There is no science without political science, it seems. Availability of nonprescription medicines is based on three major public health drivers: meeting a distinct need for an undertreated population (e.g., oxybutynin for overactive bladder); access (e.g., nicotine replacement therapy for smoking cessation); and cost-shifting (e.g., second generation antihistamines for allergy). Secondary drivers include convenience and cost-savings, which are not well studied and never a part of the U.S. drug approval process.

Few if any Rx-to-OTC switches embroil emotions to the point of overflow into the national psyche and court system. The vast majority of switches in the U.S. are characteristically straightforward evaluations of scientific studies demonstrating the likelihood of safe consumer medication-taking behavior post-approval. The questions advisory committees consider are predictable, science-based and reasonably objective with limited controversy. Enter Plan B, the poster child for the battle between science and politics.

It seems right to separate science from politics. After all, creativity and risk management considerations relating to drug approvals should be unfettered by political bias. Yet, democratic government is built on the premise that all voices are important. This is why the Food and Drug Administration (FDA) uses a public venue for its advisory committee meetings to consider major first-in-class Rx-to-OTC switches. The process allows for the formal presentation of views from all who are potentially affected by corporate proposals and/or federal public health decisions. Importantly, the democratic system allows additional recourse through the courts and Congress to challenge decisions if all else fails. Time has shown this to be a good process. But when the government administration is at odds with its own scientists, then things become murky.

None will deny that it is FDA’s responsibility to approve drugs that are safe and effective for their intended use based on the scientific evidence. This is true for prescription and nonprescription medicines. The Center for Drug Evaluation and Research routinely analyzes data from the company sponsor and other external sources and applies a risk/benefit assessment consistent with its standard drug review process. The agency’s decision-making is based on a body of scientific findings and external input from scientific advisory committees composed of health professionals with credentials to deliberate the medical and scientific issues. Specially designed

† Plan B has been called the morning-after pill. It prevents pregnancy from occurring by stopping ovulation, and it must be taken within 72 hours of unprotected intercourse. Plan B is not an abortifacient drug like mifepristone (RU-486) which terminates a pregnancy.)
studies in drug applications are also considered to address the regulatory standards for prescription or nonprescription drug use, as the case may be. This process was used for Plan B and for its successor, Plan B One Step.

In May 2004, at the request of Congressional requesters, the U.S. Government Accounting office (GAO) issued its final report entitled, 'Decision Process to Deny Initial Application for Over-the-Counter Marketing of the Emergency Contraceptive Drug Plan B Was Unusual'4. GAO noted, ‘The Plan B decision was not typical of the other 67 proposed prescription-to-OTC switch decisions made by FDA from 1994 through 2004.’ GAO cited that following incongruities:

• The Plan B Rx-to-OTC switch application was the only one from 1994-2004 that was not approved after an advisory committee recommended approval.

• The Plan B action letter was the only one signed by someone other than agency individuals who would normally sign the letter.

• No other Rx or OTC contraceptives approved by FDA up to that time had age-related marketing restrictions.

• Pediatric studies for other approved Rx or OTC contraceptives had not been previously required.

• FDA cited no issues requiring age-related limitations in the review of the original New Drug Application for Rx Plan B.

On December 7, 2011 in response to a switch petition for Plan B One Step by Teva Pharmaceuticals, FDA Commissioner Margaret Hamburg issued a public statement, stating: ‘I reviewed and thoughtfully considered the data, clinical information, and analysis provided by CDER, and I agree with the Center that there is adequate and reasonable, well-supported, and science-based evidence that Plan B One-Step is safe and effective and should be approved for nonprescription use for all females of child-bearing potential.’

Commissioner Hamburg’s statement was made in tandem with a countervailing statement by the Secretary of Health and Human Services, Kathleen Sebelius, invoking her authority under the Federal Food, Drug, and Cosmetic Act. Sebelius stated her disagreement with the Agency’s decision to allow the nonprescription marketing of Plan B One-Step for all females of child-bearing potential, and provided the following terse rationale in overruling FDA and denying Teva’s switch petition5:

‘The average age of the onset of menstruation for girls in the United States is 12.4 years. However, about ten percent of girls are physically capable of bearing children by 11.1 years of age. It is common knowledge that there are significant cognitive and behavioral differences between older adolescent girls and the youngest girls of reproductive age. If the application were approved, the product would be available, without prescription, for all girls of reproductive age.’

This type of disagreement within the US government was not new to the history of Plan B. In 2006, Simon Heller as lead attorney for the Center for Reproductive Rights commented about
the prior Bush Administration: ‘The evidence we have uncovered in the course of deposing a number of FDA scientists and officials reveals that the FDA submitted to political pressure from the Bush Administration in rejecting over-the-counter status for Plan B. Only by subpoenaing the White House will we be able to fully explore the extent of this improper influence exerted by the Administration over the FDA during the Plan B application review.’

Yet now, the storied history of emergency contraception in the U.S. continues as a ‘back to the future’ saga. Now it is the Obama Administration’s turn to be the captain of a policy ship that rocks precariously in politically-charged seas and risks swamping in the swirling currents of women’s rights, conservatism, and scientific integrity.

In April 2013, U.S. District Court Judge Edward Korman, who has overseen court proceedings on Plan B since 2005, ruled that Plan B One Step should be available to women and girls of all ages without a prescription. The Obama Administration stepped in, seeking Judge Korman to suspend his ruling while they appealed. Judge Korman returned with harsh criticism of the Administration, calling the appeal frivolous and stating in his denial of the government’s request: ‘If a stay is granted, it will allow the ... politically motivated decision of Secretary Sebelius ... to prevail – thus justifiably undermining the public’s confidence in the drug approval process.’ As of the end of May 2013, Plan B One-Step will not be available OTC for all ages, until the Appeals Court hears from all sides. In the meantime, the morning after pill will be available without a prescription for women and girls ages 15 and over. The message from all of this can only be, ‘stay tuned’.

Science and politics will likely brush up against one another from time to time. It is understandably difficult to disengage deeply held personal beliefs, balance competing views of large and vocal constituents, and tease out an objective view of the scientific evidence that will convince most if not all stakeholders. This is often at the heart of public policy derived from regulatory science. Louis Pasteur said, ‘Science is the torch which illuminates the world.’ We can only hope that politics does not hide the matches.

Plan B Timeline*

1999: US Food and Drug Administration (FDA) approves Plan B (levonorgestrel) as a two-tablet emergency contraceptive for prescription (Rx) sales, to be taken as an initial dose within 72 hours of unprotected sex and second dose, 12 hours later.

2001: A coalition of over 70 proponents of Plan B from the medical, reproductive rights and public health sectors file a citizen petition seeking to move Plan B over-the-counter (OTC). FDA has until December 7 to respond.

2003: Women’s Capital Corporation files an application to switch Plan B from prescription-only to over the counter for all age groups. In December, two FDA advisory committees, meeting jointly, vote 23-4 that Plan B should be made available without prescription to all age groups, and also voted 27-1 that Plan B can be used safely by all age groups.
2004: A week prior to FDA decision due date on OTC availability of Plan B, FDA announces it will take an additional 90 days for its decision.

In May, FDA rejects the application to make Plan B OTC for all age groups, citing insufficient safety information for girls under age 16, unless prescribed by a physician. Barr Pharmaceuticals (which had purchased the rights and assets from Women’s Capital Corporation) files revised application for Rx-to-OTC switch of Plan B for those aged 16 and over.

2005: In January, FDA misses its statutory deadline to decide on the revised switch application. Plan B proponents file a lawsuit in Brooklyn federal court seeking to force FDA to approve the original application for all ages.

In April, Sens. Patty Murray (D-WA), and Hillary Rodham Clinton (D-NY) announce they will block a Senate confirmation vote on Lester Crawford’s nomination as the new FDA Commissioner until the agency rules on Barr’s Plan B application. Threat is subsequently withdrawn. Crawford leaves FDA post after 2 months, and Andrew Von Eschenbach is nominated to replace him as FDA Commissioner.

In November, the U.S. Government Accounting Office issues its Report to Congressional Requesters, concluding the decision process to deny the initial Rx-to-OTC switch application for Plan B was ‘unusual.’ (See accompanying Text)

2006: Clinton and Murray say they will not allow a Senate vote on the nomination of Andrew Von Eschenbach until FDA decides on Barr’s revised Plan B application.

In June, FDA denies the proponents 2001 citizen petition (use in all ages).

In July, acting commissioner Von Eschenbach corresponds in writing to Barr stating no new regulations will be necessary, but that OTC access should be limited to women 18 and over. The letter is received one day prior to Von Eschenbach’s Senate confirmation hearing.

In August, at his Senate confirmation hearing, Von Eschenbach does not commit to a decision date on Plan B. Von Eschenbach’s nomination is held by Murray and Clinton until a decision is made.

In late August, FDA approves Plan B for nonprescription use for women 18 years and older, with proof of age for OTC sale and the need for a prescription for minors. Per the sponsor, OTC approval of Plan B led to a 120 percent increase in sales.

2009: U.S. District Judge Edward Korman (New York) orders FDA to lower the age restriction on Plan B to 17. Plan B One-Step (one tablet version of Plan B) is approved for Rx use in the U.S.

2011: In early December, FDA rejects Teva’s petition. Accompanying the rejection is a statement from FDA Commissioner Margaret Hamburg saying scientific evidence supports safe use of Plan B One Step in younger girls, as well as a statement from HHS Secretary Kathleen Sebelius overruling FDA’s plan to lift age restrictions on Plan B (see accompanying text). Teva submits supplemental application seeking to remove the prescription-only status for females younger than age 17 and to make Plan B One-Step nonprescription for all females of child-bearing potential.
In mid-December, FDA rejects the citizen petition. They say that since Teva’s petition was not accepted, it could not justify lower restrictions for two-pill versions of the drug, when the one-pill version was not proven sufficiently safe.

**2012:** Reproductive-rights groups re-open their lawsuit, adding HHS Secretary Sebelius as a defendant. US District Court Judge Korman orders FDA to demonstrate why the agency should not be directed to revise age and access restrictions on Plan B and other emergency contraception. Korman directs FDA to grant the citizen petition and make emergency contraception available over-the-counter to women of all ages.

**2013:** In April U.S. District Court Judge Edward Korman (NY) orders FDA to make Plan B available with no age restrictions, consistent with the first switch application 10 years earlier and FDA’s overruled decision in 2012. Subsequently, Korman denies the government’s request to stay his opinion pending appeal. The following Monday, an appeals court temporarily granted the Obama administration’s request for a stay of Judge Korman’s order.

* Taken from various press accounts and publications identified in a worldwide web search.

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**REFERENCES**


