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OP-ED

Inappropriate Obstructions to Access: The FDA's Handling of Plan B

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When prescribing or purchasing a medication or medical device in the US, most people assume that the product has been reviewed and, based on good evidence, approved as safe and effective by medical experts. This assumption is accurate in most cases; the Food and Drug Administration (FDA) is charged with the oversight, approval, and regulation of most (though not all) of these products [1, 2].

While scientific evidence and processes do not always trump nonscientific policy priorities—in such matters as job creation, transportation funding, and even grant funding by federal research agencies—in governmental decision making, they do drive decisions at the FDA. According to the 1938 Food, Drug and Cosmetic Act, the secretary of the US Department of Health and Human Services (HHS) or her delegate, the commissioner of food and drugs, is to base drug approval decisions on evidence of safety and effectiveness, quality of manufacturing and processing, and accuracy of labeling [3]. In this law, Congress specifically did not give the secretary broad latitude to base decisions on other policy considerations. The process for approving emergency contraception (levonorgestrel) to be sold "over the counter" (OTC) without a prescription marked a major departure from standard FDA procedure, with alterations to the usual approval process and obstruction of access to a safe and effective drug. That departure could set a dangerous precedent for future decisions.

Background

Prevention of unintended pregnancy is the most effective way to avoid the need for abortion [4]. Furthermore, recent data confirm that levonorgestrel-based emergency contraception does not affect what happens after implantation of a fertilized ovum but works prior to ovulation [5, 6] and thus is not an abortifacient. Hence, Plan B should not be subject to restrictions on or objections to abortion.

A very safe medication—safer, in fact, than many other OTC products [7]—Plan B and other levonorgestrel-based emergency contraceptives are more effective when used promptly (as early as possible within 72 hours after unprotected intercourse), so that the delays and hurdles involved in obtaining and filling a prescription (including limitations in doctors' schedules and pharmacy opening hours) can lessen or obviate its effectiveness. This makes the drug an obvious candidate for over-the-counter sale. Since the 2003 application for Plan B emergency contraception to become a nonprescription drug, the FDA's scientific and medical reviewers recommended full

OTC status with no age restrictions. It was ideological and political interference that made what should have been a straightforward approval process a contested one.

An Unusual Age Restriction

The saga of bringing Plan B (and now Plan B One-Step) fully over-the-counter can be broken in to three phases over ten years. As assistant commissioner for women's health at the FDA and director of the Office of Women's Health from 2000 to 2005, I observed the first few years of the tortuous, and indeed politicized, process of approving a safe and effective, but time-sensitive, contraceptive product for over-the-counter sale [8]. During the Bush Administration, approval of Plan B for over-the-counter sale was delayed several times, despite recommendations in favor of OTC status for all ages from both the FDA reviewers and its outside advisory committee [9]. As the US Government Accountability Office's (GAO) report on this decision process explains,

> The Plan B decision was not typical of the other 67 proposed prescription-to-OTC switch decisions made by FDA from 1994 through 2004. The Plan B OTC switch application was the only one during this period that was not approved after the advisory committees recommended approval. The Plan B action letter was the only one signed by someone other than the officials who would normally sign the letter [10].

The FDA leadership overruled the recommendation of the reviewers and the advisory committee and proposed an age restriction—initially age 16, then age 17—based on the premise that the studies required for an "OTC switch" application had not included enough young women under the age of 16 to determine whether they could accurately comprehend the drug's label and use it as directed. The FDA had never before required such age-specific studies before on label comprehension and "actual use" to approve a prescription drug for over-the-counter sale [9]. The GAO's report continues,

> There are no age-related marketing restrictions for any [other] prescription or OTC contraceptives that FDA has approved, and FDA has not required pediatric studies for them....GAO found that high-level management's involvement for the Plan B decision was unusual for an OTC switch application....The Acting Director acknowledged to GAO that considering adolescents' cognitive development as a rationale for a not-approvable decision was unprecedented for an OTC application, and other FDA officials told GAO that the rationale differed from FDA's traditional practices **[**10].

When the manufacturer responded by submitting an application for the dual status proposed—over-the-counter sale to adult women, but prescriptions required for younger people—FDA leadership delayed approval again and started a regulatory process to determine whether a federal regulation was needed to establish such a

dual-label approval, despite the fact that other products, like nicotine patches, had been given this age-related dual status in the past [11].

This was the point, in late 2005, at which I resigned my position as assistant commissioner of women's health. It was clear to me at the time that, even with an unwarranted age restriction, FDA leadership was going to continue to block unfettered access to this safe and effective drug for reasons unrelated to safety and effectiveness. Though it was difficult to leave my excellent and dedicated colleagues at the FDA, it was better for me to move outside of the agency and to be able to voice my concerns in public. I spent the next year speaking and writing about how science and evidence must drive our health policy decisions, particularly at the FDA. Little did I know that this was just the beginning of the story.

Half Measures

Beginning in 2005, *Tummino v. Von Eschenbach*, a lawsuit against the FDA, had been filed by a number of plaintiffs including individual women, organizations, and health professionals, based on an original petition that they had filed asking the FDA to approve all levonorgestrel-based emergency contraceptive methods for OTC status [12]. This lawsuit, with the plaintiffs represented by lawyers at the Center for Reproductive Rights, would later play a major role in leading to FDA approval of OTC status.

In August 2006, the acting FDA commissioner, who was seeking Senate confirmation as permanent commissioner, concluded that no federal regulation was needed for age-restricted OTC approval, but that the age restriction should be 18 rather than 17 [13]. He announced this decision the day before his Senate confirmation hearing, where he was to face senators, including Patty Murray (D-WA), Hillary Clinton (D-NY), and Barbara Mikulski (D-MD), who had been calling for a science-based decision on Plan B since 2004. The commissioner's announcement cleared the way for approval with an age restriction of 18, and this approval came remarkably quickly, within less than a month [14], as did his confirmation as commissioner.

From 2006 to 2009, no further regulatory actions occurred. Plan B was available in pharmacies for sale without a prescription for women 18 or older or with a prescription for women younger than 18, with little controversy. Though this constituted progress, it was certainly not ideal: these age restrictions have real consequences for women seeking emergency contraception. Because of the age restriction, levonorgestrel is held behind the counter, so that only an open pharmacy can dispense it, even to women "old enough." This may mean waiting until pharmacies open for business, and showing an ID prior to purchase can be intimidating in such a sensitive situation.

Further Obstructions

In March of 2009, the federal judge hearing the *Tummino* case issued his first ruling, ordering the FDA to immediately roll back the age restriction to 17 (on the grounds

that the change to 18 was clearly arbitrary) and to reevaluate the need for any age restriction through the usual FDA review and approval processes [15]. The FDA did roll back the age restriction to 17, but took no further action on lifting the age restrictions as directed by the court.

In late 2010, the Center for Reproductive Rights and the plaintiffs in the *Tummino* lawsuit filed new legal motions against the FDA. The FDA responded that the manufacturer had now started new studies on younger teens and that, therefore, it was waiting for a new application for over-the-counter sales rather than considering the previous 2003 application. This is an important point. The FDA did not need new research studies to have enough information to approve Plan B (or Plan B One-Step, the current formulation); the reviewers and advisory committee had recommended full approval back in 2003 and 2004 based on the previously provided data. The request for additional data on teens had been made through inappropriate interference by political leadership in 2004, not by the original reviewers or the advisory committee. FDA management was now making the same inappropriate request of the manufacturer.

More Politically Motivated Interference

The manufacturer submitted a new application with new data on younger teens in 2011. The FDA was prepared to approve the application for full OTC status of Plan B One-Step [16], but then a new and unexpected roadblock appeared. The secretary of HHS, Kathleen Sebelius, overruled the FDA commissioner and blocked approval for OTC status, stating that there was inadequate data on the ability of 11- and 12-year old girls to understand the label or use the product as directed [17]. President Obama supported her decision, stating his concern as a parent about access to emergency contraception without a prescription by young girls [18]. These last-minute concerns echoed those raised previously by the Bush Administration and by opponents of access to emergency contraception in general, but moved the age concerns even earlier to preteens—a logical leap the Guttmacher Institute described as "specious," given data showing that fewer than 1 percent of 11-year-old girls in the United States are sexually active [19]. I joined many in speaking out against the decision [20].

This was truly unprecedented: *never before* had an HHS Secretary overruled the FDA on a medical product approval [21]. Because this decision occurred in a presidential election year, it seems likely that full OTC approval was blocked to avoid political controversy. When the secretary overruled the FDA commissioner, she set a new and troubling precedent for future decisions that might be deemed politically sensitive.

Resolution

This new denial led to new legal action. The Center for Reproductive Rights renewed its lawsuit, adding Sebelius as a defendant in early 2012. By spring of 2013, US District Court Judge Edward Korman issued his ruling [22]: all levonorgestrel-based emergency contraception was to be made available over the counter within 30

days, and the FDA's decisions around Plan B were described as "arbitrary, capricious, and unreasonable" [23].

The Obama administration appealed the decision and asked the United States Court of Appeals for the Second Circuit to delay FDA action, pending the appeal. Within days the appeals court denied the request for delay, noting that the age restriction on the brand-name drug Plan B One-Step could remain if the FDA so chose, but that generic products should immediately be available without a prescription for all ages [24]. The administration promptly withdrew its appeal and approved Plan B One-Step as an OTC product without age restrictions [25]. Plan B One-Step came onto the shelves during the summer of 2013, to little fanfare or controversy. Those who had raised objections can see that the sky did not fall.

Conclusion

Now that levonorgestrel is finally approved for OTC sale without age restrictions, we have added a valuable tool to our constellation of reproductive health efforts to reduce unintended pregnancies, but it's not a magic bullet. Furthermore, new scientific questions have emerged about its efficacy for overweight or obese women. Clarification is needed on the product label to accurately reflect updated information on its mechanism of action. However, these concerns can be addressed appropriately within the scientific research community, the FDA and health care delivery systems, not in the political arena.

New debates about contraception have arisen, both in the political arena and in the courts, concerning the requirement for insurance coverage of contraception under the Affordable Care Act [26]. The scientific and medical communities must defend the clear evidence of the health benefits to women and to families of access to family planning tools, including emergency contraception. While women's reproductive health has been the focus of centuries-long political, religious, and moral debates, we must ensure that safe, effective, and beneficial drugs are made as available as possible.

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