We Need to Know More:

The Importance of Studying Medical Products That are Already Approved

Diana Zuckerman, Ph.D., President

National Center for Policy Research (CPR) for Women & Families

Statement at the FDA Public Meeting on PDUFA

Panel II

December 7, 2001

During the last two years, several very widely-used drugs were removed from the market after they had been approved. It is abundantly clear that approval of a drug or device is based on short-term information that may not tell the entire story about the safety of a medical product. Under the current Prescription Drug User Fee Act (PDUFA), user fees are not allocated for monitoring the safety of medical products that have been approved. As a result, there are very limited resources for post-market surveillance. This is a dangerous situation that must change.

The current situation is a recipe for disaster, as more and more drugs are sold to more and more people soon after approval.

Here's the recipe:

1. Approve drugs more quickly;

2. Approve medical products that have known serious complications and adverse reactions, and do nothing to ensure that physicians and patients will have the information they need to objectively weigh the risks and benefits;

3. Spend billions of dollars on direct-to-consumer advertising and promotions to physicians, which will ensure that very large numbers of consumers are taking drugs that are newly available;

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4. Rely on the manufacturers and spend very little federal resources to ensure that products are studied carefully after they are approved;

5. Spend very little to study adverse reaction reports or even to make sure that the reporting system works appropriately.

Stir this all together, and the result is going to be that some products are going to be approved that have much more serious risks than is known at the time of approval, and consumers will die or suffer from serious health problems as a result.

Because of PDUFA, there is less money than there was before for the FDA to conduct or monitor post-market surveillance. As bad as the situation is for drugs, consumers with implanted medical devices are even more vulnerable. Of course, this is part of a much larger problem because user fees are not used for medical devices at all.

I will provide three examples of the need for better post-market surveillance:

1. Fen-phen was widely used as a diet pill by thousands of women, some of whom died or experienced permanent health problems as a result. The risks were discovered by health professionals who happened to see a lot of patients with identical, and yet highly unusual, health problems, all of whom had received diet pills at the same medical facility. It was thanks to luck and some very observant health professionals that this was discovered – if the women had received their fen-phen through the Internet or another clinic, the doctors and nurses probably would not have noticed the link between the drug and the adverse reaction. It might have taken years before the link was discovered, and tens of thousands of other women and men would have been at grave risk.

2. Jaw implants – a permanent device used to treat TMJ disorders -- were recently approved by the FDA despite the lack of even 2 years of safety data for the majority of patients who had undergone the surgery. The FDA's Advisory Committee made it clear that careful post-market surveillance was essential. There is no evidence that this has been done. Meanwhile, some patients have reported debilitating pain, permanent damage to the jaw and skull, and other serious health problems that are caused by these implants. It is still not known how often these terrible adverse reactions occur

3. Saline breast implants were approved by the FDA last year despite a 3-year complication rate of more than 70 % among mastectomy patients. The complication rate was so high that members of the FDA Advisory Committee questioned if the data were meaningful. For example, they asked whether the pain that so many women reported was unrelenting pain that lasted for months, or merely excessive but "normal" pain after surgery. They wondered if the infections that were reported were life-threatening or easily treated. Again, the Advisory Committee made it clear that careful post-market surveillance was essential, but that has not been done. In fact, the FDA has received more than 65,000 adverse reaction reports for saline implants and more than 127,000 for silicone gel implants, and these have not yet been comprehensively evaluated. And meanwhile, studies conducted at the National

Cancer Institute raise questions about the link between several cancers and the long-term use of breast implants. However, those studies do not provide specific information about implants that are currently on the market.

These are just three examples of how drugs and devices can be approved (or in the case of fen-phen, approved drugs were used in combination) when the long-term safety is not clear. The current PDUFA requirements to spend user fees and a portion of federal funds on the drug review process means less money for post-market surveillance at a time when we need more money for surveillance. We are relying on manufacturers to do this work, and we know from experience that manufacturers are reluctant to admit that they are selling a product that can cause serious and even fatal health problems.

This is a dangerous situation for consumers across the country. A recent GAO report tells us that it has been especially dangerous for women, who have been disproportionately harmed by approved drugs that were later removed from the market. It is essential that this situation be changed, by strengthening the system and resources for post-market surveillance. There are many ways to do this:

- changing the system of post-market surveillance;
- increasing user fees and including the cost of comprehensive post-market surveillance;
- requiring user fees for medical devices;
- changing the formula used in the allocation of federal funds for various FDA regulatory and scientific activities;
- dramatically increasing the amount of federal funds available for post-market surveillance of drugs and devices; or
- some combination of these strategies.

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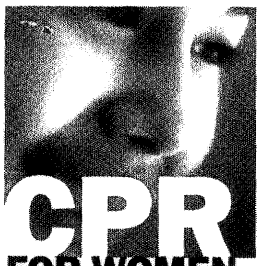

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Here's the recipe:

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Stir this all together, and the result is going to be that some products are going to be approv that have much more serious risks than is known at the time of approval, and consumers will di or suffer from serious health problems as a result.

Because of PDUFA, fewer resources have been available to the FDA to conduct or monitor post-market surveillance. As bad as the situation is for drugs, consumers with implanted medic devices are even more vulnerable. Of course, this is part of a much larger problem because user fees are not used for medical devices at all.

I will provide three examples of the need for better post-market surveillance:

1. Fen-phen was widely used as a diet pill by thousands of women, some of whom died or experienced permanent health problems as a result. The risks were discovered by health professionals who happened to see several patients with identical, and yet highly unusual, health problems, all of whom had received diet pills at the same medical facility. It was thanks to luck and some very observant health professionals that this was discovered – if the women had received their fen-phen through the Internet or another clinic, the doctors and nurses probably would not have noticed the link between the drug and the adverse reactions. It might have taken years before the link was discovered, and tens of thousands of other women and men would have been at grave risk.

2. Jaw implants – a permanent device used to treat TMJ disorders -- were recently approved by the FDA despite the extremely high patient attrition rate in the manufacturers' studies. The FDA's Advisory Committee made it clear that careful post-market surveillance was essential. There is no evidence that this has been done. Meanwhile, some patients have reported debilitating pain, permanent damage to the jaw and skull, and other serious health problems that are caused by these implants. Health care professionals agree that terrible adverse reactions can occur, but because of the lack of research it is not known how often they occur.

3. Saline breast implants were approved by the FDA last year despite a 3-year complication rate of more than 70 % among mastectomy patients. The complication rate was so high that members of the FDA Advisory Committee questioned whether the data were meaningful. For example, they asked whether the pain that so many women reported was unrelenting pain that lasted for months, or merely excessive but "normal" pain after surgery. They wondered whether the multiple surgeries were due to problems with the implants or nipple

reconstruction. Again, the Advisory Committee made it clear that careful post-market surveillance was essential, but that has not been done. In fact, the FDA has received more than 65,000 adverse reaction reports for saline implants and more than 127,000 for silicone gel implants, and these have not yet been comprehensively evaluated. And meanwhile, studies conducted at the National Cancer Institute raise questions about the link between several cancers and the long-term use of breast implants. However, those studies do not provide specific information about implants that are currently on the market.

These are just three examples of how drugs and devices can be approved (or in the case of fen-phen, drugs approved separately were used in combination) when the long-term safety is not clear. The current PDUFA requirements to spend user fees and an increasing portion of federal funds on the drug review process has meant less money for post-market surveillance at a time when we need **more** money for surveillance to keep up with the increasing number of approved drugs. We are relying on manufacturers to do this work, and we know from experience that manufacturers are reluctant to admit that they are selling a product that can cause serious and even fatal health problems.

This is a dangerous situation for consumers across the country. A recent GAO report tells us that it has been especially dangerous for women, who have been disproportionately harmed by approved drugs that were later removed from the market. It is essential that this situation be changed, by strengthening the system and resources for post-market surveillance. The FDA needs much more money and staff to do post-market surveillance and related activities. However, they also need more regulatory muscle and the will to regulate medical products that are already approved – especially implanted devices and drugs that are taken for chronic conditions, whether they are diet drugs or drugs to lower cholesterol. There are many ways to do this:

- changing the system of post-market surveillance, with a stronger regulatory role for the FDA;
- increasing user fees and including the cost of comprehensive post-market surveillance;
- requiring user fees for medical devices, pre and post-market;
- changing the formula used in the allocation of federal funds for various FDA regulatory and scientific activities;
- dramatically increasing the amount of federal funds and staff available for post-market surveillance of drugs and devices; or
- some combination of these strategies.

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