

Sex, Politics, and Morality at the FDA: *Reflections on the Plan B Decision*

BY FRANK DAVIDOFF

On September 3, 2005, I resigned my consultant position with the Food and Drug Administration. I did this to protest the agency's August 26, 2005, decision to delay a final ruling on over-the-counter availability of Plan B, the emergency contraceptive, and I wasn't alone: Susan Wood, the FDA's assistant commissioner for women's health and director of the agency's Office of Women's Health, also resigned at about the same time. What in the world has been going on at the FDA?

Plan B consists of two relatively large doses of a single ingredient, levonorgestrol, a constituent of many birth control pills. Taken twelve hours apart within seventy-two hours after unprotected intercourse, the drug is about 75 percent effective in preventing pregnancy. Importantly for the question of over-the-counter availability, the drug's contraceptive efficacy decreases dramatically during this seventy-two hour window.

Plan B has been available by prescription since 1999. In April 2003, Women's Capital Corporation, which produces Plan B, filed an application with the FDA for approval of over-the-counter marketing of the drug. (Women's Capital Corporation later transferred ownership of the drug to Barr Laboratories.) As it often does in considering such applications, the agency then convened a joint meeting of its Nonprescription Drug and Reproductive Health Drug Advisory Committees (NDAC and RHDAC, respectively) in December 2003 to obtain in-

dependent expert opinion on the application. The briefing materials for the meeting were more extensive than usual; they weighed eighteen pounds.

During two days of intensive hearings and discussion, the committees carefully examined the pros and cons of over-the-counter availability; they also heard comments from several dozen members of the public, nearly all in support of approval. In the course of their deliberations, the committees voted twenty-eight to zero that the drug was safe (one member of NDAC commented that the single ingredient of Plan B, levonorgestrol, is the safest drug the committee had yet considered); they voted twenty-seven to one that consumers could properly use Plan B as recommended on the proposed labeling (as judged from the "actual use study" that was part of the sponsor's application); they voted twenty-eight to zero that women were unlikely to use Plan B as a regular form of contraception; and they voted twenty-seven to one that the actual use study data were generalizable to the overall population of over-the-counter users, including adolescents. At the end of the day, they voted twenty-three to four in favor of approval for over-the-counter availability (I was one of the twenty-three).

In sum, the committees agreed that Plan B met all of the FDA's criteria for over-the-counter availability: 1) an acceptable safety profile based on prescription use and experience; 2) a low potential for abuse; 3) an appropriate safety and therapeutic "index" (the ratio between the toxic and the therapeutic dose); 4) a positive benefit-risk assessment; and 5) demonstrable need for treatment of a condition or illness that is self-recognizable, self-limiting, and requires minimal intervention by a health care practitioner.

While all of that is true, the committees spent most of their time during the hearings considering several complex social, behavioral, and ethical issues—both benefits and side effects or "toxicities"—associated with over-the-counter availability of emergency contraception. FDA advisory committees do occasionally take up issues of that kind; in other meetings, for example, the NDAC struggled at length with the problem that acetaminophen, the active ingredient in Tylenol, is often used for suicidal overdose. But many of the issues raised in connection with the proposed over-the-counter switch of Plan B differed, both quantitatively and qualitatively, from the usual biological and clinical concerns raised by other over-the-counter switches. To start with, the proposed benefits for the switch of Plan B—and the primary explicit rationale for the over-the-counter switch application—were as much social, behavioral, and ethical as they were clinical. They included the likelihood that over-the-counter availability would prevent a large number of unwanted pregnancies and, consequently, a substantial proportion of elective abortions; that it would be of particular importance on weekends, since much unprotected intercourse probably takes place on Friday and

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Saturday nights, when it is particularly difficult to find a doctor to write a prescription; and that it would cut down on inappropriate, and dauntingly expensive, emergency room visits as a source of prescriptions on short notice for the many women who have no established relationship with a doctor.

But the list of potential social, behavioral, and ethical side effects and toxicities of Plan B's over-the-counter availability was also substantial. First, some members of the RHDAC suggested that requiring a prescription for emergency contraception forces women to see doctors, who can then provide medical evaluations plus education and counseling on contraception. These members argued that over-the-counter availability of Plan B would deprive women of that presumed benefit. Second, because the mechanism by which the drug prevents pregnancy isn't definitely known, some on the committees argued that levonorgestrol could, at least at times, prevent implantation of a fertilized ovum, which some view as a form of abortion, hence unacceptable. Third, easy availability of Plan B could have the social side effect of increased promiscuity, since impulsive sexual encounters might be seen as not having the consequence of an unplanned pregnancy. A related, secondary effect might be an increase in sexually transmitted disease. Fourth, over-the-counter availability might discourage the use of other means of regular contraception. Finally, and importantly, some committee members were concerned about the possibility that the social and behavioral side effects and toxicities associated with over-the-counter availability might be greater in women aged sixteen and younger because women in that age group may be less capable of understanding and following instructions and making appropriate judgments.

During the discussion the committees dealt with each of these issues in considerable depth. As is evident from the votes, the overwhelming majority of committee members appeared to be convinced, largely by the rather extensive published evidence and by the special studies submitted by the sponsor, that the overall benefits of over-the-counter availability of emergency contraception far outweighed its potential risks and harms, whether social, behavioral, or clinical.

The increased control that easier availability would give women over their reproductive lives appeared to most committee members to outweigh concerns about women bypassing doctor visits. After all, women generally consult doctors for contraceptive advice when their sexual activity is to some degree planned. But not all sexual activity is planned, so many women who have had no reason to seek out contraception from a doctor are inevitably exposed to the risk of unplanned and unwanted pregnancy.

The available evidence on mechanism of action, limited as it is, strongly indicates that levonorgestrol is a contraceptive, rather than an abortifacient; that is, it appears to prevent fertilization rather than preventing implantation of the fertilized ovum. Among other evidence, the drug is known to be ineffective once pregnancy is established; moreover, as one member of the RHDAC pointed out, this is the same drug that is given to preserve pregnancies in women with spontaneous "threatened abortion."

A variety of clinical studies, some in the United States and others in countries where contraception is available without prescription (there are many), indicate that promiscuity or sexually transmitted diseases do not increase when emergency contraception is available over the counter, nor does use of conventional, preventive contraception decrease. In addition, Plan B frequently produces nausea and vomiting, and repeated use leads to menstrual irregularity, so it is unlikely that women will depend exclusively on it for contraception. Finally, although relatively few women aged sixteen and younger were included in the actual use studies of Plan B,

the data that were presented indicated that the youngest women who were studied actually used the drug correctly about as often as older women.

As is evident from the twenty-three to four vote, the majority of committee members appeared convinced that the benefits of over-the-counter emergency contraceptive availability far outweighed its potential risks and harms, whether social, behavioral, or clinical.



As I thought about the hearings after getting home, I realized that the discussion hadn't considered the issue of spontaneous abortion, a serious omission that in my view prevented the committees from reaching a clear and balanced understanding of the whole abortion issue. Accordingly, several days after the hearings I wrote a letter to the agency,

to be included in the public record, which laid out the following concerns. The best studies, using sensitive hormonal assays, have shown that about 30 percent of all pregnancies in women who are using no contraception are spontaneously lost very early after conception, well before the woman knows she is pregnant. Assuming that Plan B prevents pregnancy by preventing fertilization—an entirely reasonable assumption, given current evidence—the over-the-counter availability of Plan B could therefore result in a large decrease in the loss of fertilized ova; in effect, use of Plan B could actually decrease the overall number of “abortions” that would otherwise have occurred (in this case, spontaneously). Moreover, since levonorgestrol is, in fact, a progestational agent that is used to prevent threatened abortion, it is even possible that many, and perhaps most, of the 25 percent of pregnancies that occur despite the use of Plan B (Plan B “failure”) could be those that would have otherwise been spontaneously lost early on if the woman had not taken the drug. In this latter case, emergency use of levonorgestrol could, at least in theory, virtually eliminate very early spontaneous “abortion.” These considerations suggest that even if Plan B were to prevent as many as 30 percent of pregnancies by preventing implantation of fertilized ova, rather than by preventing fertilization, the overall early loss of fertilized ova in any group of women using Plan B would be no greater than if the drug was not used at all, although drug-induced early loss would replace spontaneous early loss—a tradeoff of uncertain moral significance.

Advisory committee recommendations are not binding on the agency, but the FDA rarely makes decisions that are contrary to those recommendations. Moreover, as a high-level FDA staffer explained to me informally, in the few instances in which the agency’s approval decisions went against advisory committee votes, the votes (for reasons that were usually not clear) had been inconsistent with the sense of the committees’ own discussions—clearly not the case in the Plan B hearings. It was therefore a considerable surprise, not to mention a serious disappointment, to many of us when the FDA announced its decision in May 2004 that Plan B was “not approvable” for over-the-counter use. The decision seemed to me to be so obviously inconsistent with the evidence that I seriously considered resigning at that time, but I decided not to. I felt an obligation to finish my full term.

It was anyone’s guess in May 2004 what drove the FDA to behave in such a seemingly irrational way. True, we had learned during the Plan B committee hearings that some members of Congress had written to the FDA opposing over-the-counter availability, apparently on the grounds that it might foster promiscuity, and some statements in the public hearings had raised concern about the social and behavioral side effects. Moreover, two or three members of the RHDAC had made it clear that they had serious moral concerns because of the possibility, however remote, that in some women Plan B might be acting as an abortifacient. But there was no “smoking gun” to indicate that the agency had actually yielded to direct political pressure from social conservatives. On

the other hand, there was no other obvious explanation, either.

In fact, the FDA’s May 2004 “not approvable” decision for Plan B did not close the door entirely on the over-the-counter option. The agency offered the sponsor the option of “two tier,” age-dependent marketing—that is, making Plan B available over the counter to women over age sixteen, but only by prescription to younger women. As pointed out later, this option is very limited: it would discriminate not only against younger women, but also against those over sixteen who do not have drivers’ licenses—usually poor women and those from inner-city neighborhoods.¹ Moreover, being “carded” by a pharmacist in order to buy the drug—a very public process—would be a serious and humiliating invasion of privacy that would intimidate many women and prevent them from obtaining the drug. Despite these disturbing concerns, and despite the fact that such marketing for over-the-counter drugs is virtually unprecedented (nicotine preparations for smoking cessation are not approved for over-the-counter availability to people under age eighteen, but that restriction is consistent with the age restriction for tobacco sales), Barr Laboratories apparently decided it was better to settle for half a loaf and refiled their over-the-counter switch application, which included a plan for dual-level availability.

While this was happening, the FDA’s then newly appointed commissioner, Lester Crawford, made a public commitment as a condition of his appointment that the agency would make a definite decision on Plan B’s over-the-counter approvability by September 1, 2005. On August 26, 2005, however, the FDA, apparently as the result of a sudden and unexpected *crise de nerfs* over the unprecedented nature of a two-tier marketing system, announced that it would require a ninety-day comment period before it could make a final ruling on over-the-counter availability. Those familiar with the FDA’s rule-making recognized immediately that this nondecision ruling meant the agency could put off a decision on over-the-counter approvability almost indefinitely. There’s an old saying that seemed to capture the situation very well: “Fool me once, shame on you; fool me twice, shame on me.” At that point, therefore, I decided that the irrationality of the FDA’s decision process had crossed the line, and the time had come for me to resign. (Since my term on the NDAC officially ended in May 2005, the position I resigned was actually as a consultant.)



Other information that has surfaced along the way strengthens the inference that the presumed inability of younger women to use Plan B correctly was a smoke screen (or, perhaps more appropriately, a “fig leaf”) used to obscure the real pressures for nonapproval. First, it became increasingly clear that many people confuse Plan B with mifepristone, or RU-486—the “French pill”—which is a progesterone antagonist used explicitly to induce abortion.² Second, as reported in *Time* magazine, prior to the FDA’s August 2005 decision, socially conservative organizations were

encouraging their members to flood the White House and Congress with letters and calls opposing over-the-counter approval. Third, W. David Hager, an obstetrician-gynecologist recruited directly by the Bush White House to serve on the RHDAC and one of the four committee members who voted against over-the-counter availability, confirmed that after the committee hearings he had sent the FDA a “minority report” at the behest of “someone at the FDA,” whose name he says he is not at liberty to reveal, asking for “more studies” and for “more data on the use of Plan B by young girls.”³ It was also later revealed that in speaking about Plan B to an audience at a Christian college, Hager had said “God has used me to stand in the breach for the cause of the Kingdom.”

These suspicions of social conservative pressure received further strong support from the report of the Government Accountability Office released in November 2005.⁴ Produced in response to a request by forty-eight members of the U.S. Senate and House of Representatives, the report documents four unusual aspects of the initial “not approvable” Plan B decision process. First, the FDA staff who would normally have been responsible for signing the not-approvable letter disagreed with the decision and refused to sign. Second, high-level FDA management was more involved in the review of Plan B than in the review of any other over-the-counter switch application. Third, the decision not to approve the application may have been made before the scientific reviews were completed. And lastly, the rationale for the decision (the presumed inability of younger women to use the drug appropriately) did not follow the FDA’s usual practices—it normally considers extrapolating data from older to younger adolescents to be scientifically appropriate. The exercise of such pressures should not be surprising, however, when we recognize that the FDA is part of the executive branch of government. The FDA commissioner therefore reports to the secretary of the Department of Health and Human Services who, in turn, reports directly to the president; and the current president makes no secret of his determination to implement a socially conservative agenda by whatever means necessary.



The distressing history of Plan B teaches lessons on at least two points: the special vulnerabilities of the FDA, and the vagaries of resignation as a form of social protest. As a regulatory agency, the FDA is caught in crossfire from several sources. There is pressure from free market advocates, most obviously those in industry, for whom the agency—like all Federal regulators—is anathema; free marketers truly believe that the economy, medicine, and the public interest would all be better off without the FDA’s “paternalistic” control. Accordingly, industry has worked hard, and with considerable success, to reshape the FDA’s regulatory role to

be more in line with its own interests.⁵ Industry has exerted its influence largely through Congress, both because many members of Congress share its free market perspective, and because Congress in turn does possess some control over the shape, size, and function of the FDA. On the other hand, when it perceives that the FDA has allowed the public to be exposed to preventable risks and harms, Congress apparently sees no internal (and political) contradiction in taking the opposite position, coming down hard on the agency and pushing for more stringent regulation. The 1962 Kefauver-Harris amendments mandating that drugs must be shown to be effective as well as safe before they can be marketed came about because of the thalidomide tragedy. The FDA is also subject to direct political pressure from the executive branch, as was apparently the case with the Plan B decision. And finally, the FDA is under

constant, detailed, and intensive scrutiny by the media and, consequently, the public. The public’s judgments can be swift and harsh, particularly when it perceives that the agency is roiled by conflict of interest, bureaucratic paralysis, and lack of transparency.

Managing these pressures while trying to get its basic scientific and administrative job done is a huge challenge for the agency. Its priority, then, is to manage relationships with the outside world, and for that it requires public trust. Unfortunately, corruption of the decision-making process by political forces, as has happened in the case of Plan B, squanders that trust and tarnishes the agency’s image.⁶ But the FDA also needs to manage the effects of those pressures internally, particularly their impact on its own employees. Virtually all the

It was anyone’s guess in May 2004 what drove the FDA to decide Plan B was not approvable for over-the-counter use. While there was no smoking gun to indicate it yielded to direct political pressure, there was no other obvious explanation, either.

FDA staff who worked with the advisory committees struck me as being knowledgeable, professional, competent, and hard working. And although I suspect many FDA staff could have made considerably larger incomes in industry or even academia, several made it clear to me that they chose to stay with the agency because they felt their work was both rewarding and important. I found it particularly distressing, therefore, to be told in September 2005 by a high-level agency official that the staff had become “demoralized and depressed” by the Plan B decision, and to learn that Susan Wood had resigned.

Resigning from an organization is hardly as visible as signing a petition or taking out an ad, nor is it as strident as rioting in the streets; but resigning in protest is certainly a time-honored practice. I had never before resigned in protest, however, and since no one ever taught me in school how to go about it, I was on my own. At first, I wondered whether to do it at all. I would be withholding my expertise, such as it was, from the FDA at a time when it probably needed outside expert help more than ever, and I did feel I had something useful to offer. I knew that, by resigning, I would be letting down my colleagues on the NDAC. And I also knew that my leaving might lead to the appointment of someone worse—someone who believed that social and religious values should trump a rational decision process, based on scientific evidence, which is the agency’s mandate.

In the end, I simply decided that the potential value of such a protest outweighed the down side. At the same time, however, just resigning quietly made no sense at all. (As one of my friends put it, “If an FDA committee member falls in the forest and no one hears it, does it make a noise?”) In my resignation letter, I therefore told the FDA that I was resigning “publicly,” thus declaring my intention to use my resignation actively as leverage for reconsideration of the Plan B decision. (I also told them I would encourage other members of the NDAC to resign, but later reconsidered that decision after a colleague persuaded me that the potential damage to the FDA of multiple simultaneous resignations might be greater than the value of the protest.) Having no clear idea how to turn my resignation into an active protest—how to get the word out, use it for some leverage, “make a fuss”—I fell back on the storied method of social protest: writing a letter to the *New York Times*. Unfortunately, my letter got to the *Times* two days after Hurricane Katrina

hit New Orleans, and like so much else, it was washed away in the flood.

It was only when, about two weeks later, I got a call from a *Hartford Courant* reporter asking for an interview that it seemed my protest might gain some traction. The reporter’s interest, it turns out, came about only because I had mentioned my resignation to a colleague, and the conversation was passed on through a network of personal connections—the vagaries of chance. The resulting article appeared a few days later as the cover story in *Northeast*, the *Courant’s* Sunday magazine.⁷ Since the media seems to find blood in the water irresistible, the *Courant* story was immediately followed by an intense but short-lived media frenzy, which included tapings by National Public Radio, Fox news, and ABC news, not to mention Associated Press and Reuters stories in various newspapers (including the *New York Times*), as well as reports in “The Tan Sheet” and the *British Medical Journal*. But it was only when I began getting e-mail a few days later from friends and colleagues in far-flung places—London, Rome, and Bangkok—that I appreciated fully the reach and power the Internet has given to the media. A number of advocacy groups also approached me, offering to put on press conferences in which I could talk about the Plan B “debacle.” That idea seemed attractive at first, but when I considered the possibility of getting tangled up in the agendas of groups I knew nothing about, I decided against it.



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Has my resignation made any difference at all? It’s hard to say. It did lead directly to my being contacted by staffers of two U.S. senators who had questions about “decision-making at the FDA,” and this gave me an opportunity to talk at length with them about the Plan B decision. When the GAO report was released, I was invited to discuss it on *The NewsHour with Jim Lehrer* (which I unfortunately couldn’t do). I did learn in passing about one or more bills being considered by Congress that would require a definitive decision, up or down, from the FDA on Plan B by “date certain,” the default being that over-the-counter availability would be automatically approved if the decision weren’t forthcoming by that date. Any relief I felt from the prospect that rationality might be restored to the Plan B decision was quickly extinguished, however, by the realization that such a law

would set the terrible precedent of drug approval directly by the unruly politics of Congress, rather than by sober and balanced review of the evidence by the FDA.

How did we get ourselves into such a mess? In my view, what has brought out the harsh, controlling streak in so many people is that emergency contraception has to do with sex, and that the resultant commingling of sex with politics and morality is highly corrosive. Why does sex get people's backs up? Like all powerful forces—terrorism, hurricanes, pandemics—the power of sex can seem appalling, terrifying, something that must therefore be controlled at all costs. And since men exert most organized social control, the control over sexuality is asserted primarily by controlling the sexual and reproductive lives of women. A small number of women apparently also share these views. Furthermore, although several other serious and legitimate concerns—including interests of the state and society, as well as personal, humanistic issues—attach to abortion, one can argue that the abortion issue—particularly not permitting very early abortion—is also in substantial part an expression of the need to control women's sexual lives.

How can we get ourselves out of this mess? It may be both necessary and possible to “fight back” against political attacks on science,⁸ but that strategy is likely to be successful only in the short run; deeper structural changes are probably required in the long run to keep from having to fight those battles over and over again. Although a simple solution is unlikely, at least two approaches might help. The first is a greatly increased reliance on transparency. That is, rather than imposing rigid and absolutist control over the availability of a safe and effective drug like Plan B, both doctors and patients would be better off if the public had greater access to the drug, but only on condition that everyone is fully informed about the issues associated with its use. For example, providing everyone with full information about the facts on spontaneous early abortion and possible effects of Plan B on early pregnancy loss would allow those doctors and those women who have serious moral concerns about abortion to make informed choices about using the drug. At the same time, access would not be limited for women for whom these concerns are not a serious barrier to the drug's use. Providing this information through appropriate wording on the package label should be quite possible; I suggested such wording in my December 2005 follow-up letter to the FDA.

The second approach would be to find a way to protect the FDA without diluting its effectiveness. The agency, like all regulators, is currently caught in the crossfire precisely because, by design, it is positioned in the no man's land between the commercial and “guardian” (governmental, academic, legal, religious, and military) worlds. It is therefore subject to the contrasting, often clashing and conflicting “moral syndromes” and pragmatic interests of these two worlds. As the social critic Jane Jacobs has argued, both worlds are necessary for a healthy and well-functioning society.⁹ But when one world takes over the functions of the other, the result is a “monstrous hybrid”—think of the Soviet Union's effect on

commerce, or, conversely, the effect of commercialism on managed care and HMOs in the United States.¹⁰ However, although each of these worlds needs to keep well within its own domain, they need to interact closely with one another, balancing their interests and working out mutually acceptable solutions if the larger society is to prosper.

That balancing act is a tough one for everyone, and particularly for regulatory agencies, all of which are caught in the middle; moreover, the FDA carries a large added burden because protection of the public health is such a sensitive issue. It has occurred to me, therefore, that it would make sense to convert the FDA into a quasigovernmental agency, like the Federal Reserve and the National Academy of Sciences—supported by public funds and with binding decision-making power over both the standards of scientific evidence and the flow of commerce, but largely out of reach of direct political pressure. I made that suggestion during my discussions with the senate staffers. Unfortunately, they didn't seem impressed.

1. A.J.J. Wood, J.M. Drazen, and M.F. Greene. “A Sad Day for Science at the FDA,” *New England Journal of Medicine* 352 (2005): 1197-99.

2. *60 Minutes*, “The Debate over Plan B,” <http://www.cbsnews.com/stories/2005/11/22/60minutes/main1068924.shtml>.

3. *Ibid.*

4. United States Government Accountability Office, “Decision Process to Deny Initial Application for Over-the-Counter Marketing of the Emergency Contraceptive Drug Plan B Was Unusual,” Report GAO-06-109, <http://www.gao.gov/cgi-bin/getrpt?GAO-06-109>.

5. M. Angell, *The Truth about the Drug Companies: How They Deceive Us and What to Do about It* (New York: Random House, 2004).

6. Wood, Drazen, and Greene, “A Sad Day for Science at the FDA.”

7. R. Buck, “Plan B Casualties,” *Northeast Magazine*, October 2, 2005: 3-5.

8. L. Rosenstock and L.J. Lee, “Attacks on Science: The Risks to Evidence-Based Policy,” *American Journal of Public Health* 92 (2002): 14-18.

9. J. Jacobs, *Systems of Survival: A Dialogue on the Moral Foundations of Commerce and Politics* (New York: Random House, 1992).

10. F. Davidoff, “Medicine and Commerce. 1: Is Managed Care a ‘Monstrous Hybrid?’” [Editorial] *Annals of Internal Medicine* 128 (1998): 496-99; J.G. Coombs, *The Rise and Fall of HMOs: An American Health Care Revolution* (Madison: University of Wisconsin Press, 2005).