Some Biblical Contributions to Business Ethics

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How does the Bible guide us in the midst of business decisions? We have provided three case studies from the pharmaceutical industry that illustrate the consequences of decisions and actions by the company and government regulators. The cases studies are:

1. Eisai Medical Research, Inc., and decisions and actions surrounding the marketing of a popular medicine for treatment of the symptoms of Alzheimer's disease in late 2009
2. McNeil Consumer Products Company (a division of Johnson & Johnson) and the decisions and actions surrounding tampering with Extra Strength Tylenol Capsules in 1982 and 1984
3. McNeil Consumer Healthcare (a division of Johnson & Johnson) and decisions and actions surrounding the manufacture of OTC drug products in 2008 and 2009

These case studies were selected because they are: current (Cases 1 and 3); well documented in public government records (Cases 1 and 3); in the press and widely known (Case 2); and in a state where decisions were made with defined consequences. They were also selected because the pharmaceutical industry operates within a framework of governmental laws, regulations, and guidance documents that are often subject to interpretation. Because the laws, regulations, and guidance documents are not always black and white, the industry must often make decisions about the "gray" areas. It is usually the gray areas that present the most difficult decisions, and where companies spend significant effort "managing risk."

To help companies and their employees make decisions about the gray areas of the law and better manage risk, companies have created many internal statements and policies to aid employees in making the right decisions. Typically, they fall into one of two categories—*Company Values* or *Codes of Conduct.*

Company Values

1. quality
2. integrity
3. respect for people
4. community
5. collaboration/teamwork
6. leadership

7. performance
8. innovation

Codes of Conduct

1. accuracy of public disclosures
2. advertising and promotional standards
3. antitrust and competition
4. business records and internal controls
5. conflicts of interest
6. environmental, health, and safety laws
7. false reporting to government agencies
8. food, drug, and medical device laws
9. gifts and entertainment policy
10. improper payments in the public and private sectors
11. standards on relationships with medical professionals
12. intellectual property and confidential information
13. international trade controls
14. discrimination in employment and unlawful harassment
15. money laundering
16. political contributions
17. privacy laws
18. securities transactions

But even with all these policies and procedures, poor decisions are still made and companies suffer the legal, public, and financial consequences.

In all fairness to the companies listed above, it must be noted that the FDA also issues dozens of Warning Letters every year to other companies for similar circumstances. Our intent is not to criticize or commend these particular companies, but to use them as examples of the decision making that occurs in the pharmaceutical industry. Reference materials for cases are presented in the appendix to this paper.

The presentation of the cases in Part I comes primarily from Dr. Radebaugh, while reflections on biblical principles in Part II come primarily from Dr. Poythress.

Part I: Cases

Case Study 1

This case study is based on a Warning Letter from the U.S. FDA, which is posted on the FDA Web site and is reproduced in the appendix at the end of this article. The company's response to the letter is classified as confidential.

Setting: A prescription pharmaceutical company, Eisai Medical Research, Inc., received a Warning Letter from the FDA in early 2010 for misleading advertising for a drug product (Aricept) to treat mild to moderate Alzheimer's disease.

General findings: The company was accused by the U.S. FDA of violating the Federal Food, Drug, and Cosmetic Act and the 21 CFR 202.1 by overstating the efficacy of the drug, thereby misbranding the drug.

Specific findings: The company created TV ads that depicted patients with Alzheimer's symptoms, before and after use of Aricept. The FDA accused the company of presenting drastic improvements in the patient's cognitive abilities that were not supported by the clinical data.

Requesting Action: The company was requested to immediately cease disseminating promotional materials that violate the law.

Possible Ethical Questions: (1) Did the company knowingly violate the law by overstating efficacy, or did the company in good faith interpret the clinical data differently than the FDA did? (2) Did the company knowingly violate the law on the assumption that the temporary use of the TV ads would give financial benefits that would outweigh the potential penalties? (3) What policies did the company have in place to guide employees in their decision making, and were they adequate? (4) What is the moral authority for the policies? (5) What reward system was in place for the employees, and did it provide incentive to make the decisions that were made? (6) If the ads were the result of a good faith difference of opinion, how will the company learn from this experience so that the violation does not occur again?

Biblical Questions: (1) Does the Bible provide clear guidance such that, if known and followed, it would have prevented this violation of the law? (2) How would the Bible help navigate the "gray" areas of the law that are subject to interpretation? (3) How can biblical principles be built into company policies?

Case Study 2

This case study is based on many press reports. Even today, this case study is taught in business schools as a model for effective crisis management.

Setting: In 1982, several bottles of Tylenol Extra Strength Capsules were tampered with through the addition of cyanide, and placed on pharmacy shelves in the Chicago area. Seven people died from ingesting the cyanide-laced capsules from the tampered-with bottles. In 1984, a second round of tamperings occurred, but there were no known deaths as a result of these tamperings.

General findings: The major product of a leading consumer health care company, McNeil Consumer Products of Johnson & Johnson, was a victim of external tampering that caused death to unsuspecting customers. The company was faced with the dilemma of resolving the problem without damaging/destroying the reputation of the company and its most profitable product. Based on the principles of the J&J Credo, putting public safety first as opposed to the company, the company reacted to the tamperings in such a way that public trust in the product and the company was restored.

Company Actions: In the first round of tamperings, bottles of Tylenol Extra Strength Capsules were purchased from Chicago area pharmacies and tampered with by replacing the contents of the hard gelatin capsules with cyanide. The bottles were then placed back on pharmacy shelves and purchased by unsuspecting customers. Some

customers who did not notice the tampering died from ingesting capsules laced with cyanide. The perpetrator of the crime was not apprehended and convicted. Even though the company was not responsible for the tamperings, it assumed responsibility for public safety. As a remedy, the company recalled all products that had left the factory (31 million bottles) and replaced them at no cost to the public (in excess of $100 million cost to the company). In addition, it began selling the capsules in tamper-evident packaging. In the second round of tamperings (viewed by some as copycat tamperings), there were no deaths, but a crisis of confidence in the product was rekindled in the public. Again the product was recalled and replaced at company expense. Because the company could not develop technology that could prevent the hard gelatin capsules from being emptied and refilled with poisons, it withdrew the hard gelatin capsule from the market and replaced it with caplet-shaped solid tablets. Due to company decisions and actions (senior management embracing the J&J Credo), confidence in the product and the company was restored. The Tylenol tamperings have become a textbook business example of how a company successfully managed a crisis, using the ethical principles of its credo, and prevented irreparable damage to the company and a major product.

Ethical Questions: (1) Could the company have made the same business decisions without the Credo? (2) What is it about the Credo that guided the senior executives in their decision making?

Biblical Questions: (1) Does the J&J Credo embrace biblical principles, and if so, which ones? (2) How could the Bible help guide decision making and enhance the principles of the Credo?

Case Study 3

This case study is based on documents posted on the FDA Web site, namely, an FDA Warning Letter and the company's response to the Warning Letter. The documents are reproduced in the appendix at the end of this article.

Setting: On January 15, 2010, McNeil Consumer Healthcare received a Warning Letter from the FDA for violation of quality regulations in the manufacture of various OTC drug products. Multiple products were recalled from the marketplace as a result of violations.

General findings: In 2008 and 2009, the company became aware of product contamination (via complaints from consumers of "uncharacteristic odors" and gastrointestinal distress) that led to the recall of several lots of Tylenol Arthritis Relief Caplets. The company determined that the odor was due to the presence of TBA, which is a degradant of TBP, a pesticide used to treat wooden pallets for transporting packaging materials. The FDA expressed concern about the company's response to the problem, based on timeliness, thoroughness, and resolution of the issues. FDA deemed that management at J&J and McNeil Consumer did not take appropriate action to ensure the quality, safety, and integrity of its products. Additional consequences are that FDA may withhold approval of export certificates, or approval of new products until the violations are corrected, and quality management systems are put in place that ensure compliance with FDA regulations.

Requested Actions: The company was requested to recall additional products, and put quality management systems in place to ensure compliance with FDA regulations. The product could not be manufactured until the TBA problem was resolved.

Ethical Questions: (1) Given that the J&J Credo that existed in 1982, still existed in 2009, why was the response to this crisis handled differently than the Tylenol tampering crisis in 1982 and 1984? (2) Did the Credo cover this situation? What is needed besides written credos and policies? (3) In addition to the Credo, were there written compliance policies that should have covered this situation? Why were they not followed? (4) Were these issues the result of poor management and/or a deficiency in moral judgment?

Biblical Questions: (1) Did the company violate or compromise biblical principles? (2) What guidance could the Bible have provided that might have remediated the situation sooner or prevented it from happening?

Part II: Reflection on Biblical Principles

Let us begin with Case Study 1, which involved Eisai. The FDA accused Eisai of misleading advertising for a drug product, Aricept, which is used in treating Alzheimer's disease.

The Eisai case at first glance may appear to be one-dimensional. The advertising by overreaching violated specific federal statutes, namely the FD&C Act and 21 CFR 202. The most obvious ethical issue, then, is the principle of obedience to the authority of civil government, which is expounded most fully in the Bible in Romans 13:1–10, but also comes up for discussion elsewhere (1 Peter 2:13–17) and is one aspect of a larger issue of submission to authorities of various kinds (Eph. 5:21–6:9; 1 Peter 2:18–3:6; Ex. 20:12; Deut. 17:8–20).

Several Dimensions in Ethical Responsibility

This case contains greater complexity than what appears on the surface. A closer inspection reveals several dimensions. To begin with, we must deal with the issue of truth. The Bible stresses the importance of telling the truth (Ex. 20:16; Ps. 101:7; Prov. 6:19; 8:7; 12:17, 19; 14:5, 25; 19:5, 9; Eph.4:25). Did the advertising do that? Moreover, TV advertising includes a visual element, and the visual accompaniment of words can suggest much more than the words convey in themselves. What did the visual accompaniment suggest? Did it suggest more than the product could deliver?

Because of the power of visual imagery, we need also to ask about the potential for manipulation. Viewers may be enticed and lured into interest in the product not because of the virtues of the product but because of the humorous mood or the pleasant smiles or scenes of happy family activity. The advertiser needs a larger biblical view of the world and of fellow human beings, a view that would remind him that he should regard the client with respect as a human being, and not as a virtually subhuman object to be trapped into a commitment against his better judgment.

On the other hand, we should take into account the larger context of modern advertising. Decades of TV advertising have created a cultural context in which most viewers are sophisticated. Many viewers, one might suggest, know some of the aims and techniques of advertising, and have developed a distant attitude that makes them resistant to manipulation. They may have a kind of tacit bargain with the advertiser: If you the advertiser present something humorous, clever, or engaging, I in return will consent to devote a little attention to what you have to say about your product. I know beforehand that you are going to present your product in the most favorable light, and not introduce all possible qualifications or drawbacks. That is part of the "game" that I the viewer and you the advertiser play. Given that context, the advertiser has considerable freedom.

We can also explore the aspect of promising that belongs to many advertisements. Some advertising may make direct promises: "We promise that if you buy our product, you will see improvement within three days, and you will be satisfied with your purchase." Much advertising is less direct, but still contains an implicit element of promise. Promises are a specific kind of commitment that has ties with the broader area of personal responsibility and commitment making. The Bible expresses this commitment making through its discussion of "covenants." God makes covenants with various human beings. God is a person who can make commitments. We as human beings made in His image can also make commitments. We are responsible for those commitments, by analogy with the central commitments that come to expression in God's covenants. What implicit commitments did the advertising make, and were these commitments that the product could realistically fulfill? (The FDA letter to Eisai notes that the Eisai ads include "the superimposed text, 'Individual results may vary,'" but states that this inclusion "does not mitigate these misleading presentations" [p. 4].)

The joint presence of many dimensions in advertising makes moral evaluation more complex. In this case study, Dr. Radebaugh legitimately raises the question of whether someone in Eisai was deliberately violating the statutory rules, or whether the advertisement fell in a "gray" area and was not clearly in violation. Was the conflict due to two distinct interpretations of the statutes, one by the FDA and one by Eisai? If so, did the FDA allow any discussion or appeal of its initial ruling? If it did allow discussion, officials within Eisai would have to employ wisdom to decide whether to pursue further discussion or just concede the case.

The case also contains many challenges about the internal processes at Eisai. What procedures and relationships among the employees at Eisai led to the initial decision to go forward with the advertising? If we are seeking to be guided by biblical principles, we should try not only to find ways to express elements of biblical ethics in company procedures and guidelines, but also to help the individual employees and clusters of employees to grow in discernment when confronted with similar issues in the future. We must be concerned for the people (the principle of love) as well as the rules (moral standards).

In particular, Dr. Radebaugh asks, "What was the reward system that was in place, and did it provide incentive to violate the law?" The Bible is realistic about sin. The Lord's Prayer includes the petition, "Lead us not into temptation" (Matt. 6:13 ESV), partly because sin does root itself in people's hearts. Whether we are Christians or not, we are

prone to temptation (James 1:14–15). Companies need to be realistic about fallen human nature. If company policies promise rewards for concrete accomplishments, such as advertising, but provide no specific incentives with respect to the issues of violating the law or lying or dealing underhandedly, the reward system may end up undermining any verbal policies that have nice-sounding moral phraseology but no "teeth," no "bite" within the company's system of rewards.

The concern for people also comes to the surface in Dr. Radebaugh's question, "How will the company learn from this experience so that the violation does not occur again?" If patterns of policy and behavior have become systematically entrenched, it may not be enough simply to say to the guilty party, "Don't do it again!" Taking more time to understand how things go wrong is not only the kind thing to do for the people involved, but may also be the wise thing to do for the long-term benefit of the company as a whole, since it may uncover ways in which the broader atmosphere and morale of the employees can be influenced for the better.

Such efforts are particular important when we deal with "gray" areas in which civil laws leave room for interpretation. Companies and employees have a natural tendency to interpret any gray areas in their favor. Up to a point, this latitude in interpretation may be legitimate. Those who make the laws are reasonable, and want to allow space for legitimate advertising that stresses a product's positive features. But employees under pressure may easily slide into unreasonable "bending" of the law, or even deliberate violation. Internal company discussion needs to address these temptations frankly and realistically.

Perspectives

A complex, multidimensional situation like this one demands not only attention to biblical standards for ethics, but creativity in discerning how standards come to bear on a particular business situation. Creativity can be enhanced if we use multiple perspectives on a situation. John Frame's work on biblical ethics presents a biblical basis for three main perspectives, which he has termed the *normative* perspective, the *existential* (or *personal*) perspective, and the *situational* perspective.[1]

The *normative* perspective asks about the norms, the ethical rules that bear on human living. The Ten Commandments are a summary of God's norms. In the Eisai case, norms include obedience to civil authority, coming to focus in the fifth commandment (Ex. 20:12), and telling the truth, coming to focus in the ninth commandment (Ex. 20:16).

The *personal* perspective focuses on the persons in the situation and their motives. In the Eisai case, we ask whether an employee deliberately violated a statute, and whether the reward system unwittingly encouraged the pursuit of unethical motives.

The *situational* perspective focuses on the situation: Eisai is a prescription drug company working in U.S. territory, subject to particular statutes with respect to drug advertising. The situation includes the "culture" of advertising and viewer expectations, as well as the "culture" of Eisai, including policies it may have in place specifying ethical standards, the answerability of employees to superiors, and the responsibility of the company as a whole to its board and stockholders.

These three perspectives do not come out of thin air. Biblical ethics gives us norms, in the Ten Commandments. It tells us to pay attention to persons (the principle of love), including God, who is the most important Person in our lives. It tells us to pay attention to our situation when it commands us to bless others, to do good, and to promote the glory of God (Rom. 12:14; 1 Peter 3:9; 4:19; 1 Cor. 10:31). These three aspects—norms, persons, and situation—fit together, because God gives us the norms, He created us as persons, and He providentially controls our situations. He has promised that we will never be in a situation where we have no good alternative, where we are "compelled" to sin (see 1 Corinthians 10:13). But situations may be difficult. It may sometimes look as if we have no alternatives.

Each of the three perspectives is actually a perspective on the whole of ethics. The norms tell us to pay attention to persons and to motives, and therefore they implicitly include the personal perspective. The norms also tell us to pay attention to our situations, and to exercise discernment (Phil. 1:9). Thus the normative perspective points to the situational perspective. Similarly, the situational perspective points to the normative perspective. God is the most important person in our situation, so a robust consideration of the situation includes God. It therefore includes God's norms (His evaluations) as well. The same holds for all three perspectives. It is nevertheless useful to have all three, because we may then be encouraged to notice what we may have previously overlooked. The personal perspective tells us to pay attention to employees' motives, their temptations to sin, and the way in which a reward system may unwittingly encourage improper behavior.

Divine Resources

The intersection of moral standards (norms) with situations leads to pressure on people, and people need the resources of Christ. Jesus Christ Himself was fully man, and He did not ever sin. He faced the uniquely difficult situation of his crucifixion and death. Hebrews reminds us that "we do not have a high priest who is unable to sympathize with our weaknesses, but one who in every respect has been tempted as we are, yet without sin" (Heb. 4:15 ESV). It also exhorts us to pray: "Let us then with confidence draw near to the throne of grace, that we may receive mercy and find grace to help in time of need" (Heb. 4:16 ESV). We have access to God through Christ our high priest, and through Him we "may receive mercy and find grace to help." Specifically, it is "help in time of need." These promises hold for a person in Eisai dealing with a tempting opportunity to advertise Aricept, or people in McNeil Consumer Products dealing with contaminated products.

The "help" can take the form of sustenance when we are tempted to do something that is clearly wrong (as might have been the case with the Eisai example). It can also take the form of sustenance emotionally and spiritually when company executives must face a crisis that is not at all their fault (McNeil, 1982 and 1984), when perhaps they feel that it is all "unfair" and may be tempted to despair. And it can take the form of a renewed creativity and boldness that fellowship with God supplies. God the Creator is the source of creativity, and we are meant to be bold in following his ways even when we

cannot see how it will turn out for good ("We walk by faith, not by sight" [2 Cor. 5:7 ESV]).

This boldness in doing good has particular relevance in addressing business temptations to cut corners, morally speaking, for the sake of short-term gains in money, power, or prestige. In 1982 and 1984 the officials at McNeil could easily have argued to themselves that money was all-important and that it was too expensive (more than $100 million in 1982) to recall all the Tylenol. Instead, they followed the hard course of recalling the bottles. But in the long run, this hard course helped the company by restoring public confidence.

Or consider the Eisai case. Dr. Radebaugh asked, "Did the company knowingly violate the law on the assumption that the temporary use of the TV ads would give financial benefits that would outweigh the potential penalties?" The situation becomes even more tempting if no clear violation of law is at stake. For example, it appears that in 2008 and 2009 McNeil made at least a minimal effort to solve the problem of contamination with TBA. Presumably key officials within McNeil thought that they had solved the problem through minimal investigations and minimal changes, and this minimum would have been justified as monetarily the best solution. But it proved inadequate.

We can see the same issue rise again when we consider the importance of looking at employee motives, employee relationships, and employee morale. The personal perspective invites us to pay attention to these dimensions. In the long run, paying attention to these dimensions helps a company. But in the short run it may look like an unnecessary bother. The one-dimensional businessperson may tell himself that he needs to go full steam ahead, caring only about profit, not about the employees.

The temptations also increase when business employees tell themselves, "No one will ever know." Or at least "no one will ever know until I am long out of the picture." They may tell themselves, "No harm will come to the public, and in the meantime I increase the company's profit and enhance my own career prospects." It is a useful antidote to remind oneself in response, "God knows. Christ knows." And also God controls situations. He controls monetary success and company reputation as well as having authority over ethical standards. In many instances doing the right thing ethically, as McNeil attempted in 1982 and 1984, issues eventually in situational changes that are a blessing to the company. Proverbs is full of examples reminding us that following God's way can lead to blessing, often in this life as well as in the next. But we cannot guarantee company success by some kind of ironclad mechanics of the marketplace. The company employee in a tight spot must believe God, even when he cannot by sheer calculation of future consequences assure himself that the outcome will be prosperous.

The Universal Claims of Christ

I have framed the discussion in Christian terms. I believe that only in this way can we fully appreciate the resources found in the Bible. Let me further expand the horizons by reflecting on the larger salvific context given by the Bible, within which we carry on ethical decision making.

The Bible is not designed by God merely to be a moral handbook, to give us some boundaries for ethics. It does indeed give us moral norms. It also shows that the norms lead to personal and situational perspectives on ethics. But in addition, it is a book communicating salvation. The gospel is "the power of God for salvation to everyone who believes" (Rom. 1:16 ESV). At its center is the salvation accomplished by Jesus Christ, the great high priest (Heb. 4:15). This salvation is an exclusive salvation, found only in Christ (John 14:6; Acts 4:12). Only in Christ are we going to find the "mercy" and "grace" we need (Heb. 4:15–16), in the sphere of business as well as in every other area of life. Ethics cannot be detached from God. And God is the God who opens access to Himself only through Christ. Through Him we receive power that transforms our hearts, that clarifies our moral compass, that enables us to do what is right, and that stimulates us to find ways to bless others around us.

Furthermore, we learn from the Bible that Christ is Lord of all of life, not merely a narrowly "religious sphere": "All authority in heaven and on earth has been given to me" (Matt. 28:18 ESV; see also Ephesians 1:20–22). All of life should be in service to Christ. The person who is a disciple of Christ has committed everything to Him (Luke 14:26–27, 33). We are never "off duty." Leisure, rest, and family activities as well as work belong to Him. Every aspect of business rightly belongs to Him. Today we have popular language about "full-time Christian service," but in actuality every Christian is supposed to be serving Christ all the time. The issue of who is paying for our service is secondary. Loving God with all our hearts implies that we are to be loving Him all the time. Thus, the Bible challenges us not merely with respect to a few ethical principles, which might apply only in a few scattered situations, but all the time, in all activities. Our motives and our actions always have an ethical dimension. And God the Judge of all evaluates all human motives and actions. The goal for life is not merely individualistic or private, but universal allegiance to Christ throughout the world, "so that at the name of Jesus every knee should bow, in heaven and on earth and under the earth, and every tongue confess that Jesus Christ is Lord, to the glory of God the Father" (Phil. 2:10–11 ESV). This universal allegiance includes in principle the transformation of the whole world of business, to bring it to display the glory of Christ.[2]

The Pluralistic Challenge

The exclusiveness of salvation in Christ and the absoluteness of His claims create real challenges in a pluralistic world. How do we negotiate these challenges? The obvious answer is the one that Hebrews 4:15–16 already gives: God in Christ must provide power, wisdom, creativity, humility, and boldness, to invigorate us to face the challenges. There is a way through, even if we do not yet see it.

We also have examples in Scripture of people who lived in pluralistic situations or lived in faith to God in situations of idolatry. We can look at Joseph in Egypt (Gen. 39–50), Daniel and his three friends in Babylon (Dan. 1–6), Jeremiah's and Ezekiel's messages to exiles in Babylon, Esther in Persia, Paul in the Roman Empire, and the instructions in the New Testament letters, which are directed to Christians, who were a

minority. Throughout history, exemplary disciples did not compromise their faith, and at the same time they became a testimony and a blessing to pagans around them.

Bridge Building with Pluralism

The Bible provides resources for navigating modern pluralism. But in our own thinking we should assess realistically the deep differences that stem from religious commitments rather than paper them over. Christ is Lord over all, whether non-Christians are aware of it or not. They owe allegiance to Him as universal Lord, and they are guilty of rebellion whether they are aware of it or not. The Bible tells us that people are either in rebellion against God or in submission to Him. The world of people is divided by this great divide. The transition from rebellion to submission comes from God's work of salvation, which takes place through Christ. There is no other way.

Much of modern pluralism does not like these truths. It likes neither the exclusiveness of Christ's claims, nor His universal Lordship, nor the separation between followers and opponents of Christ. But in principle Christians are in a better position than anyone else to live in pluralistic situations, because they know the actual situation. They know that Christ is Lord and Judge (Acts 17:31). They recognize that the need for salvation extends into the specifics of the business world and every other sphere of life. They can look with honesty at the depth of the difficulties that come with human disagreements. Moreover, the Christian message tells us to love our enemies, and to be agents of reconciliation in the midst of painful differences (2 Cor. 5:18–21). The opportunities are great.

Many dimensions go into the foundations for bridge building:

1. All people are made in the image of God (Gen. 1:26–28). We have a foundation for sympathy and understanding.
2. All people, even people who are deeply wrong in their ideas or in their actions, can still be respected for what they were created to be (James 3:9).
3. All people except Christ in His human nature have been caught in the tangle of sin. They are guilty before God (Rom. 3:23; 6:23). The effects of sin are radical, and influence us in every aspect of life. Followers of Christ should not present themselves as morally superior or proud, but as those who themselves still confront temptations and need forgiveness. And we should demonstrate the reality of the forgiveness we receive by our readiness to forgive others (Matt. 6:12, 14–15).
4. All people know God, though in rebellion they try to suppress the truth about God (Rom. 1:18–25).
5. All people have a sense of right and wrong, though that sense can be twisted by sin (Rom. 1:32; 2:14–15).
6. All people have longings that can only be fulfilled in communion with God, but which people vainly try to fulfill with idolatrous substitutes (Rom. 1:21–25). These substitutes can include not only the worship of images (physical idols) that took place in the ancient world, but heart commitments to false religions or to secular goals that are made into ultimate commitments, goals such as money, power, fame, sex,

pleasure, or even the goal of being a morally admirable, "good" person.[3] These idolatrous goals crop up in the business world as well as all other areas of life.

7. God is gracious to both good and evil people. People get better than they deserve. And this graciousness of God includes restraint of sin. People are not as bad in practice as their sinful rebellion could lead them to be. Non-Christians, as well as Christians, accomplish good things in the world. This graciousness of God to people outside Christ has been called "common grace."

8. Christ is universal Lord, and is Savior of all who place their trust in Him. The offer of salvation goes out to all.

These various commonalities can serve as bridges for communication and encouragement of others in the workplace, even when opportunity does not arise for Christians to explain all the dimensions of their own understanding of God and the world.

Discussion of the Eisai Case

We may take the Eisai case as an example. Suppose Sue is a Christian employee of Eisai and participates in the internal discussion within Eisai responding to the FDA. She employs the three perspectives on ethics: normative, personal, and situational. From the normative perspective, she brings into the discussion the principles of obedience to civil government, truth-telling, fulfilling promises, and endeavoring to serve customers (customers being one form of "neighbor" in biblical terminology). All of these principles are found in the Bible. All of these principles come from God, who is sovereign Creator and who created each individual with a moral sense (conscience).

Sue knows these things more clearly and more accurately because she has instruction from the Bible. But even people with no contact with the Bible know these truths dimly. God has given to each human being a conscience, a moral sense, and some knowledge of God and His character. Moral principles have probably been written into some of the specific policy statements that Eisai already has in place. Sue can at many points agree with both general policy statements and the individual convictions of fellow employees about what is the right thing for the company to do, even if the individual employees and the authors of the policy statements are not Christians. The policy statement from Johnson & Johnson, "Our Credo," is a good example of the operation of common grace. The policies formulated there are in accord with biblical principles, though no direct appeal is made to the Bible.

But Sue may also find points of sensitivity and potential conflict. Individuals will not always agree about what is right, even on the level of more general principles. Even if people have a measure of agreement on a general principle, their views on the implementation of the principle may differ. For example, just how does the principle of truth-telling intersect the principle of serving the company by maximizing its success? And under what circumstances is it permissible to "shade" the truth without falling into a blatant lie? The company policy statements may be morally flawed; or they may be so general that their implications for advertising Aricept are not clear.

Sue should recognize, on the basis of the teaching of the Bible about her own imperfections and the possibility of self-deceit (Jer. 17:9), that she herself is not perfect in moral discernment. When her judgment differs from someone else's, she needs to listen respectfully, not merely assume that she is superior because she is a Christian. Christian grace includes humility. On the other hand, Sue should recognize that the direct instruction of the Bible, and the work of the Holy Spirit in purifying her conscience, gives her potentially an advantage in the clarity of her moral discernment. She can in many situations become a moral leader. On occasion, she may have to stand for obedience to God even when everyone else opposes her.

Sue's interaction with other people in Eisai must also use the personal perspective. People matter. Eventually some decision has to be made, one way or the other. But Sue should be eager to express respect to others with whom she disagrees ("speaking the truth in love" [Eph. 4:15 ESV]), no matter whose opinions win out in one particular case. Building bridges to people, and not merely narrowly "getting the job done," form part of her responsibility. Sue can find a foundation for bridge building in the commonality of human nature, made in the image of God, and in the biblical principle of respecting human beings with whom she disagrees.

Sue also looks at the situation. She wants to take into account the limitations that exist because a company like Eisai is a public company set up with guidelines and specifications. She wants to consider the situation involved in the process leading to the production of the advertising, and consider possible alterations that will head off a repetition of the same mistake in the future. For her as a Christian, knowing the reality of temptation, it should be natural to ask, "What reward system was in place, and did it provide incentive to violate the law?" Others can join with her in this discussion because considerations of this kind make good practical sense, even if the others do not consciously operate from a biblically grounded framework.

The Inescapability of God and of Christian Redemption

But the reality of deep differences ought also to be faced. Sue knows that Christ as Lord makes universal claims, not merely on her but even on non-Christians. Those claims are normative, and they are also part of the situation. Sue has to reckon with these realities, even though others do not accept them. Sue does not merely fit in. She has a different knowledge of the total "situation." In addition, things that are going on in her mind and her spirit do not match "the world," that is, the world in rebellion against God (1 John 2:15–17; John 15:18–21).

Moral standards go back to God. Persons and their value go back to God, who created them. If Sue is following the Bible's instruction, she learns to think about the world in personal terms, with God as a person at the center. Moral standards are not just abstract principles sitting in the air, but reflect the character of a personal God. Knowing God the infinite person helps in discerning the meaning and applicability of His standards to difficult cases and so-called gray areas where the implications of a particular federal statute may not be crystal clear. Non-Christians also, as we have observed, know God inescapably (Rom. 1:21). But their knowledge is clouded and problematic. That will have

effects on their understanding of moral principles, including principles of obeying authority and principles of truth-telling. The effects may be very subtle; but at times they may also be dramatic. Sue needs to be instructed by the Bible at this point, and not to be naive about the reality of differences.

Sue's personal perspective also includes her communion with God. She should be devoting herself to God in body and in spirit throughout the day's activities (Rom. 12:1–2). She can offer up praises and petitions. She may be praying for God-honoring decisions within Eisai, for God-honoring ethical principles, and for God to work in the people in Eisai. She prays for people to come to know Christ as Savior, because that is the foundational remedy not only for individuals but for the world, including the "world" of business. At the same time, short of that fundamental change, she prays for incremental changes that are in line with biblical principles.

Significance of Differences

We may wonder about the reasons for the differences in the earlier and later cases that confronted McNeil Consumer Products. As Dr. Radebaugh points out, McNeil had the same policy, "Our Credo," in 1982–84 and in 2008–2010. What made the difference? It might be the case that in 1982–84 key officials were more personally in tune with the depth motivations of the "Credo," which according to a Christian view go back to God in his personal character. At a later point, in 2008–2010, it is possible that officials, whether Christian or non-Christian in name, suppressed this depth dimension in the "Credo" and treated it as little more than wishful verbiage, with little personal depth and little situational relevance. Norms have meaning in interaction with persons and situations (using the three perspectives)—they are not rightly treated as impersonal abstractions.

The differences between human viewpoints impinge even more painfully when we consider redemption. Suppose that at Eisai someone deliberately violated the law. What is the remedy? Does he get fired? Does he get a slap on the wrist? Does he merely get sympathy? If we listen to the Bible, we realize that the deliberate violation was a sin, not merely a human violation against a human rule. Christ is the only remedy for sin. But we cannot force redemption on anyone. People are saved only by the power of God. As a minimum, we can pray for the person at fault. But depending on the situation, a Christian might or might not have opportunity to share with the person at fault the deeper recesses of the problem.

In a typical public company, or even in an explicitly Christian company, Christians have to weigh the situation and the personal dimension, which may include specific resistance, on the part of some people, to any overt Christian message. Many situations are difficult, and require us to seek creativity from God.

Fundamental Loyalties

Within these situations, we should recognize that our loyalty to Christ rises above all other loyalties. And this loyalty includes as one aspect the importance of announcing Christ's claims. Peter and the apostles said, "We must obey God rather than men" (Acts

5:29 ESV). The apostles disobeyed recognized human authorities who had been put in place through God's providence. Normally we must obey the authorities over us. Why did the apostles do otherwise? Their loyalty to God and to Christ trumped the claims of human authorities.

The same principles apply today. If human authorities within a company tell us to sin, whether by way of lying or fraud or disobedience to civil government, we cannot consent. Neither do we consent when human authorities tell us to keep quiet about the realities of Christ. That was the issue to which the apostles more than once responded by pointing to the ultimacy of divine authority (Acts 4:19–20; 4:29–33; 5:29).

Christians confront resistance in this area for several reasons. First, human authorities are tempted to imagine that their authority is absolute. Second, they do not like people who upset the apple cart by going against "standard policy." Third, people are incited both by sin and by the devil to try to suppress the Christian message and its effects. Sometimes they use as an excuse the disruptive character of the Christian message (Acts 16:20–21; 19:26–27; 24:5), which of course is partly related to its exclusiveness, but also to its absoluteness. Businesses or civil governments or other authorities may put in place rules against "proselytism" or religious "insults" or "offensive [religious] language" or other specifications that have as one effect the suppression of free propagation of the gospel. We should recognize that all such suppression is at root rebellion against God Himself. It only pretends to be neutral. God *commands* the proclamation of the gospel of the universal lordship of Christ. No one has the right to undo or oppose what God commands.

Businesses—including "nice-sounding" businesses—can have policies that explicitly contradict God's commands in this area. We must face the fact that this is an evil, and that it comes from businesses and their policies, not from Christians who find that sometimes for conscience' sake they must violate those policies. (Of course, immature Christians can sometimes be obnoxious or indiscreet; but I am addressing the issue of illegitimate suppression.) This is not an evil that is easily removed. It belongs to a larger culture of evil.

Let us follow this concern a little further. Do we, in some cases, confront a culture that loves prosperity and economic pragmatism, a culture in which economic goals become new idols? The culture wants smoothly functioning businesses, and that means marginalizing the ferment engendered by religious debate. People allegedly have the "right" to have their religious views undisturbed (and unused!) in the workplace. Religion must be made irrelevant for the sake of smooth business economics. This kind of culture wants "peace" in opposition to the disruptive challenges of the gospel, a gospel that proclaims the kingdom of God and the necessity of change by submission to the lordship of Christ. This is a serious difficulty. When we confront it, we should pray for change, rather than imagining that worldly weapons are our primary resource.

Christians must also recognize that in these cases we, like the apostles, "must obey God rather than men" (Acts 5:29 ESV). That takes wisdom. The form that our obedience takes cannot be compromised merely on the basis of human rules. But in some situations it may be wisest to find a way around the rules rather than directly violating them. Christians can pray and work for change in human rules or a revised understanding

of the implications of the rules. They can discuss difficulties with their superiors beforehand. The Bible counsels us to make our defense of Christian faith "with gentleness and respect" (1 Peter 3:15 ESV). With all the creativity and power that the Holy Spirit supplies, we should make every effort to talk and act winsomely. "Keep your conduct among the Gentiles honorable, so that when they speak against you as evildoers, they may see your good deeds and glorify God on the day of visitation" (1 Peter 2:12 ESV). "For this is the will of God, that by doing good you should put to silence the ignorance of foolish people. Live as people who are free, not using your freedom as a cover-up for evil, but living as servants of God" (1 Peter 2:15–16 ESV). "But even if your should suffer for righteousness' sake, you will be blessed. Have no fear of them, nor be troubled, but in your hearts regard Christ the Lord as holy, always being prepared to make a defense to anyone who asks you for a reason for the hope that is in you; yet do it with gentleness and respect, having a good conscience, so that, when you are slandered, those who revile your good behavior in Christ may be put to shame. For it is better to suffer for doing good, if that should be God's will, than for doing evil" (1 Peter 3:14–17 ESV).

Forgiveness

A Christian should also recognize from the Bible the role of forgiveness in human relationships. What should a company do with a person who has violated the law, as might have been the case with Eisai? Even if a guilty person does not repent thoroughly, it may be wise to give him another chance. Or maybe not. Here again we confront the challenge of wisely and discerningly weighing norms, persons, and situations. For example, the situation may be such that the violation was flagrant, serious, and repeated. It is time to fire the person, both for the protection of the future of the company, for the protection of the integrity of fellow workers, and for his own good (he must feel the consequences). True love, in biblical terms, cares about the person and is ready to forgive. But caring about the person may also mean bringing consequences, to strengthen the person's resolve not to sin again. This principle holds true within the Christian community, where we can experience the full power of Christian redemption. But in an analogous way it can also be applied—with careful attention to the difference in situations—to situations of "common grace" outside the Christian community. We are called on to be a blessing to non-Christians even when they remain outside the Christian faith (Gal. 6:10).

Conclusion

When we as Christians attempt to bring principles like these to bear within a situation of religious and ethical "pluralism," we need both to care about the blessing that non-Christians can receive from Christian principles, and to take into account the fundamental disagreements that remain in place between Christian faith and "the world." We endeavor to explain our principles winsomely, not obnoxiously thrusting forward our Christian underpinnings on those who wish not to hear them, but also being honest about the fact

that our understanding is informed by deeper roots. The endeavor to do justice to both sides of the situation requires wisdom and graciousness and humility and creativity. Once again, we confront our need for the power of the Spirit of Christ.

Notes

1. John M. Frame, *Perspectives on the Word of God: An Introduction to Christian Ethics* (Eugene, OR: Wipf and Stock, 1999); John M. Frame, *The Doctrine of the Christian Life* (Phillipsburg, NJ: Presbyterian and Reformed, 2008).
2. See Abraham Kuyper, *Lectures on Calvinism* (Grand Rapids: Eerdmans, 1931).
3. Timothy Keller, *Counterfeit Gods: The Empty Promises of Money, Sex, and Power, and the Only Hope That Matters* (New York: Dutton, 2009).

Appendix: Supporting Documents

1. Warning letter from FDA to Eisai Medical Research Inc., http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM201238.pdf (accessed April 28, 2010).
2 "Our Credo" from Johnson & Johnson, http://www.jnj.com/connect/about-jnj/jnj-credo/ (accessed April 26, 2010).
3. Warning letter from FDA to McNeil, January 15, 2010, http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm197811.htm (accessed April 28, 2010).
4. Response from McNeil to the FDA, February 5, 2010, http://www.fda.gov/downloads/AboutFDA/CentersOffices/ORA/ORAElectronicReadingRoom/UCM204455.pdf (accessed April 28, 2010).

Warning letter from FDA to Eisai Medical Research Inc.

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM201238.pdf (accessed April 28, 2010).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Gary Wieczorek, Associate Director, Regulatory Affairs
Eisai Medical Research Inc.
300 Tice Blvd
Woodcliff Lake, NJ 07677

RE: NDA # 20-690
Aricept (donepezil hydrochloride) Tablets
MACMIS #18244

Dear Mr. Wieczorek:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed two consumer broadcast television ads (TV ads) for Aricept® (donepezil hydrochloride) Tablets ("Beach" (ARU00435) and "Garden" (AAR00036)) submitted by Eisai Medical Research Inc. (Eisai) under cover of Form FDA-2253. The TV ads are misleading because they overstate the efficacy of the drug. Thus, the TV ads misbrand Aricept in violation of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 352(n), and FDA implementing regulations. 21 CFR 202.1(e)(5)(i) & (e)(6)(i).

Background

According to its FDA-approved product labeling (PI), Aricept is indicated for "the treatment of dementia of the Alzheimer's type. Efficacy has been demonstrated in patients with mild to moderate Alzheimer's Disease, as well as in patients with severe Alzheimer's Disease."

According to the CLINICAL PHARMACOLOGY section of the PI, Aricept was tested in mild to moderate Alzheimer's disease in two randomized, double-blind, placebo-controlled studies (the Fifteen-Week and Thirty-Week Studies). In each study, the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog) was used. This subscale is a multi-item instrument that examines selected aspects of cognitive performance, including elements of memory, orientation, attention, reasoning, language, and praxis. After 24 weeks of treatment, the mean differences in the ADAS-cog change scores (scored from 0 to 70) for Aricept-treated patients compared to placebo were 2.8 and 3.1 units for the 5 mg/day and 10 mg/day treatments, respectively. The Fifteen and Thirty week studies also analyzed Aricept's ability to produce an overall clinical effect using a Clinician's Interview Based Impression of Change that required the use of caregiver information (CIBIC plus). The CIBIC plus examined general, cognitive, and behavioral function and activities of daily living on a 7-point scale ranging from "markedly improved" to "markedly worse." The CIBIC plus results in the Thirty-Week Study (Figure 3 in the PI) are presented in the following graph:

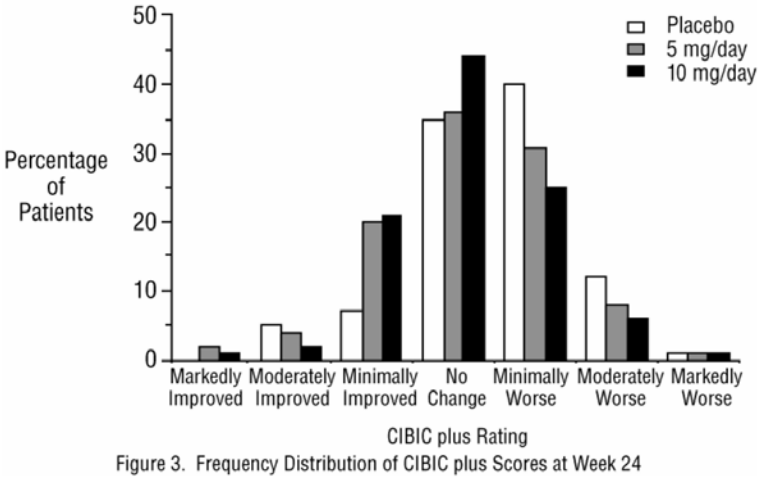

Figure 3. Frequency Distribution of CIBIC plus Scores at Week 24

In patients with severe Alzheimer's disease, the effects of Aricept on cognitive function were tested in a 24 week study (Japanese study), which evaluated patients on both the Severe Impairment Battery (SIB) and CIBIC plus. In addition, a randomized, double-blind, placebo-controlled clinical trial (the Swedish 24-Week Study) assessed cognitive function using the SIB and daily function using the Modified Alzheimer's Disease Cooperative Study Activities of Daily Living inventory for Severe Alzheimer's Disease (ADCS-ADL-severe), which is a subset of 19 items, including ratings of the patient's ability to eat, dress, bathe, use the telephone, get around, and perform other activities of daily living. After 24 weeks of treatment, the mean difference in the ADCS-ADL-severe change scores (scored from 0 to 54) for Aricept-treated patients compared to placebo was 1.8 units. The following graph shows the effect of Aricept on ADCS-ADL-severe in the Swedish 24-week study (Figure 9 in PI):

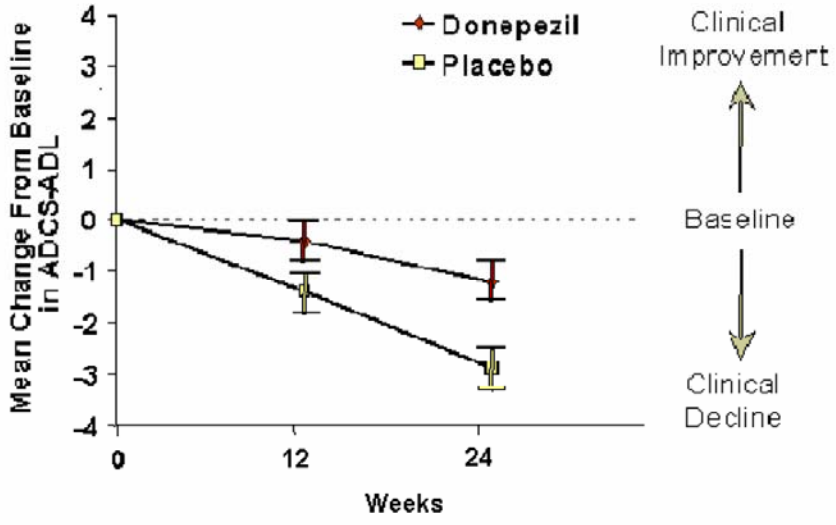

Figure 9. Time course of the change from baseline in ADCS-ADL-severe score for patients completing 24 weeks of treatment.

Aricept is contraindicated in patients with known hypersensitivity to the drug or to piperidine derivatives. Aricept is also associated with serious risks as reflected in the WARNINGS section of the PI, including syncopal episodes and gastrointestinal bleeding, especially in patients with a history of ulcers or in patients who are taking concurrent nonsteroidal anti-inflammatory drugs (NSAIDS). The most common adverse reactions associated with Aricept in severe Alzheimer's disease are diarrhea, anorexia, vomiting, nausea, and ecchymosis. In mild to moderate Alzheimer's disease, the most common adverse reactions are nausea, diarrhea, insomnia, vomiting, muscle cramps, fatigue, and anorexia.

Overstatement of Efficacy

Promotional materials are misleading if they represent or suggest that a drug is more effective than has been demonstrated by substantial evidence or substantial clinical experience.

The "Beach" TV ad presents an elderly man staring off into space, appearing distant, confused, and disinterested, while the rest of his family walks on the beach, and the man's daughter has a look of concern on her face. While this beach scene is taking place, the man's daughter makes the following statements:

- "Dad had been repeating things and acting disoriented for a while, like something was stealing him away from us."
- "We wanted to be there for him, to hold on to him." (While this statement is being made, a young boy clasps the man's hand.)

The ad then shows the man and his daughter discussing Aricept with his doctor. Specifically, the daughter states:

- "Dad's doctor said his symptoms were signs of Alzheimer's, a type of dementia, and that prescription Aricept could help." (While this statement is being made, the daughter poignantly clasps her father's hand.)

After the patient and his daughter discuss Aricept with the doctor, the man's behavior changes dramatically. The man is shown happily interacting with his family members, moving more quickly and with greater focus. For example, he pats his grandson on the head while pouring cereal, winks while feeding the dog under the table, energetically cheers and points at a soccer game while following the plays, and clasps his daughter's hand. While these scenes are taking place, the ad makes the following statements:

- "Studies showed Aricept slows the progression of Alzheimer's symptoms."
- "It improves cognition and slows the decline of overall function."
- "If it helps Dad be more like himself longer, that's everything to us."
- "Don't wait. Talk to your doctor about Aricept."

The "Garden" TV ad presents an elderly woman looking away from family members, appearing confused, aloof, and disoriented. While these scenes are taking place, the woman's daughter makes the following statements:

- "We'd been noticing mom acting forgetful and confused, like she was drifting away."
- "We wanted to be there for her, to hold on to her." (While this statement is being made, a young girl clasps the woman's hand.)

Similar to the "Beach" ad, this ad then shows the woman and her daughter discussing Aricept with her doctor. Specifically, the ad states:

- "Studies showed Aricept slows the progression of Alzheimer's symptoms."
- "It improves cognition and slows the decline of overall function."

After the woman and her daughter discuss Aricept with the doctor, the woman's behavior changes dramatically. The woman is shown interacting happily with her daughter and her grandchildren, trying on a hat, helping them plant seeds, and working with them in the garden. At the end of the ad, the daughter looks at her mother, smiling and hugging her, and the woman clasps her daughter's hand.

The totality of the above claims and presentations misleadingly overstates the efficacy of Aricept, implying a greater benefit than has been supported by substantial evidence or substantial clinical experience. As described above, the beginning segment of each ad presents patients with Alzheimer's disease looking blank, confused, distant, and walking off apart from their family members. However, after talking to their doctors about treatment with Aricept, the patients are seen interacting and communicating with their family members, happily and actively involved in activities with them. These presentations imply that, as a result of Aricept treatment, patients' cognitive and daily functioning, specifically aspects of attention and focus, orientation, communication, and social interaction and engagement, will be restored to normal.

The results from the Aricept efficacy trials in patients with mild to moderate and severe Alzheimer's disease do **not** support such a drastic improvement. According to the CLINICAL PHARMACOLOGY section of the PI, the mean differences in the ADAS-cog change scores for Aricept-treated patients compared to placebo were **only 2.8 and 3.1 units** (scored from 0 to 70) for the 5 mg/day and 10 mg/day treatments, respectively, after 24 weeks of treatment. Furthermore, the distribution of CIBIC plus scores in patients in the Thirty-Week Study (see Figure 3 in Background section) indicates that **less than 5%** of patients treated with Aricept at either dose were "markedly improved" or "moderately improved." The majority of patients experienced no change or became worse on Aricept treatment. Moreover, Figure 9 (see Background section) indicates that although the Aricept-treated group in the Swedish 24-Week Study reached a statistically significant result in change from baseline in ADCS-ADL-severe scores versus placebo, the mean difference was **only 1.8 units** (scored from 0 to 54), and patients on Aricept continued to show clinical decline over time.

Therefore, the claims and presentations in both TV ads are **not** representative of the results from the clinical trials for Aricept, and misleadingly overstate the efficacy of the drug. The inclusion of the superimposed text, "Individual results may vary," does not mitigate these misleading presentations.

Conclusion and Requested Action

For the reasons discussed above, the TV ads misbrand Aricept in violation of the Act, 21 U.S.C. 352(n), and FDA implementing regulations. 21 CFR 202.1(e)(5)(i) & (e)(6)(i).

DDMAC requests that Eisai immediately cease the dissemination of violative promotional materials for Aricept such as those described above. Please submit a written response to this letter on or before February 18, 2010, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Aricept that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials. Please direct your response to me at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD 20705-1266, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS # 18244 in addition to the NDA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Aricept comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Sharon M. Watson, PharmD
LCDR, USPHS
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20690	ORIG-1	EISAI INC	ARICEPT

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SHARON M WATSON
02/03/2010

“Our Credo” from Johnson & Johnson

http://www.jnj.com/connect/about-jnj/jnj-credo/ (accessed April 26, 2010).

Our Credo

We believe our first responsibility is to the doctors, nurses and patients,
to mothers and fathers and all others who use our products and services.
In meeting their needs everything we do must be of high quality.
We must constantly strive to reduce our costs
in order to maintain reasonable prices.
Customers' orders must be serviced promptly and accurately.
Our suppliers and distributors must have an opportunity
to make a fair profit.

We are responsible to our employees,
the men and women who work with us throughout the world.
Everyone must be considered as an individual.
We must respect their dignity and recognize their merit.
They must have a sense of security in their jobs.
Compensation must be fair and adequate,
and working conditions clean, orderly and safe.
We must be mindful of ways to help our employees fulfill
their family responsibilities.
Employees must feel free to make suggestions and complaints.
There must be equal opportunity for employment, development
and advancement for those qualified.
We must provide competent management,
and their actions must be just and ethical.

We are responsible to the communities in which we live and work
and to the world community as well.
We must be good citizens — support good works and charities
and bear our fair share of taxes.
We must encourage civic improvements and better health and education.
We must maintain in good order
the property we are privileged to use,
protecting the environment and natural resources.

Our final responsibility is to our stockholders.
Business must make a sound profit.
We must experiment with new ideas.
Research must be carried on, innovative programs developed
and mistakes paid for.
New equipment must be purchased, new facilities provided
and new products launched.
Reserves must be created to provide for adverse times.
When we operate according to these principles,
the stockholders should realize a fair return.

Johnson & Johnson

Warning letter from FDA to McNeil, January 15, 2010

http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm197811.htm (accessed April 28, 2010).

U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

McNeil Consumer and Specialty Pharmaceuticals 1/15/10

Department of Health and Human Services

Public Health Service
Food and Drug Administration
San Juan District
466 Fernandez Juncos Avenue
San Juan PR 00901-3223
Telephone: (787) 474-9500
FAX: (787) 729-6658

January 15, 2010

WARNING LETTER
SJN-2010-01

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Peter Luther, President, NA OTC
McNeil Consumer Healthcare
7050 Camp Hill Road Mb # 204
Fort Washington, PA 19034

Dear Mr. Luther:

This is regarding an inspection of your pharmaceutical manufacturing facility, McNeil Healthcare LLC, located at Road 183, Km. 19.8, Sector Montones, Las Piedras, Puerto Rico 00771, conducted by investigator J. Lopez and chemist R. Gonzalez and concluded on January 8, 2010. The inspection identified significant violations of the Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations (C.F.R.), Parts 210 and 211. These violations cause your drug products to be adulterated within the meaning of Section 501 (a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)] in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with CGMP regulations. In addition, our inspection revealed that you failed to submit NDA Field Alert Reports (FARs) to FDA in compliance with 21 C.F.R. § 314.81 (b)(1)(ii), as required by section 505(k) of the Act [21 U.S.C. § 355(k)].

Specific violations observed during the inspection include, but are not limited, to:

1. Failure to thoroughly investigate any unexplained discrepancy or the failure of a batch or any of its components to meet any of its specifications whether or not the batch has already been distributed. In addition, you failed to extend the investigation to other batches of the same product and other products that might have been associated with the discrepancy as required by 21 C.F.R. § 211.192.

Your company has determined that the "uncharacteristic odor" complaints, some of which were associated with adverse event reports (gastrointestinal distress), for several of your OTC drug products are due to 2,4,6 Tribromoanisole (TBA) contamination in the product and/or bottles. TBA, which has a musty, mildew-type odor, is a known degradant of 2,4,6, Tribromophenol (TBP). TBP is a pesticide and flame retardant used to treat wooden pallets for transporting packaging materials and finished product. TBA is organoleptically detectable at parts per trillion. You are currently attributing the cause of the uncharacteristic odor to be contamination of the drug product containers from TBP treated wooden pallets. You have concluded that TBP from the wooden pallets degraded into TBA, which contaminated product containers and the finished product in those containers.

The contamination, first noted in 2008, occurred again in 2009, leading to recalls of several lots of Tylenol

Arthritis Relief caplets, 100 count bottles, 650 mg. More recalls are being conducted including multiple other OTC drug products.

We are aware of the complaint information available to your company, the sequence of events, and the extent of your firm's follow up measures during this period. We have concluded that your company did not conduct a timely, comprehensive investigation.

Your initial investigation into the root cause of the odor was unjustifiably delayed and terminated prematurely. Numerous complaints were received over a four month period in 2008 before they were considered a trend and before actions were initiated to determine the root cause. When microbiological testing in August 2008 did not support an initial speculation that microbial contamination was the root cause of the odor, the investigation was closed. No other possible root causes were pursued. Your firm lacked adequate justification for this decision.

Complaints of uncharacteristic odor were reported again in April 2009. Approximately 112 similar complaints were received by August 3, 2009. Although your firm had test results indicative of contamination with TBA as the source of the off odor on the complaint samples since September 2009, these results were not shared with FDA until after the initiation of the inspection and following several requests for this information made by the district office.

In October 2009, you concluded that the most probable root cause of the odor in the Tylenol Arthritis Relief caplets was the exposure of drug product bottles to wood pallets chemically treated with TBP. You did not expand the scope of the investigation to other lots and products potentially affected by this deviation. This would include, for example, products packaged in bottles from the same supplier that used the same type of wooden pallets, and other products manufactured by your facility for which odor complaints were received.

2. Failure of your Quality Control Unit to ensure a thorough investigation in accordance with 21 C.F.R. § 211.192 with conclusions and follow up accomplished as required by 21 C.F.R. § 211.198. As described above, the timing and depth of your investigative efforts regarding uncharacteristic odor complaints were insufficient to meet good manufacturing practice. Your firm's management, including the Quality Control Unit, was not proactive in response to consumer complaints. In addition, during the 2008 examination of complaint samples, your firm's analysts noted that the tablets, once removed from the bottle, did not have an unusual odor but the bottle retained a strong odor. Nonetheless, you did not pursue chemical testing at that time.

Your firm's quality management should have ensured the start of chemical testing far earlier. Failure to do so prolonged identification and resolution of the problem, resulting in continued consumer exposure. Quality problems must be thoroughly investigated, root cause determined, and appropriate corrective and preventive actions implemented as quickly as possible to limit exposure of the public to substandard drugs.

3. Failure to submit NDA-Field Alert Reports (FARs) within three (3) working days of receipt of information concerning any bacteriological contamination, or any significant chemical, physical, or other change or deterioration in the distributed drug products as required by 21 C.F.R. § 314.81 (b)(1)(ii).

Your firm received numerous uncharacteristic odor consumer complaints during the period of April 2008 through September 2008 for your product Tylenol Arthritis Relief caplets. Nevertheless, you failed to submit a FAR to FDA within three working days to inform the Agency of the nature of the problem and the steps that you were taking to address it. You did not submit the FAR until September 18, 2009, after again noting an adverse, continuing trend of numerous complaints over the course of a several month period.

The Agency is concerned about the response of Johnson & Johnson (J&J) to this matter. It appears that when J&J became aware of FDA's concerns about the thoroughness and timeliness of McNeil's investigation, whether all potentially affected products had been identified, and whether the recall was adequate in scope, J&J did not take appropriate actions to resolve these issues. Corporate management has the responsibility to ensure the quality, safety, and integrity of its products. Neither upper management at J&J nor at McNeil Consumer Healthcare assured timely investigation and resolution of the issues.

Neither this letter nor the observations noted on the FDA-483 is intended to be an all-inclusive list of the deficiencies that may exist at your facility. In addition, the Agency may send further correspondence based upon continued review of the inspectional findings. It is your responsibility to ensure that your operations at this facility and all other facilities under your control are in full compliance with all applicable requirements of federal law and FDA regulations. You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure, and injunction. Other federal agencies may take this warning letter into account when considering the award of contracts. Additionally, FDA may withhold approval of requests for export certificates, or approval of pending new drug applications listing your facility as a manufacturer until the above violations are corrected. A reinspection may be necessary.

Within 15 working days of receipt of this letter, please notify this office in writing of the specific steps that you

have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you cannot complete corrective action within 15 working days, state the reason for the delay and the time within which you will complete the correction.

Please contact the District Office to schedule a meeting to discuss your proposed corrective actions and time frames, as well as your plan for ensuring timely and meaningful involvement of corporate management (local and global) in resolving significant public health issues in the future. Please contact Margarita Santiago, Compliance Officer, at (787) 474-4789 to schedule a meeting at the FDA, San Juan District Office.

Your reply to the Warning Letter should be sent to the Food & Drug Administration, San Juan District Office, 466 Fernandez Juncos Ave., San Juan, PR 00901-3223, to the attention of Margarita Santiago.

Sincerely,

/S/

Maridalia Torrres
District Director
San Juan District

Cc:
Mr. William C. Weldon, CEO, Johnson & Johnson
Ms. Nuria Ramirez Ordonez, General Manager, McNeil Healthcare, LLC, Las Piedras, PR

Links on this page:

Response from McNeil to the FDA, February 5, 2010

http://www.fda.gov/downloads/AboutFDA/CentersOffices/ORA/ORAElectronicReadingRoom/UCM204455.pdf (accessed April 28, 2010).

McNeil
Consumer Healthcare

Peter Luther
Président

e-mail: (b) (4)

CONFIDENTIAL
February 5, 2010

Margarita Santiago
Food and Drug Administration
San Juan District Office
466 Fernandez Juncos Ave.
San Juan, PR 00901-3223

Subject: Response to the Warning Letter dated January 15, 2010

Dear Ms. Santiago:

On behalf of McNeil Consumer Healthcare, Division of McNEIL-PPC, Inc. ("McNeil"), please find our written response to the Warning Letter issued to us on January 15, 2010 (the "Warning Letter"). This document provides a summary of the corrective actions to the issues raised in the Warning Letter. The second document is the more detailed response to the FDA Form-483 ("483") issued January 8, 2010. Therefore, in considering this response to the Warning Letter, the FDA should also consider and reference the more detailed 483 response document.

McNeil and Johnson & Johnson management are taking this issue very seriously and are committed to ensuring that McNeil implements all necessary corrective and preventive actions to improve the McNeil quality systems.

McNeil shares FDA's primary concern of ensuring the safety and efficacy of our products and understands the important obligation we have to the consumers that use them. Given this obligation, our quality systems are of utmost importance to us and we appreciate the feedback and input received from the FDA in the Warning Letter. We have already begun implementing the corrective actions detailed in this response.

McNeil Investigation

McNeil acknowledges the concerns raised by the FDA in the 483 and the Warning Letter with respect to the thoroughness and timeliness of various aspects of this investigation. The corrective actions detailed below directly and indirectly address FDA's concerns and will improve the thoroughness and timeliness of our investigations in the future.

As an initial matter, it's important to review the scope of the investigation that led McNeil to the source of the contamination, the primary root cause of the 2, 4, 6-tribromoanisole ("TBA"), and the decision to recall various McNeil products. Reviewing this investigation has been critical to our development of an effective corrective action plan. The components of this corrective action plan, which are highlighted below, and detailed in the 483 submission, are being implemented systemically throughout McNeil.

In McNeil's experience, many of the challenges raised by this particular investigation were unique. Only after we engaged (b) (4) an external forensic laboratory, that has unique testing capabilities, did we determine that TBA was a likely source of the uncharacteristic odor. After McNeil confirmed the source of the odor, we were able to launch a comprehensive investigation focused specifically on how TBA could have entered the McNeil supply chain.

While (b) (4) has the appropriate analytical equipment and methodologies capable of detecting trace amounts of TBA in parts per trillion ("ppt") levels, the nature of this testing was, and continues to be, limited to only 8 samples per day. We continue to evaluate other laboratories capable of conducting this testing; however, very few laboratories have been able to meet our ppt sensitivity requirements and no laboratories, as of the date of this letter, have been able to validate at these levels. In parallel, we are pursuing in-house development of this testing capability.

Our next challenge was to determine how TBA could have entered the supply chain. This stage of the investigation led us to review multiple potential sources of contamination, including, but not limited to caps/liners, bottles/resins, pallets, manufacturing/packaging lines, bulk product, and ingredients. We also conducted extensive literature searches and worked with toxicology experts to help us better understand the chemical and how to evaluate its potential toxicity. From this, we learned that there was no toxicity data available for TBA. Relevant Health Hazard Evaluations ("HHEs") were developed and provided to FDA. The scope of the investigation widened significantly before it narrowed. Each time our knowledge increased, we expanded our search for affected or potentially affected products.

Based on this comprehensive forensic investigation, we traced TBA from certain bottles to wood pallets, and then, more specifically, to wood used to build the pallets that was sourced from (b) and treated with 2, 4, 6-tribromophenol ("TBP"). From the literature, we know TBP can lead to the formation of TBA under certain environmental and handling conditions. Once we confirmed via analytical testing that these wood pallets were treated with TBP and were likely the primary cause of the TBA, we expanded our review to include other sites that had received these pallets and decided on January 14, 2010 to initiate the very broad recall of any potentially impacted products.

Our investigation continues and we will be providing an update to you at our February 11, 2010 meeting.

In the Warning Letter, FDA identified the following 3 specific violations that were observed during the inspection:

1. *Failure to thoroughly investigate any unexplained discrepancy or the failure of a batch or any of its components to meet any of its specifications whether or not the batch has already been distributed. In addition, you failed to extend the investigation to other batches of the*

same product and other products that might have been associated with the discrepancy as required by 21 C.F.R. Section 211.192.

2. *Failure of your Quality Control Unit to ensure a thorough investigation in accordance with 21 C.F.R. Section 211.192 with conclusions and follow up accomplished as required by 21 C.F.R. Section 211.198. As described above, the timing and depth of your investigative efforts regarding uncharacteristic odor complaints were insufficient to meet good manufacturing practice. Your firm's management, including the Quality Control Unit, was not proactive in response to consumer complaints. In addition, during the 2008 examination of complaint samples, your firm's analysts noted that the tablets, once removed from the bottle, did not have an unusual odor but the bottle retained a strong odor. Nonetheless, you did not pursue chemical testing at that time.*

   Your firm's quality management should have ensured the start of chemical testing far earlier. Failure to do so prolonged identification and resolution of the problem, resulting in contained consumer exposure. Quality problems must be thoroughly investigated, root cause determined, and appropriate corrective and preventative actions implemented as quickly as possible to limit exposure of the public to substandard drugs.

3. *Failure to submit NDA-Field Alert Reports (FARs) within three (3) working days of receipt of information concerning any bacteriological contamination, or any significant chemical, physical, or other change or deterioration in the distributed drug products as required by 21 C.F.R. Section 314.81(b)(1)(ii).*

   Your firm received numerous uncharacteristic odor complaints during the period of April 2008 through September 2008 for your product Tylenol Arthritis Relief caplets. Nevertheless, you failed to submit a FAR within three working days to inform the Agency of the nature of the problem and the steps that you were taking to address it. You did not submit the FAR until September 18, 2009, after again noting an adverse, continuing trend of numerous complaints over the course of a several month period.

McNeil is implementing a corrective action plan, described below, and in more detail in the 483 response, which we believe addresses each of these 3 items in a comprehensive way. We have the appropriate knowledge, resources and direction to execute these enhancements and improvements. As the President of McNeil, I understand that I and McNeil's Management Board have final oversight responsibilities to ensure that the commitments described in our responses are addressed and given priority attention by our organization.

The key elements of the corrective action plan for the Warning Letter include:

- Enhancements to the Quality System
- Organizational Changes
- Senior Management Oversight

Enhancements to the Quality System

Based on our investigation, we recognize opportunities to enhance our Quality System. As a result, we have immediately implemented the following improvements:

- *Changes to complaint review process:* McNeil recognizes the importance of appropriate categorization of complaints in helping to facilitate accurate, timely, and actionable trending of complaints based on reported defect types. Based on this, McNeil has reassessed all complaint categories with specific focus on categories that may require subjective interpretation. These categories have been redefined or combined to increase consistency in complaint defect coding and to ensure accuracy in trending. Accurate complaint categories will increase our ability to identify signals and trends faster, and to take action more effectively.

  All affected employees have been trained in these new complaint category definitions. The implementation of the new complaint categories will occur in February 2010.
  Concurrent to the development of the new categorization, the existing procedural requirements for quality investigators to evaluate and correct complaint categorization during daily file review have been reinforced through training. This training was completed in January 2010.

  Relevant changes to the complaint review process are reflected in SOP (b) (4) "Requirements for Complaint Handling" attached to the 483 response.
- *Changes to complaint handling procedures:* McNeil recognizes the important role of appropriate complaint handling procedures in ensuring that trends are detected early and investigated thoroughly. McNeil will continue to investigate all complaints associated with our products pursuant to SOP (b) (4) In addition, we have developed (b) (4) based on severity or frequency, for trends above baseline levels for all products. This approach in trending will enhance our ability to identify and recognize trends for product families, product lots, and across product lines. This trending will enable the early identification of issues requiring an expanded investigation, management notification and prioritization of action. This trending will be done on a continuous basis including monthly and quarterly reviews by the McNeil quality organization.

  These changes to the complaint handling procedures are reflected in SOP (b) (4) "Requirements for Complaint Handling" attached to the 483 response.

- *Change to Investigation Procedures:* We are amending the current investigation SOP to require that if an (b) (4) (b) (4) (b) (4) (b) (4) Such decisions will be documented and are intended to ensure the broadest investigatory approach. (b) (4) (b) (4) (b) (4)

  This change to investigation procedures will be reflected in SOP (b) (4) attached to the 483 response.

- *Change to Central Complaint Vigilance Quarterly Process:* We will expand our Central Complaint Vigilance Quarterly Process, where we currently review complaints, to include a more extensive review of adverse event trends across all McNeil product lines, and will formally include (b) (4) and (b) (4) This expanded process will be in place in April 2010.

  These changes to the Central Complaint Vigilance Quarterly Process are reflected in SOP (b) (b) (4) "Requirements for Complaint Handling" attached to the 483 response.

- *Change in Field Alert Reporting Requirements for Complaint Trends:* To help ensure more timely notification to FDA of NDA-Field Alert reports, the McNeil FDA Field Alert procedure has been revised to require the issuance of a Field Alert once a confirmed complaint trend where bacteriological contamination or significant chemical, physical, or other change or deterioration in a distributed drug product cannot be ruled out. This Field Alert will be issued within 3 business days of McNeil becoming aware of a complaint trend. In addition to timely communications, this interpretation of Section 314.81(b)(1)(i) and (ii), as codified in Title 21 of the Code of Federal Regulations, will likely result in more frequent communications with FDA.

  These changes to the Field Alert Reporting Requirements for Complaint Trends are reflected in SOP (b) (4) attached to the 483 response.

Organizational Changes

McNeil has already begun implementing organizational changes that it believes will strengthen our focus on quality and compliance. Dr. Veronica Cruz has been appointed to the position of Vice President of Quality Assurance, OTC, effective February 15, 2010, and will be a member of the McNeil Management Board. Dr. Cruz has extensive experience in Quality within the API and pharmaceutical dosage manufacturing environment. She has supported manufacturing and distribution to global markets of OTC liquids and solids and spent much of her career in Puerto Rico, including previous experience in McNeil's Las Piedras site. She moves to this role from the position of Vice President, North America Quality Operations for Johnson & Johnson's Global Pharmaceutical Supply Group. Throughout her career, she has also developed and implemented various quality systems and processes resulting in significant improvement in the compliance level of the site quality systems.

As announced in the appointment of Dr. Cruz, she will now report directly to Sam Jiwrajka, who has been appointed to the role as head of Quality for the Johnson & Johnson Group of Consumer Companies. This move is part of changes already underway within the Johnson & Johnson Consumer organization which we believe will further strengthen our Quality operating model. Under this new model, McNeil will receive increased support from the Johnson & Johnson Consumer quality organization; however, the McNeil Management Board, consisting of executive leaders from various functions, will continue to be directly accountable for product quality and regulatory compliance of McNeil. This will allow these organizations to realize the benefits of Johnson & Johnson Consumer's scale and scope while continuing to preserve the benefits and accountabilities of our decentralized structure.

Senior Management Oversight

McNeil senior management is committed to more detailed and frequent oversight of our quality systems and quality-related issues with our products.

We are in the process of initiating enhanced Quarterly Executive Board Quality System reviews. These reviews will include the McNeil Management Board as well as relevant members of the McNeil quality organization, plus participants from Johnson & Johnson. While Executive quality reviews were initiated in 2009, we have identified opportunities to improve the depth and breadth of these reviews. Therefore, they will now include a review of all of our quality system elements with very specific management action plans established and tracked. This will provide senior management with the appropriate level of visibility and will ensure adequate support and prioritization of key issues.

In addition to the Quarterly Executive Board Quality System Reviews, we will be adding complaint updates to our monthly McNeil Management Board meeting. This will give the McNeil Management Board greater visibility to complaint trends earlier to ensure that they are given appropriate prioritization, attention, and action at a senior level in the organization.
These senior management quality review processes are reflected in SOP (b) (4) attached to the 483 response.

In addition to the Quality System enhancements outlined above, Dr. Cruz will lead a comprehensive assessment of the McNeil quality system in coordination with resources from Johnson & Johnson Quality & Compliance Worldwide. This assessment will be completed by the end of April 2010. Based on this assessment, Dr. Cruz will develop a plan that would continue to strengthen our focus on complaint vigilance, corrective and preventive actions ("CAPAs") and quality systems. We will share this plan with FDA to underscore our ongoing commitment to improving our quality system.

Remediation Plan related to Pallets

In addition to the corrective actions outlined above, McNeil has also developed a remediation plan specifically directed to TBA and wood pallets. Based on our determination that TBP-treated wood used to make pallets are the primary cause of the TBA contamination, a remediation plan was immediately developed which included the following:

- All existing McNeil components from the (b) (4) plant shipped on wood pallets, where the pallets could not be confirmed to be TBP-free, are in the process of being destroyed (along with the pallets themselves).

- McNeil packaging lines and warehouses are being cleaned at all sites per a protocol developed in consultation with an external TBA expert. A similar cleaning procedure was also used at the aforementioned component supplier, (b) (4)

- McNeil has required of all in-coming material suppliers that any pending shipments or future shipments are to be on heat-treated, TBP/phenol-free pallets. An inspection process has been instituted to evaluate incoming materials to confirm that they are only shipped on heat-treated pallets. In addition, documentation from wood/pallet suppliers is required to confirm that the pallets are TBP/phenol-free. Materials on pallets not meeting these requirements are not

accepted into any McNeil facility. This process is also being rolled out to our third-party manufacturing sites. Monitoring of compliance with this pallet requirement will be conducted.

Conclusion

McNeil recognizes the seriousness of this situation and has identified this corrective action plan as our top priority. We are dedicated to providing the resources, time, effort and executive oversight to ensure that our quality systems meet all requirements and operate effectively and efficiently. We are confident that this corrective action plan provides the approach necessary to identify and implement systemic actions that will improve and enhance our quality processes and systems while addressing the concerns raised by the FDA in the Warning Letter and the 483.

We look forward to our February 11 meeting and the opportunity to engage with you more fully on our corrective actions and plans moving forward and on our on-going investigation. Please feel free to contact me by phone at (b) (4) if you have any questions or concerns.

Sincerely,

Peter Luther
President

cc: Maridalia Torres