Plan B: Politics and Values at the FDA, Again

by Rebecca Dresser

Plan B is an emergency contraceptive that the U.S. Food and Drug Administration approved for prescription use in 1999. In 2003, a company called Barr Pharmaceuticals submitted to the FDA an application to switch Plan B from prescription to over-the-counter (OTC) status. At a joint meeting late that year, the FDA's Nonprescription Drugs Advisory Committee and Advisory Committee for Reproductive Health Drugs recommended that the agency approve the application. But in a May 2004 letter, FDA officials notified Barr that the application was "not approvable at this time."

The letter, signed by the acting director of FDA's Center for Drug Evaluation and Research, Steven Galson, said that the company had failed to supply data establishing that Plan B would be safe for younger women using it without professional supervision. A drug can qualify for OTC status only if it confers benefits that outweigh its risks, and the manufacturer tries to show that it does by offering evidence of acceptable product performance in a study of actual consumer use. Label comprehension is also a central concern. Because consumers will take the drug without a clinician's guidance, the label must include clear instructions for safe and effective use.[1]

Barr's application to sell Plan B without a prescription relied primarily on a study of 585 women. Though the data overall met the OTC standards, the sample size for young adolescents was inadequate, Galson asserted: just twenty-nine subjects were under sixteen and none was under fourteen. Barr had also submitted an alternative (and novel) proposal to assign Plan B a dual status—OTC for women over sixteen and by prescription for younger women. But Galson denied this proposal because it was incomplete.

The FDA letter described what Barr could do to gain approval for OTC status. First, it could furnish more data showing that young adolescents could use Plan B safely without professional assistance. Alternatively, it could submit a more complete application for dual status. The latter option would be more complicated, however. Barr would have to describe a satisfactory labeling, marketing, and education approach that took into account the different age groups and access routes for a dual status product. The FDA would also have to verify its statutory authority to approve a drug as prescription-only for some people and OTC for others.

Although Galson denied that the agency was under political pressure to decide as it did, skeptics charged that Plan B had become a pawn in the presidential campaign. Groups supporting OTC status charged that the decision was actually motivated by the administration's quest to win votes in the November election. Conservative groups and members of Congress had opposed the switch, claiming that an easily available emergency contraceptive could promote unsafe sex among teenagers. They also said that OTC status would conflict with the administration's other policies favoring abstinence for teens.[2]

But pro-choice and medical organizations argued that the data were more than adequate to support the switch. According to the existing data, Plan B reduces the pregnancy rate after unprotected sex from 8 percent to 1 percent. The drug is most effective when taken within twenty-four hours after intercourse, which is much easier to do if the drug has OTC status. Researchers have detected no serious side effects in women and no harm to children born to women taking the drug. Like several other contraceptives, Plan B fails to protect against sexually transmitted diseases, but OTC supporters cite studies indicating that women with convenient access to emergency contraceptives do not decrease their use of condoms.[3]

Researchers say that Plan B may act in two ways to prevent pregnancy. One is by preventing ovulation and the other is by preventing the fertilized egg from implanting in the uterus. The latter possibility makes the drug objectionable to people who think it is wrong to terminate developing human life after conception. Those favoring OTC status say that the objection can be addressed by product labeling that allows women who hold this moral view to avoid using the drug.

The Hybrid Nature of FDA Decisions

Much of the negative reaction to the Plan B ruling labeled the decision "unscientific." For example, an editorial in the *New England Journal of Medicine* stated that: "Until now, [FDA] approval has been based on scientific evidence from well-designed clinical trials with adequate power to establish safety and rule out toxicity with some reasonable level of confidence. Political considerations have wisely been kept out of the decision-making process."[4] Yet the Plan B decision was only the latest of a long line of FDA rulings that were controversial because of disagreements over which values should take priority in drug-approval decisions. Like most other science policy decisions, drug-approval decisions necessarily build on judgments

about both science and values. And interest groups often lobby the agency to make choices that will reflect their constituents' values.

The events surrounding RU-486 offer one illustration. By the early 1990s, this drug had been approved for clinical use in several countries, but pro-life and pro-choice forces struggled for more than a decade before the FDA deemed the product safe and effective for U.S. women. Although the debate was presented as hinging on the adequacy of medical evidence concerning safety, it was substantially influenced by abortion politics. Indeed, when RU-486 was linked to a California woman's death in 2003, abortion opponents claimed once again that the product was unsafe and petitioned the FDA to restrict access to the drug.[5]

Silicone-gel breast implants were the focus of another values conflict at the FDA. In 1992, former commissioner David Kessler restricted the availability of implants on the ground that adequate safety data were lacking. According to his ruling, implants could not be provided to women for breast augmentation, but could be available for breast reconstruction to women enrolled in clinical trials evaluating the devices. In Kessler's judgment, the risks of implants were too great to allow their use for enhancement purposes, but acceptable in studies of implants to relieve the effects of disease.

Kessler invoked values in defense of his ruling: "Certainly as a society, we are far from according cosmetic interventions the same importance as a matter of public health that we accord to cancer treatments."[6] In turn, critics said Kessler had inappropriately devalued the benefits of breast augmentation: "In waving aside the benefits of breast implants for most women who had them, Kessler appeared to be introducing an impossibly high standard for the devices: since there were no benefits, there should be no risks."[7]

The values conflict over breast implants continues even today. In 2003, an FDA advisory committee found that trial data collected since Kessler's ruling were sufficient to demonstrate safety and efficacy. A majority of the committee recommended that implants be approved for both augmentation and reconstruction, but critics charged that several committee members were plastic surgeons with financial interests in making implants more widely available. The FDA later denied the application, saying that more data on long-term safety were needed.[8]

Values in FDA Decisions

Value judgments are implicit in any FDA approval decision because determinations about a product's safety depend partly on judgments about the importance of the benefit it offers. If a product appears to reduce burdensome symptoms or extend life in many seriously ill patients, the agency is likely to approve the product even if it also presents material risks to some of those patients. The agency is less likely to accept such risks if a product targets only mild symptoms, and even less likely if the benefits are seen as purely cosmetic. Similar judgments affect the agency's evidentiary requirements. The FDA's accelerated approval program exemplifies its willingness to be less demanding about safety and efficacy data when drugs offer significant benefits to seriously ill patients.

It is disingenuous for either side in the Plan B controversy to suggest that the dispute is simply about the amount or quality of scientific data. Like the disagreements over RU-486 and silicone-gel breast implants, the disagreement over whether Plan B should become an OTC drug reflects conflicting ethical judgments about the possible consequences of such a situation. People who see unwanted pregnancy as a serious harm are more likely to consider Barr's study data adequate, while those worried about preserving traditional norms surrounding marriage and procreation are more likely to find the data deficient.

Rather than criticizing FDA officials for taking values into account, we should criticize them for failing to disclose which values affected the decision. Certain features of the FDA's "not approvable" ruling suggest that it relied on unarticulated value preferences. The FDA notification letter said that the data on Plan B use by young teenagers were insufficient, but it did not say which risks warranted further investigation. The letter failed to cite specific physical or other potential harms to girls under seventeen or concerns related to their ability to understand the product label. These omissions left the agency vulnerable to complaints that the decision was based on different, undisclosed considerations.

The Plan B dispute at the FDA, like others before it and others that will follow it, is about what matters to the participants. Rather than attempting to disguise value conflicts as disputes over data, it would be better to recognize them, as Kessler did in his decision about breast implants. Participants in FDA deliberations should be required to explain the values underlying their judgments about the adequacy of research data so that others have the opportunity to examine, and possibly challenge, those judgments. We cannot banish values and politics from FDA decisionmaking, but we can insist that they be brought into the open.

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2. M. Kaufman, "Debate Intensifies over 'Morning After' Pill," *The Washington Post*, February 13, 2004.

3. B. Vastag, "Plan B for 'Plan B'?" *JAMA* 291 (2004): 2805-06.

4. J.M. Drazen, M.F. Greene, and A.J.J. Wood, "The FDA, Politics, and Plan B," *NEJM* 350 (2004): 1561-62.

5. M. Kaufman, "Death after Abortion Pill Reignites Safety Debate," *The Washington Post*, November 3, 2003.

6. D.A. Kessler, "The Basis of the FDA's Decision on Breast Implants," *NEJM* 326 (1992): 1713-15.

7. M. Angell, *Science on Trial: The Clash of Medical Evidence and the Law in the Breast Implant Case* (New York: Norton 1996), 63.

8. L. Neergaard, "FDA Nixes Bid on Silicone Implants," *The Washington Post*, January 8, 2004.