

# CASE TEACHING NOTES

*for*

## "Amanda's Absence: Should Vioxx Be Kept Off the Market?"

*by*

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### INTRODUCTION

When chronic pain forces a top student to withdraw from college, biology instructor Dr. Sharpe learns that medications may be removed from the market for many reasons, including safety concerns. As the case unfolds, students learn how the FDA balances drug safety against medical needs.

The storyline of the case is based on an actual student's experience, but all names and identifying details have been changed. The texts of the original press release and testimony in Parts II and III are in the public domain and were obtained from the U.S. Food & Drug Administration's public web site (<http://www.fda.gov>). Both were edited heavily for brevity, but no relevant facts have been altered.

As written, the case is appropriate for a non-majors course. I have found that most students can participate in a relevant discussion without any prior background. To adapt the case for a more advanced course in cell biology, pharmacology, or biochemistry, the instructor could write more topic-specific questions for Part I and substitute the 2004 Science article by Egan, et al., listed under "Further Reading" below for the press release in Part II. This case also could be modified to explore statistical analysis ("What is a significant difference?"), specific analytical methods used for risk/benefit analysis, and bioethical issues. The complete transcript of Dr. Sandra Kweder's testimony before Congress (used in Part III and cited in the sources) touches on all of these topics, and so remains an ideal resource.

This interrupted case can be run over the course of one or two class periods. If introductory-level students work in groups and consider just the first two questions for each part, the case can be completed in 50 minutes. If students discuss all of the questions, the case can be extended to 75 minutes. Rather than having students read just the one-page excerpt from Dr. Kweder's congressional testimony, the instructor may choose to have them read the entire transcript. If so, the case should be conducted over two days, giving students time to read the transcript as homework. The fourth part of this case is an optional homework writing assignment; if it is not used, another assignment should be given that requires students to summarize their position and thoughts on the case.

This case can be extended considerably for advanced students, especially those who have some background in biology and chemistry. They can examine the biochemical paths affected by Vioxx, the mechanisms by which it increases risk of heart attacks, or the costs of bringing a chemical compound to market under the current FDA system. For these students, the instructor should plan to spend more time than what is given above. It may be necessary too to revise the text of Parts II and III, based on the amount of experience that students have.

The first lawsuit by a family member against Merck resulted in a large award, and other cases are pending. Given these, students might be asked to write a different final assignment—one that examines the responsibility of the pharmaceutical manufacturer in this process in terms of patient safety. They might also look further at how after-market testing is conducted, and how this relates to the costs of drug development.

## **Objectives**

Upon completing this case, introductory level students should be able to:

- Describe in general terms the purpose and structure of a clinical trial.
- Explain how the decision is made to bring pharmaceutical drugs on and off the market.
- Describe or define in general terms the concept of risk/benefit analysis.
- Distinguish between relative risk and absolute risk.

If the instructor modifies Parts I and II to fit their particular topic, additional learning objectives can be achieved as well.

## **CLASSROOM MANAGEMENT / BLOCKS OF ANALYSIS**

Students read and discuss the questions for each part of the case in small groups of four to seven. During the ensuing classroom discussions in which the entire class participates, the instructor asks each group to report their answers.

In Part I, students learn that while the decision to recall or withdraw a drug usually is a slow, methodical process, in some instances clinical trial data is so convincing that the withdrawal occurs suddenly, as was the case with Vioxx. However, withdrawal rarely is a simple issue. Inevitably there is a long-term toll on quality of life for individuals who had relied on the drug, a factor often overlooked by the popular press as it moves on to other news. Part I attaches these issues to a character (a student) that case readers can empathize with.

Students read Part I when they first come to class, then discuss it in their small groups and then as an entire class before proceeding to Part II. Alternatively, Part I can be a pre-lecture reading assignment. When using this case in an introductory level class, students should be allowed to ask for definitions of concepts or terms. If the students have some relevant background, it would be appropriate to require students to explain concepts to one another (i.e., team learning) rather than ask the instructor.

Parts II and III are read in class and the questions at the end of each part are discussed following the same procedure as for Part I described above. Part II introduces some of the factual data for the case. The abridged press release that appears in this part of the case summarizes the regulatory history of the drug and why it was approved originally. Briefly, two separate studies, one in 2000 and a second one conducted in 2004, showed a 2-fold increased risk of heart attacks in patients taking Vioxx.

Part III is an abridged and edited excerpt of testimony Dr. Sandra Kweder, Deputy Director of the Office of New Drugs, presented on November 18, 2004, to the U.S. Senate's Finance Committee regarding Vioxx's withdrawal. Dr. Kweder outlines the drug approval strategy of the FDA concisely and the agency's policy of continued monitoring. She underscores the fact that no drug is safe in all situations. Finally, she explains that the decision to withdraw a drug depends on many factors, not just its safety profile. The full transcript of her testimony is quite long. If an instructor wants to focus on cell biology, pharmacology, or some other specific issue, they can extract the relevant portions for their students rather than have the students read the entire document.

When teaching this case, it is recommended that the class time be split so that students spend approximately 25% of the time discussing Part I, 35% of the time discussing Part II, and 40% discussing Part III. If the instructor wants to encourage more in-depth discussion, students can be assigned a larger excerpt of the testimony transcript to read as homework. In this situation, Part III would be discussed at a second class meeting.

The final, optional homework assignment in Part IV was designed with four goals in mind:

- Each student must state and defend his or her position independently of their group, thus demonstrating they have understood the issues of the case.
- It is a defined end product that can be graded as a supplement to the participation grade.
- It extends the case beyond the data presented and provides an opportunity for further study and research.
- It gives students time to think about the issues, and go back and review all three parts of the case.

Ideally, students would have at least five days to read, discuss, and compose their position papers. A good starting point for further information is the FDA web site from which students can link to press reports, testimony, and clinical trial data.

Alternatively, instructors may choose to let students role-play their responses as Dr. Sharpe or another member of the FDA approval panel. Another final exercise might be to ask students how patients might protect themselves from future risks associated with medications. The instructor might ask them to list questions they would ask a health care provider or to examine the role of the package insert in products.

## ANSWER KEY

Answers to the questions posed in the case study are provided in a separate answer key to the case. Those answers are password-protected. To access the answers for this case, go to [the key](#). You will be prompted for a username and password. If you have not yet registered with us, you can see whether you are eligible for an account by reviewing our [password policy and then apply online](#) or write to [answerkey@sciencecases.org](mailto:answerkey@sciencecases.org).

## REFERENCES & FURTHER READING

### References

Food & Drug Administration. 2004. FDA Issues Public Health Advisory on Vioxx as its Manufacturer Voluntarily Withdraws Product. Accessed June 26, 2005.  
<http://www.fda.gov/bbs/topics/news/2004/NEW01122.html>

\_\_\_\_\_. 2004. Statement of Sandra Kweder, M.D., before Committee on Finance, United States Senate. Accessed June 26, 2005.  
<http://www.fda.gov/ola/2004/vioxx1118.html>

\_\_\_\_\_. 2005. COX-2 Selective (includes Bextra, Celebrex, and Vioxx) and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). Accessed June 26, 2005.  
<http://www.fda.gov/cder/drug/infopage/COX2/default.htm>

Jenkins, J.K. 2005. Analysis and recommendations for Agency action regarding non-steroidal anti-inflammatory drugs and cardiovascular risk (PDF). Accessed June 26, 2005.  
<http://www.fda.gov/cder/drug/infopage/COX2/NSAIDdecisionMemo.pdf>

### For Further Reading

Egan, K.M., Lawson, J.A., Fries, S., Koller, B., Rader, D.J., Smyth, E.M., Fitzgerald, G.A. 2004. COX-2-derived prostacyclin confers atheroprotection on female mice. *Science* 306 (5703):1954–57.

Egan, K.M., Lawson, J.A., Fries, S., Koller, B., Rader, D.J., Smyth, E.M., Fitzgerald, G.A. 2005. Cyclooxygenase-2-derived prostacyclin confers atheroprotection on female mice. *Obstetrical & Gynecological Survey* 60(5):309–1.

## ***Helpful Web Sites***

The drug approval process:

<http://www.fda.gov/cder/handbook/develop.htm>

<http://www.fda.gov/cder/regulatory/applications/default.htm>

<http://www.fda.gov/fdac/special/newdrug/benefits.html>

Costs of research and development:

<http://www.phrma.org/issues/researchdev/>

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