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Perspective

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A Sad Day for Science at the FDA

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The Food and Drug Administration (FDA) has again postponed issuing a decision about making emergency contraception available to women without a prescription. This decision — or nondecision — deserves serious scrutiny, since it appears to reflect political meddling in the drug-approval process.

Emergency contraception in the form of Plan B has been available by prescription in the United States since 1999, but its manufacturer, Barr Laboratories, has proposed that it be sold over the counter. Plan B consists of two 0.75-mg levonorgestrel tablets to be taken 12 hours apart as soon as possible, and within 72 hours, after an act of unprotected or inadequately protected intercourse. Time is of the essence, since the contraceptive efficacy decreases over time even within the recommended 72 hours after intercourse. The risk of pregnancy increases from 0.4 percent if contraception is initiated within 24 hours to 2.7 percent if it is initiated 48 to 72 hours after intercourse.

Currently, after an episode of unprotected intercourse, contraceptive failure, or rape, a woman has to recognize the availability of emergency contraception, find and make contact with an available physician who is willing and able to prescribe Plan B, obtain a prescription for the drug, find a pharmacy that stocks and will dispense it (not a trivial consideration in some parts of the country), fill the prescription at the pharmacy, and ingest the drug — all while the time window for efficacy is closing. Unprotected intercourse may occur at times — for instance, weekends — when it is likely to be difficult to reach a physician, particularly for women who do not have an ongoing relationship with a particular doctor. It therefore seemed logical to consider making Plan B available over the counter, as it is in many other countries.

After the manufacturer requested over-the-counter status, the FDA convened an advisory committee meeting in December 2003. The committee, made up of experts both in obstetrics–gynecology and in over-the-counter drug availability, voted overwhelmingly (23 to 4) that emergency contraception should be made available to U.S. women over the counter. Even the small number who voted against over-the-counter status acknowledged at the time that they did so for reasons other than concern about its demonstrated efficacy or safety. Yet these are

the only legitimate considerations for FDA approval. The committee reviewed the world literature, heard presentations of all points of view, and came to a conclusion, which under normal circumstances would have been accepted by the FDA. Subsequently, the FDA's own professional staff endorsed that conclusion and recommendation.

However, FDA management rejected the application in May 2004, citing concerns about the effects of over-the-counter availability on the sexual behavior of young teenagers. Data demonstrating that ready access to Plan B by adolescents as young as 15 did not lead to increased irresponsible sexual behavior were available in December 2003 and had been reviewed by the advisory committee. Moreover, the agency was conspicuously unable, then or later, to cite any data to support different safety or efficacy profiles in different age groups — a damning indictment of the basis for their disapproval.

After the May 2004 decision, a dual marketing plan was suggested: the drug could be made available over the counter to women over 16 and only by prescription below that age. In a surreal twist, however, the FDA commissioner seems to have belatedly discovered that the FDA has never before allowed two identical dosage formulations to be sold simultaneously over the counter and by prescription. Owing to his apparent ignorance of this problem, the approval has again been delayed to allow a 60-day comment period so that the dual-status issue can be addressed. It is, frankly, not credible to us that the commissioner and his staff did not recognize this problem when they initially floated the idea of age-restricted over-the-counter marketing. The problem was widely recognized and has been a major strategic issue for pharmaceutical companies that are switching drugs from prescription to over-the-counter status.

Why is the FDA considering age-based restrictions on the over-the-counter availability of emergency contraception? The stated reason is that there is uncertainty about the drug's safety in younger women. But the FDA has not pointed to any data to support that position, nor has the agency demanded such evidence in the case of other drugs that have been switched to over-the-counter status. All involved acknowledge that Plan B is extraordinarily safe. Even the advisory committee members who subsequently voted against its over-the-counter availability had acknowledged its appropriate safety earlier at the December 2003 meeting, when the committee voted 28 to 0 that the drug was safe.

In contrast, other over-the-counter drugs, such as acetaminophen and aspirin, can cause death when taken inappropriately. At a meeting of a similar FDA advisory committee, data were presented indicating that acetaminophen ingestion results in 56,680 emergency-department visits, 26,256 hospitalizations, and 458 deaths in the United States every year; a large number of these events affect persons younger than 17 years of age.[1] The FDA has shown no inclination to restrict the availability of these drugs to young people by requiring them to have a prescription. Why not?

Studies presented to the advisory committee at its meeting about Plan B and additional studies published more recently demonstrate clearly that women given ready access to emergency contraception do not routinely use less effective regular contraception, do not engage more often in high-risk sexual behavior, do not become more promiscuous, and do not have increased rates of pregnancy or sexually transmitted diseases — all findings that contradict claims made by those outside the FDA who oppose wider availability of emergency contraception.

Although the real reason behind the attempts to introduce an age restriction on Plan B are at best unclear, the effect would be to intimidate women of all ages. The only way to enforce such a restriction would be to insist that all those attempting to purchase emergency contraception provide proof of age — that they be "carded," or required to produce a driver's license or other government-issued identification. The provision of such identification to a store clerk, who might be the customer's peer, could be humiliating, and in destroying any semblance of privacy, such a requirement would deter women from purchasing emergency contraception.

Imagine the scene at the checkout counter: with a line of impatient customers waiting behind you, you must show an identification card to a sales clerk in order to purchase a product that clearly reveals your exposure to unprotected intercourse during the past few hours. If chain pharmacies followed the rules they have used for beer and cigarettes (whose sales are currently subject to similar age restrictions), only clerks over a certain age would be allowed to authorize sales — which would delay the

purchase even longer and expose the purchaser to further embarrassment. Moreover, many potential users of all ages — particularly poor women and those from inner-city neighborhoods — have no driver's licenses. Such women would not be able to obtain emergency contraception even if they were older than the arbitrary age limit set by the FDA.

Finally, it is likely that because of the age restrictions, many pharmacies would choose to hold their entire stock of Plan B "behind the counter" to ensure that all purchasers had to document their eligibility. American women should not have to explain their need for such a product in public, in front of their neighbors and friends, at such a painful, frightening, and vulnerable time.

This is a sad day for American women and for the FDA. In the absence of data to support their original decision to reject the advice of their advisory committee and their own staff analysts, one can only speculate about the real reason for the actions of the agency's leadership. Their subsequent delays, dissembling, and shifting justifications of their regulatory maneuvering and manipulation have resulted in the resignation of Susan F. Wood, the assistant FDA commissioner for women's health and director of the agency's Office of Women's Health. Wood's departure is a statement of protest against the decision by the FDA management to bow to political pressure at the expense of women's health.

The FDA has, on occasion, been criticized for being too bureaucratic and slow to approve important new drugs, too quick to approve new drugs to please the corporate patrons who provide much of its budget, and too slow to withdraw drugs that seem to pose a danger to public health. But the agency has previously resisted political pressure to reflect a particular social policy or ideology. The recent actions of the FDA leadership have made a mockery of the process of evaluating scientific evidence, disillusioned many of the participating scientists both inside and outside the agency, squandered the public trust, and tarnished the agency's image. American women and the dedicated professionals at the FDA deserve better. Will we ever again be able to believe in the FDA's independence?

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1. Nonprescription Drugs Advisory Committee. (Accessed September 1, 2005, at http://www.fda.gov/ohrms/dockets/ac/cder02.htm#NonprescriptionDrugs.)