formulated to provide relief of cold and flu symptoms. These products are known as Alka-Seltzer Plus cold medicines. Bayer had invested considerable resources in cultivating the Alka-Seltzer Plus brand. By 1998, annual advertising expenditures totaled over \$44.8 million, of which 62% was spent on promoting the effervescent tablets.<sup>2</sup>

### **A Key Ingredient: PPA**

Perhaps the most common symptom of cold and flu is sinus congestion. Many remedies contain phenylpropanolamine (PPA) because the chemical is highly effective in providing relief of sinus congestion. PPA is a stimulant similar to amphetamine and is also used in the

---

<sup>1</sup> <http://www.bayerus.com/about/org.htm>

<sup>2</sup> Competitive Media Reporting. Ad \$ Summary: January-December 1998, Book I. New York: 1999, p. 98.

manufacture of weight loss drugs because of its ability to act as an appetite suppressant. In addition to Alka-Seltzer Plus, PPA can be found in other popular cold medicine brands such as Comtrex, Dimetapp, and Robitussin.<sup>3</sup> The medication has been on the market for 50 years with annual usage surpassing one billion doses.<sup>4</sup> While Alka-Seltzer Plus cold medicines are available in both effervescent and liqui-gel forms, only the effervescent medicines contain PPA.

### **Federal Drug Administration Organizational Overview**

As a unit of the U.S. Department of Health and Human Services, the FDA plays a critical role in the safety and security of the public health. Its mission statement is as follows:<sup>5</sup>

1. To promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner;
2. With respect to such products, protect the public health by ensuring that foods are safe, wholesome, sanitary, and properly labeled; human and veterinary drugs are safe and effective; there is reasonable assurance of the safety and effectiveness of devices intended for human use; cosmetics are safe and properly labeled, and; public health and safety are protected from electronic product radiation;
3. Participate through appropriate processes with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements; and,
4. As determined to be appropriate by the Secretary (of Health and Human Services), carry out paragraphs (1) through (3) in consultation with experts in science, medicine, and public health, and in cooperation with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products.

Of the several regulatory bodies within the FDA, the Center for Drug Evaluation and Research (CDER) focuses on both prescription and OTC drug markets. More specifically, all OTC initiatives are handled within CDER at the Office of Drug Evaluation V, Division of OTC Products. (Exhibit 3)

---

<sup>3</sup> <http://healthwatch.medscape.com>

<sup>4</sup> "Phenylpropanolamine & Risk of Hemorrhagic Stroke – Final Report of HSP." Yale University, May 2000.

<sup>5</sup> <http://www.fda.gov>

## FDA Drug Recall Policy and Process

As defined by the FDA, a recall is a “voluntary action that takes place because manufacturers and distributors carry out their responsibility to protect the public health and well-being from products that present a risk of injury or gross deception or are otherwise defective.”<sup>6</sup> In the event that manufacturers or distributors refuse or fail to undertake a FDA requested recall, the FDA may pursue a court approved seizure. An ad hoc committee of FDA scientists evaluates all drugs being recalled or considered for recall. This committee may also elect to seek outside consultation and expertise as appropriate.

There are several main factors analyzed by the committee. First, it must determine whether the drug has already caused any disease or injury. Next, the committee considers whether or not future exposure to the drug could cause health hazards such as illness or death. Finally, they assess the likelihood of the hazards occurring and the resulting consequences, short and long-term. Based upon these general guidelines, the FDA will decide whether or not a drug should be recalled.

If a recall is deemed necessary, the FDA assigns a classification to the recalled drug. The classifications are defined as follows:<sup>7</sup>

Class I – reasonable probability that exposure to or use of the drug will cause serious adverse health consequences or death.

Class II – remote probability that exposure to or use of the drug may cause temporary or medically reversible adverse health conditions.

Class III – use of or exposure to the drug is not likely to cause adverse health consequences.

In the event of a recall, the FDA will immediately notify all affected companies by phone or by visitation from an authorized FDA representative, followed by a written confirmation by mail or telegram to a company official. The notification specifies the violation, the hazard classification, proposed recall strategy, and other instructions. Upon receiving the notification, the company may be asked to provide the FDA with additional information pertinent to the drug being recalled.

Following notification, a drug manufacturer develops a recall strategy in accordance with FDA guidelines. These guidelines govern the depth of the recall, public communication, and effectiveness checks. Depending upon how hazardous the drug is and the extent of its

---

<sup>6</sup>U.S. Code of Federal Regulations, 21 CFR 7.40

<sup>7</sup>21 CFR 7.3m

distribution, the recall depth can span from wholesale levels to retail/consumer levels. Each physical product recall is unique to the circumstances surrounding the situation. Ultimately, the FDA will specify to what level the recall should extend.

The FDA may also issue warnings to alert the public of the recall. This is reserved for “urgent situations where other means for preventing use of the recalled product appear inadequate.”<sup>8</sup> Ordinarily, the FDA will issue public warnings through several channels including the general news media (national, regional, or local) or specialized news media such as the trade press to reach specific target segments (i.e., physicians, medical organizations, etc.). For a firm that decides to issue its own public warnings, the format, content, and extent of the communications must be submitted to the FDA for review and approval. All public communications must:<sup>9</sup>

Display the product by name, size, lot number(s), code(s), serial number(s) and any other descriptive labeling to accurately identify the product.

Explain the reason for the recall and the associated hazard.

Provide instructions for product returns.

Identify a means for recipients to communicate and contact the company.

The third and final component of a recall strategy is the effectiveness check. The purpose of an effectiveness check is to verify that affected parties have received the recall notifications and taken action. Normally, the drug manufacturer will be responsible for verifying the effectiveness of the recall notification, but the FDA can assist and perform audits when necessary. The FDA categorizes effectiveness checks into five levels:<sup>10</sup>

1. Level A – 100% effectiveness
2. Level B – Some of the recipients contacted, but not all
3. Level C – Less than 10% contacted
4. Level D – Less than 2% contacted
5. Level E – No effectiveness

---

<sup>8</sup> 21 CFR 7.45

<sup>9</sup> 21 CFR 7.49c

<sup>10</sup> 21 CFR 7.45b3

The FDA will terminate a recall when it determines that “all reasonable efforts have been made to remove or correct the product in accordance with the recall strategy, and when it is reasonable to assume that the product subject to the recall has been removed and proper disposition or correction has been made commensurate with the degree of hazard of the recalled product.”<sup>11</sup>

### **The PPA Controversy**

PPA has been on the market for over fifty years, and the FDA had classified the chemical as “safe and effective.” However, in the late 1970s, some concerns over its possible health hazards began to emerge. Several doctors theorized that PPA caused blood pressure to rise above normal levels, thus leading to stroke. In 1984, a research study concluded that any hemorrhagic risk related to PPA, if present at all, was very small (less than 1% likelihood).<sup>12</sup> By the late 1980s, lawsuits against drug manufacturers of medicines containing PPA were growing, especially the legal claims from patients and consumers of PPA alleging misconduct against the drug companies. Furthermore, case reports from medical organizations describing the occurrence of strokes after PPA ingestion were climbing.

In response to growing concerns, the FDA and several drug manufacturers jointly commissioned a research study called the Hemorrhagic Stroke Project (HSP) with the Yale University School of Medicine in late 1994. The study was comprised of 702 case subjects and 1,376 control subjects. The main purpose was to identify if there was an association between hemorrhagic stroke and the PPA found in cold remedies and appetite suppressants. By the end of the research study in May 2000, Yale University determined that “PPA increases the risk for hemorrhagic stroke. For both individuals considering use of PPA and for policy makers, the HSP provides important data for a contemporary assessment of risks associated with use of PPA.”<sup>13</sup>

On October 19, 2000, the FDA’s Nonprescription Drugs Advisory Committee (NDAC) discussed this report and other information on PPA. The NDAC determined that there is an association between PPA and hemorrhagic stroke. They recommended that PPA “not be considered generally recognized as safe for over-the-counter use as a nasal decongestant or for weight control.”<sup>14</sup>

---

<sup>11</sup> 21 CFR 7.55a

<sup>12</sup> Jick, Aselton, Hunter. “PPA and Cerebral Hemorrhage,” *Lancet*, 1984.

<sup>13</sup> “Phenylpropanolamine & Risk of Hemorrhagic Stroke – Final Report of the HSP.” Yale University, May 2000.

<sup>14</sup> <http://www.fda.gov/cder/drug/infopage/ppa/advisory.htm>

### Media Interpretation of the FDA's Actions

On November 3, 2000, Janet Woodcock, M.D., Director at the Center for Drug Evaluation and Research issued a written statement addressed to the senior management at Bayer Corporation, as well as to other OTC manufacturers (Exhibit 4). In the letter, Woodcock referred to the report that the FDA received from the researchers at the Yale University School of Medicine. The Yale report's research data suggested that PPA increases the risk for hemorrhagic stroke (bleeding into the brain or into tissue surrounding the brain) in women.<sup>15</sup> The report also determined that men who used PPA could be at risk. Woodcock's statement continued that, "as an interim measure to protect the public health, you (OTC manufacturers) should voluntarily discontinue marketing any drug products containing phenylpropanolamine. If applicable, you may reformulate such products to remove the phenylpropanolamine ingredient."<sup>16</sup>

As the news media became aware of this notice by the FDA, different interpretations of the warning began to surface in the headlines. The headline from the November 7, 2000 *Wall Street Journal* read "FDA Bans Use of Chemical Tied to Strokes." Similarly, the *USA Today* headline from the same day reported, "Drugmakers, stores move on FDA ban – Reformulated remedies on way for colds." The *New Jersey Star-Ledger* and *Pittsburgh Post-Gazette* also reported that the FDA would take steps to ban all use of PPA in cold remedies and appetite suppressants.

In reality, the FDA never issued a ban on the sale or use of PPA, but rather requested a voluntary recall of the product by the manufacturer's whose products contained the chemical. Given the portrayals of the major newspapers, the public reaction had the potential to be much stronger than what was intended by the FDA or anticipated by companies like Bayer. Now, Bayer had to address the public perception that the FDA had banned the use of PPA, making cold remedies, such as Alka-Seltzer, dangerously unsafe.

### Bayer's Dilemma

It is clearly ironic that Bayer was among several cold medicine manufacturers who funded the Yale University study that served as the basis for the FDA's decision. Despite the conclusions of the FDA, Bayer management still believed in the safety of all Bayer products, including those containing PPA.<sup>17</sup> However, management was also intent on maintaining the trust and confidence of Bayer consumers.<sup>18</sup> These facts would undoubtedly influence the

---

<sup>15</sup> Ibid.

<sup>16</sup> FDA Letter to Manufacturers of Drug Products Containing Phenylpropanolamine, November 3, 2000.

<sup>17</sup> [http://www.alka-seltzer.com/info\\_ppa.htm](http://www.alka-seltzer.com/info_ppa.htm)

<sup>18</sup> Ibid.

decision of whether or not to comply with the FDA's requested voluntary recall of all medicines containing PPA as an ingredient.

Several cost considerations would also impact Bayer's decision. At the time of the FDA's decision, management felt the costs of implementing the recall had the potential to reach \$60 million.<sup>19</sup> Bayer would have to reimburse all retailers carrying its effervescent medicines for the costs of physically removing and returning the products to Bayer. Additionally, money spent on advertising campaigns, point-of-sale promotional displays, and slotting fees for the effervescent medicines would be lost. Finally, Bayer would have to make a decision about outstanding promotions that had been sent to consumers prior to the issuance of the FDA's decision. One such promotion was a coupon entitling customers who purchased an Alka-Seltzer Plus product to a free container of orange juice.

These outstanding consumer promotions were especially problematic considering the dynamics of supplying Alka-Seltzer Plus to retailers. Demand forecasts are prepared well ahead of anticipated deliveries because the production lead-time for Alka-Seltzer Plus products, both effervescent and liqui-gels, is approximately three months. The FDA's call for a voluntary withdrawal of PPA products took place in early November 2000, the beginning of what is considered the peak season for cold and flu medicines. Bayer had not anticipated the FDA's decision, and the production of liqui-gels was not adjusted during the months preceding the peak season. If a recall were implemented, the effervescent products would become unavailable and retailers would experience stock-outs of substitute Bayer products. Supply of Bayer substitutes would not be available to meet demand until after the conclusion of the peak cold and flu season. One thing was certain: if Bayer did not take action, the positive brand equity of Alka-Seltzer Plus, as well as the reputations of Bayer's other OTC brands, would suffer immensely.

---

<sup>19</sup> "Phenylpropanolamine & Risk of Hemorrhagic Stroke - Final Report of the HSP," Yale University, May 2000.

### Questions

1. How should Bayer respond to the media's portrayal of the voluntary recall as an FDA ban of PPA?
2. Should Bayer continue to claim that its products containing PPA are safe? If so, should this message be consistent with a voluntary recall of products containing PPA?
3. What is the most effective medium for communicating Bayer's message? Is there a danger of further misinterpretation by the media?
4. What marketing strategy should Bayer implement given the outstanding Alka-Seltzer Plus coupons and the company's inability to supply the product or comparable substitutes?

Do Not Copy

**Exhibit 1: History of Alka-Seltzer**

**1931:** Alka-Seltzer is introduced on the market.

**1950s:** Alka-Seltzer gains mass popularity through national advertising.

**1969:** Alka-Seltzer Plus products are introduced on the market.

**1970s:** Health concerns about PPA begin to surface.

**1980s:** Lawsuits against OTC manufacturers are filed.

**1984:** The first study of the relationship between PPA and strokes is conducted.  
A minimal association is found.

**1994:** The FDA and OTC manufacturers jointly commission a research study at  
Yale University School of Medicine.

**1995:** Bayer introduces Alka-Seltzer Plus caplets.

**1996:** Bayer introduces Alka-Seltzer Plus liqui-gels.

**May 2000:** Yale University releases the results of the research study to the FDA's  
Nonprescription Drugs Advisory Committee (NDAC).

**October 2000:** NDAC reviews the results and recommends that PPA not be considered safe.

**November 2000:** The FDA requests a voluntary recall by the OTC manufacturers of all products  
containing PPA.

Do Not Copy

Do Not Copy

**Exhibit 4: FDA Letter**

DEPARTMENT OF HEALTH HUMAN SERVICES

Food and Drug Administration

Rockville MD 20857

November 3, 2000

Dear CEO or President:

This letter concerns drug products containing phenylpropanolamine and its salts marketed by prescription or over-the-counter (OTC), which are now or have previously been manufactured, relabeled, repacked, or distributed by your firm. Phenylpropanolamine is currently available by prescription and OTC as a nasal decongestant, and OTC for weight control. Your firm is receiving this letter based on information in the Food and Drug Administration's (FDA) Drug Listing System or because you have a new drug application (NDA) or abbreviated new drug application (ANDA) for a product containing phenylpropanolamine.

This letter is to inform you of recent developments relating to phenylpropanolamine. Earlier this year, FDA received a report entitled "Phenylpropanolamine & Risk of Hemorrhagic Stroke: Final Report of the Hemorrhagic Stroke Project" from scientists at Yale University School of Medicine. This report, which is on display in Docket No. 8 1 N-0022 in the FDA Dockets Management Branch, states that the data suggest that phenylpropanolamine increases the risk for hemorrhagic stroke.

On October 19, 2000, the Agency's Nonprescription Drugs Advisory Committee (NDAC) discussed this report and other information on phenylpropanolamine. NDAC determined that there is an association between phenylpropanolamine and hemorrhagic stroke and recommended that phenylpropanolamine not be considered generally recognized as safe for OTC use as a nasal decongestant or for weight control.<sup>1</sup>

Based on these recent developments, FDA intends to initiate rulemaking to classify phenylpropanolamine as nonmonograph (not generally recognized as safe and effective) for OTC use. Based on the recent research findings, FDA also has significant concerns about the continued use of phenylpropanolamine in prescription drug products. FDA also intends to take action to remove phenylpropanolamine from prescription drug products. FDA plans to issue a Public Health Advisory on phenylpropanolamine to alert consumers and health professionals about the report.

---

<sup>1</sup> In the mid-1970s, phenylpropanolamine was classified as Category I (safe and effective) by two OTC drug advisory review panels. The Cough-Cold Panel's recommendations on phenylpropanolamine as a nasal decongestant appeared in the FEDERAL REGISTER of September 9, 1976 (41 FR 38312) and the Miscellaneous Internal Panel's recommendations for weight control use appeared on February 26, 1982 (47 FR 8466). However, FDA deferred its classification of phenylpropanolamine because of subsequent safety issues that were raised, pending completion of additional studies.

Page 2

FDA also believes that, as an interim measure to protect the public health, you should voluntarily discontinue marketing any drug products containing phenylpropanolamine. If applicable, you may reformulate such products to remove the phenylpropanolamine ingredient.

If you have any questions or want additional information, including information about options for reformulating products that contain phenylpropanolamine, please contact Jerry Racbanow or Robert Sherman at 301-827-2241.

Your cooperation and prompt attention to this matter will be appreciated.

Sincerely,

Janet Woodcock, M.D.  
Director Center for Drug Evaluation and  
Research

Do Not Copy