

SEX, DRUGS, AND ADVISORY COMMITTEES:
AN ANALYSIS OF PHARMACEUTICAL
INDUSTRY MANIPULATION OF FDA
VULNERABILITY TO SOCIOPOLITICAL
INFLUENCES ON MATTERS
OF WOMEN'S HEALTH

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INTRODUCTION

Under a mandate to protect the public health, the Food and Drug Administration (FDA) is charged with ensuring the safety and efficacy of drugs sold in the United States.¹ Given the high level of scientific expertise required to judge a drug's safety and efficacy, the FDA uses independent, expert advisory committees to perform a scientific risk-benefit analysis of the drug when deciding whether to approve a drug for marketing.² In light of the FDA's rigorous, scientific analysis of the safety and efficacy of new drugs, David Kessler, a former FDA Commissioner, once characterized the FDA drug approval process as "the international gold standard."³ However,

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1. *What We Do*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/WhatWeDo/> (last updated Feb. 11, 2017) [hereinafter FDA, *What We Do*]; 21 U.S.C. § 393 (2012); 21 U.S.C. § 355 (2012).

2. *See* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY ADVISORY COMMITTEES: IMPLEMENTING SECTION 120 OF THE FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT OF 1997 1 (1998) [hereinafter FDA SECTION 120 GUIDANCE].

3. *Revitalizing New Product Development From Clinical Trials Through FDA Review: Hearing on S. 1477 Before S. Comm. on Labor & Human Res.*, 104th Cong. 97 (1996) (statement of David A. Kessler, Comm'r, U.S. Food & Drug Admin.); *see also* Michelle Meadows, *Promoting Safe and Effective Drugs for 100 Years*, FDA CONSUMER MAG. (Jan./Feb. 2006), <http://www.fda.gov/AboutFDA/>

like many other agencies, the FDA sometimes falls prey to political influence that threatens the integrity of its decision-making processes.⁴ Specifically, the FDA has shown particular vulnerability to sociopolitical influences on matters of women's health. The agency displays a number of biases that distort scientific analysis, from normative judgments about women's sexuality to a patronizing sense that women require heightened protection against the risks posed by otherwise effective drugs.⁵

In August of 2015, following an advisory committee recommendation in favor of approval, the FDA approved the drug flibanserin (now marketed under the name Addyi) for the treatment of Hypoactive Sexual Desire Disorder in pre-menopausal women.⁶ The drug, which was rejected in two previous review cycles, has engendered quite a bit of public controversy.⁷ While some claim that the FDA's delay in approving the drug was the product of gender bias that caused the FDA to undervalue female sexual pleasure and over-protect women against the risks posed by the drug, others have criticized the FDA's approval as a capitulation to political pressure to approve a drug that is neither safe nor effective, following a public campaign for approval of the drug orchestrated by flibanserin's manufacturer, Sprout Pharmaceuticals.⁸

WhatWeDo/History/CentennialofFDA/CentennialEditionofFDAConsumer/ucm093787.htm ("Today, the drug review process in the United States is recognized worldwide as the gold standard.").

4. Michael R. Taylor, *Protecting the FDA's Ability to Protect Public Health*, 61 FOOD & DRUG L.J. 805, 805 (2006) ("[I]t is not surprising that FDA is often pushed and pulled in directions that take attention away from its core mission, in the name of values and interests that many people, outside and inside the agency, consider important.").

5. See *infra* notes 98–101.

6. Press Release, U.S. Food & Drug Admin., FDA Approves First Treatment for Sexual Desire Disorder (Aug. 18, 2015), www.fda.gov/newsevents/newsroom/pressannouncements/ucm458734.htm; Sindhu Sundar, *FDA Advisers Back Sprout's Drug to Boost Female Sex Drive*, LAW360 (June 4, 2015), www.law360.com/articles/663843/fda-advisers-back-sprout-s-drug-to-boost-female-sex-drive.

7. Sabrina Tavernise & Andrew Pollack, *Aid to Women, or Bottom Line?: Advocates Split on Libido Pill*, N.Y. TIMES (June 13, 2015), <http://www.nytimes.com/2015/06/14/us/aid-to-women-or-bottom-line-advocates-split-on-libido-pill.html>.

8. *Id.*; Andrew Pollack, *'Viagra for Women' is Backed by an F.D.A. Panel*, N.Y. TIMES (June 4, 2015) <http://www.nytimes.com/2015/06/05/business/panel-backs-a-drug-to-increase-womens-sex-drive.html>; Ray Moynihan, *Evening the Score on Sex Drugs: Feminist Movement or Marketing Masquerade?*, BMJ (Oct. 17, 2014), <http://www.bmj.com/content/349/bmj.g6246>.

Debate continues as to whether the FDA's approval of flibanserin was appropriate.⁹ However, the very manner in which advisory committee review of flibanserin proceeded demonstrates that interest groups, whether industry or public interest driven, have become adept at utilizing the Open Public Hearing portion of advisory committee meetings, in conjunction with public campaigns, to exploit the FDA's vulnerability to sociopolitical influences on issues of women's health. Such infiltration of the advisory committee process distorts the scientific risk-benefit analysis performed by advisory committees, which, in turn, damages public accountability and agency integrity, and frustrates effective judicial oversight of FDA decision-making.¹⁰

Part I of this Note discusses the FDA's mandate, the New Drug Application process, and judicial oversight of FDA decisions regarding new drugs. Part I also discusses the role of expert advisory committees in the new drug approval process and the requirements imposed on expert advisory committees by the Federal Advisory Committee Act.

Part II of this Note addresses the FDA's historical vulnerability to sociopolitical influences on matters involving women's health products. To demonstrate how pharmaceutical companies have become adept at manipulating the FDA's susceptibility to political manipulation with regard to women's health, Part II discusses the case of flibanserin, a female libido drug that was approved in August of 2015. Part II pays special attention to industry infiltration of the advisory committee process, arguing that political distortion of advisory committee risk-benefit analyses is inconsistent with FDA advisory committees' statutory mandate, and is especially problematic because it frustrates public accountability and appropriate and effective judicial oversight of FDA decision-making.

9. See, e.g., Hylton V. Joffe et al., *FDA Approval of Flibanserin—Treating Hypoactive Sexual Desire Disorder*, 374 *NEW ENG. J. MED.* 101 (2016) (arguing that approval of flibanserin was appropriate); Moynihan, *supra* note 8 (arguing that FDA approval of flibanserin was inappropriate).

10. See Sidney A. Shapiro, *Public Accountability of Advisory Committees*, 1 *RISK: ISSUES IN HEALTH & SAFETY* 190, 191–92 (1990); see also Gillian Metzger, *The Interdependent Relationship Between Internal and External Separation of Powers*, 59 *EMORY L.J.* 423, 431 n.34 (2009) [hereinafter Metzger, *Separation of Powers*] (briefly discussing the role of advisory committees as an important procedural check on the politicization of the FDA).

Part III of this Note argues that the FDA should issue sub-regulatory guidance limiting who can speak at advisory committee public hearings and for what purpose. Part III does not argue against societal and industrial interests being afforded a voice in the FDA process. Rather, Part III advocates for a bifurcation of the consideration of (i) social agendas/concerns and (ii) the advisory committee's analysis, so as to bolster the integrity of the risk-benefit analysis performed by the advisory committee and promote transparent and proportionate responses to bias that may distort expert risk-benefit analysis.

I. BACKGROUND

Pursuant to a mandate to protect the public health, the Food and Drug Administration (FDA) is responsible for affirmatively determining that a given drug meets requirements of safety and efficacy before that drug may be marketed to the public.¹¹ With few statutory or judicial constraints, the FDA has broad latitude in how it conducts pre-market reviews of new drugs.¹² However, courts will scrutinize FDA decision-making more closely where it appears that a decision to approve or reject a new drug was, at least in part, the product of political forces rather than scientific judgment.¹³ While such a system of non-absolute deference is often appropriate in the context of the FDA's highly technical decision-making, this system also may put pressure on FDA actors to dishonestly articulate politically or socially motivated decisions as entirely scientifically-founded so as to avoid searching judicial review.¹⁴

The FDA employs the assistance of independent, expert advisory committees to perform the highly technical, scientific risk-benefit analysis required to determine if a new drug will be granted

11. FDA, *What We Do*, *supra* note 1; Peter Barton Hutt, *A Historical Introduction*, in *FOOD AND DRUG LAW: CASES AND MATERIALS* 4–5 (Peter Barton Hutt et al. eds., 3d ed. 2007) [hereinafter Hutt, *Introduction*] [hereinafter *FOOD AND DRUG LAW*].

12. Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, in *FOOD AND DRUG LAW*, *supra* note 11, at 6.

13. See discussion *infra* pp. 158–160 for a discussion of judicial deference to administrative decision-making and its limits.

14. See *infra* note 62 in support of the conclusion that policies that limit judicial deference to scientific decision-making incentivize agencies to justify all decisions as scientifically-founded, even though the decision may be the result of other forces.

market approval.¹⁵ These advisory committees are governed by the Federal Advisory Committee Act (FACA), which requires, among other things, that advisory committees be both fairly balanced and open to public participation.¹⁶ As technical/scientific advisory committees, FDA advisory committees meet the fair balance requirement of FACA by ensuring the committees are comprised of experts whose educational and professional backgrounds reflect a balance of expertise with regard to the scientific field in which an advisory committee operates.¹⁷ To comply with the public participation requirements of FACA, FDA advisory committees hold open public hearings during every new drug review, among other things.¹⁸ While these open public hearings serve the important function of promoting public accountability and open discussion about important issues of public health, by liberally entertaining public comment, open public hearings may also serve to enflame emotions and politicize judgments at the advisory committee meetings during which risk-benefit analysis is performed.¹⁹

A. FDA Mandate and Overview

What is now the FDA has existed in the United States, in various forms, since the late 1800s. While its role has changed dramatically over time, the mission of the FDA has essentially remained the same: to protect the public health by ensuring that products intended for human consumption are safe and are accurately labeled.²⁰

By granting the FDA the authority to deny market access to drug manufacturers who have not shown the safety of their drug, the

15. Elizabeth Glode, *Advising Under the Influence?: Conflicts of Interest Among FDA Advisory Committee Members*, 57 FOOD & DRUG L.J. 293, 294–97 (2002).

16. Shapiro, *supra* note 10, at 189; 5 U.S.C. app. § 2 (2012).

17. See discussion *infra* pp. 163–165 for a discussion of the FDA's compliance with FACA's fair balance requirement.

18. See discussion *infra* pp. 165–166 for a discussion of FDA advisory committee open public hearings in the context of FACA's transparency, openness, and public participation requirements.

19. See Glode, *supra* note 15, at 299; DIVISION OF HEALTH CARE POLICY, INSTITUTE OF MEDICINE, FOOD AND DRUG ADMINISTRATION ADVISORY COMMITTEES 180 (Richard A. Rettig et al. eds., 1992).

20. Hutt, *Introduction*, *supra* note 11, at 4–5. Hutt notes, however, that this description of the FDA's mandates “oversimplifies the agency's current responsibilities, which encompass a much larger role in the development, testing, introduction, and marketing of these products.” *Id.* at 5.

Federal Food, Drug, and Cosmetic Act of 1938 (FDCA) marked a major shift in the FDA's role from one of policing drugs already on the market to one of market gatekeeper.²¹ The 1962 amendments to the FDCA cemented this shift by requiring that, before any manufacturers may introduce a new drug into the market, the FDA must affirmatively determine that the drug is both safe and effective based on evidence from clinical trials.²²

The 1962 amendments not only crystallized the FDA's pre-market veto power, but also had the effect of shifting the FDA's view of its own role in consumer protection: the FDA began to view itself as a "warrantor of manufacturer compliance with the rules that govern drug development and marketing."²³ In this role, the FDA shares responsibility with manufacturers for the introduction of any harmful drugs into the market.²⁴ Some argue that this has made FDA officials overly cautious, while others argue that FDA officials have failed to live up to the demands of this responsibility.²⁵

In light of the broad mandate to protect the public health granted by the FDCA,²⁶ the FDA articulates its mission, with respect to regulating the introduction of drugs into the market as, "protecting the public health by ensuring the safety, efficacy, and security of . . . drugs . . ."²⁷ The FDA further states that the agency "is [also] responsible for advancing the public health by helping to speed

21. Merrill, *supra* note 12, at 5, 676; Meadows, *supra* note 3.

22. See Larry J. Lesko & Janet Woodcock, *Pharmacogenomic-Guided Drug Development: Regulatory Perspective*, in FOOD AND DRUG LAW, *supra* note 11, at 670; Note, *Drug Efficacy and the 1962 Drug Amendments*, in FOOD AND DRUG LAW, *supra* note 11, at 578–79; U.S. FOOD & DRUG ADMIN., CREATING A MANDATE FOR DRUG SAFETY, LACKING A MANDATE FOR DRUG EFFICACY 1, 5–8 (2012).

23. Merrill, *supra* note 12, at 5, 676.

24. *Id.*; Hutt, *Introduction*, *supra* note 11, at 5.

25. See Hutt, *FDA Licensure of New Drugs*, in FOOD AND DRUG LAW, *supra* note 11, at 576–77 [hereinafter Hutt, *FDA Licensure*]; Lauren M. Azebu, *The FDA's Risk/Benefit Calculus in the Approvals of Qsymia and Belviq: Treating an Obesity Epidemic While Avoiding Another Fen-Phen*, 69 FOOD & DRUG L.J. 87, 95 (2014).

26. Carol R. Berry, *The Dividing Line Between the Role of the FDA and the Practice of Medicine: A Historical Review and Current Analysis* (1997) (unpublished term paper, Harvard Law School) (on file with LEDA at Harvard Law School), <https://dash.harvard.edu/bitstream/handle/1/8846812/cberry.html?sequence=2> ("The basic purpose of the Federal, Food, Drug and Cosmetic Act of 1938 . . . is for the protection of the public health and safety. Congress clearly intended that the FDA's jurisdiction 'be as broad as its literal language indicates' . . .").

27. FDA, *What We Do*, *supra* note 1.

innovations that make medical products more effective, safer, and more affordable and by helping the public get . . . accurate, science-based information”²⁸

B. New Drug Approvals

In order for a new drug to be introduced into the market, the FDA must certify that the drug is safe, effective, and properly labeled.²⁹ In a lengthy and expensive process,³⁰ drug sponsors obtain FDA approval by submitting a New Drug Application (NDA) to the FDA that contains scientific information, gathered through clinical trials, about the safety and effectiveness of a new drug.³¹

The FDA drug approval process has been subject to minimal formal statutory or judicial constraint.³² Instead, FDA officials rely on less formal rules, such as non-regulatory guidance documents (guidance), to inform agency action. “The FDA product approval system is, in short, remarkably free from conventional legal restraint.”³³ However, FDA guidance is predicated on both statutory and judicial rules that, though highly deferential to agency decision-

28. *Id.* For a description of the various functions of the FDA and how such functions fit within the FDA’s mandate, see Leonard Sacks, *Structure and Mandate of FDA*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/downloads/Training/ClinicalInvestigatorTrainingCourse/UCM378261.pdf> (last visited Feb. 11, 2017).

29. Hutt, *FDA Licensure*, *supra* note 11, at 577.

30. A 2014 study by the Tufts Center for the Study of Drug Development reported that the average total cost of developing a drug that receives FDA market approval is just under \$2.6 billion. Rick Mullen, *Cost to Develop New Pharmaceutical Drug Now Exceeds \$2.5B*, SCI. AM. (Nov. 24, 2014), <http://www.scientificamerican.com/article/cost-to-develop-new-pharmaceutical-drug-now-exceeds-2-5b/>. The same study found the average time from synthesis to approval to be 128 months. JOSEPH A. DIMASI, DIRECTOR OF ECONOMIC ANALYSIS, TUFTS CTR. FOR THE STUDY OF DRUG DEV., INNOVATION IN THE PHARMACEUTICAL INDUSTRY: NEW ESTIMATES OF R&D COSTS (Nov. 18, 2014). Note that not all of the cost and time associated with bringing a drug to market can be attributed to FDA review, and the \$2.5 billion estimate is inclusive of failures and cost of capital. *Id.* at Slide 5. Strictly speaking, a single round of NDA review (post submission) is expected to take ten months, but often takes longer, and drugs often go through multiple rounds of NDA review. *Id.* at Slide 18; *Frequently Asked Questions About the FDA Drug Approval Process*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/ResourcesForYou/SpecialFeatures/ucm279676.htm> (last updated Feb. 7, 2017).

31. Azebu, *supra* note 25, at 93–94.

32. Merrill, *supra* note 12, at 6.

33. *Id.*

making, provide outer-limits on what action the FDA may take and in what manner.³⁴

1. Risk-Benefit Analysis

To the extent that the FDCA does provide a formal statutory framework for the approval of new drugs, the statute mandates that drug sponsors make a showing that a drug is both safe and effective.³⁵ Specifically, drug sponsors must demonstrate effectiveness by a showing of “substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling”³⁶ To gain approval, a sponsor must also submit “adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling”³⁷

While the FDCA provides meaningful guidance as to what constitutes “substantial evidence,” setting forth a clinical trial mandate that has been expanded upon through strict FDA regulatory requirements, it does not attempt to set any sort of minimum level of efficacy required for approval.³⁸ So, the FDCA requires that drug manufacturers provide substantial evidence that the drug is as effective as they claim it to be, but not that the drug is substantially effective.³⁹ How effective a given drug must be in order to gain

34. See *infra* pp. 156–158 for a discussion of statutory and judicial limits on FDA discretion over the approval of new drugs.

35. Azebu, *supra* note 25, at 94.

36. 21 U.S.C. § 355(d) (2012).

37. *Id.*

38. Jonathan J. Darrow, *Pharmaceutical Efficacy: The Illusory Legal Standard*, 70 WASH. & LEE L. REV. 2073, 2075–77 (2013). The FDCA defines “substantial evidence” as:

[E]vidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

21 U.S.C. § 355(d) (2012).

39. Darrow, *supra* note 38, at 2083.

approval is left to the FDA to determine on a case-by-case basis, taking into account such factors as the risks posed by the drug and the availability of other treatment options.⁴⁰ The FDCA thus articulates a rule that is highly deferential to FDA expert judgment on whether a given drug is effective enough to be marketable, provided that such efficacy is demonstrated through rigorous clinical trials.⁴¹

Furthermore, the FDCA does not elaborate on what would or would not be “safe for use.”⁴² Indeed, no drug is completely safe in that it is free of any and all adverse side-effects.⁴³ As a result, FDA analysis of drug safety, like that of efficacy, is largely done in relative terms, considering the safety of the drug in light of its effectiveness, the availability of safer alternatives, and the feasibility of controlling risks through appropriate labeling and other risk mitigation strategies.⁴⁴ In short, in order to determine if a new drug should be approved, the FDA performs a risk-benefit analysis that weighs the risks posed by the drug against the strength of the evidence of the drug’s effectiveness.⁴⁵ The FDA does not perform this analysis in a vacuum, but instead takes into account market realities such as the availability of alternatives and the ability of physicians to oversee patient use of the drug.⁴⁶

40. *Drug Safety: Hearings Before a Subcomm. of the H. Comm. on Gov’t Operations*, 88th Cong. 150, 153–54 (1964) [hereinafter *Drug Safety Hearings*] (statement of George Larrick, Comm’r, U.S. Food & Drug Admin.); Karen Baswell, *Time for a Change: Why the FDA Should Require Greater Disclosure of Differences of Opinion on the Safety and Efficacy of Approved Drugs*, 35 HOFSTRA L. REV. 1799, 1814–15 (2006).

41. Darrow, *supra* note 38, at 2085. The Senate reports from the 1962 Kefauver-Harris drug amendments make clear that the legislature intended a high level of deference to FDA decision-making in order to enable the FDA to act on emerging scientific thought. *Id.*

42. Azebu, *supra* note 25, at 94; Baswell, *supra* note 40, at 1814–15.

43. Bernadine Healy, *What is a ‘Safe’ Drug?*, in FOOD AND DRUG LAW, *supra* note 11, at 686–87.

44. *Drug Safety Hearings*, *supra* note 40, at 150, 153–54; U.S. FOOD. & DRUG ADMIN., STRUCTURED APPROACH TO BENEFIT-RISK ASSESSMENT IN DRUG REGULATORY DECISION-MAKING: DRAFT PDUFA V IMPLEMENTATION PLAN 5–6 (2013).

45. *Drug Safety Hearings*, *supra* note 40, at 150, 153–54; Hutt, *Balancing Benefit and Risk*, in FOOD AND DRUG LAW, *supra* note 11, at 695, 696 n.1.

46. Dov Fox, *Safety, Efficacy, and Authenticity: The Gap Between Ethics and Law in FDA Decisionmaking*, 2005 MICH. ST. L. REV. 1135, 1159–60 (2005); Azebu, *supra* note 25, at 95; *Drug Safety Hearings*, *supra* note 40, at 150–54; Baswell, *supra* note 40, at 1814–15.

2. Judicial Review of FDA Decisions

Courts are generally deferential to agency discretion, particularly so with regard to technical or scientific matters.⁴⁷ Given the high level of scientific expertise required for FDA decision-making, especially in the NDA process, such deference is, broadly speaking, appropriate.⁴⁸ Not only do courts lack the expertise to effectively scrutinize the technical decisions of the FDA, but also, given courts' lack of expertise, more searching judicial scrutiny of the FDA's time-consuming and complex decision-making has the potential to thwart the effectiveness of the FDA as an agency.⁴⁹

This is not to say that FDA decisions are not ever subject to judicial scrutiny.⁵⁰ Both the Administrative Procedure Act (APA) and the FDCA afford private parties the opportunity to challenge FDA actions and decisions in court.⁵¹

With regard to NDA decisions, courts will, at a minimum, require that the FDA "articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'"⁵² However, courts will remain largely deferential to

47. Elizabeth A. Silverberg, *Looking Beyond Judicial Deference to Agency Discretion: A Fundamental Right of Access to RU 486?*, 59 BROOK. L. REV. 1551, 1566 (1994); Gillian Metzger, *Abortion, Equality, and Administrative Regulation*, 56 EMORY L.J. 865, 893 (2007) [hereinafter Metzger, *Abortion Regulation*]; Roger R. Martella, *The Legal Scrutiny Surrounding § 111(d): Will it Survive or Stumble*, 44 ENVTL. L. REP. 11058, 11060 (2014).

48. James T. O'Reilly, *Losing Deference in the FDA's Second Century: Judicial Review, Politics, and a Diminished Legacy of Expertise*, 93 CORNELL L. REV. 939, 941–42 (2008).

49. *Id.* ("As with any administrative agency, deference is the cornerstone of the FDA's effectiveness.")

50. Metzger, *Abortion and Regulation*, *supra* note 47, at 898–900.

51. Hutt, *Court Review of Agency Implementation*, in FOOD AND DRUG LAW, *supra* note 11, at 1556.

52. *Motor Vehicle Mfrs. Ass'n of the United States, Inc. v. State Farm Mutual Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (quoting *Burlington Truck Lines v. United States*, 371 U.S. 156, 168 (1962)). Actions approving a drug or requiring certain labeling will likely be reviewed under the APA's highly deferential "arbitrary and capricious" standard. 5 U.S.C. § 706 (2012); Metzger, *Abortion Regulation*, *supra* note 47, at 898–99; *Henley v. U.S. Federal Drug Admin.*, 77 F.3d 616, 620 (2d Cir. 1996) ("An agency rule may be deemed arbitrary, capricious or an abuse of discretion if the agency has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise"); Silverberg, *supra* note 47, at 1566.

the FDA's decision-making, absent indication that such judgment was the result of "arbitrariness, expansion of power, or improper influences," in which case courts will engage in a more searching "hard look" review.⁵³ Notably, courts have shown a willingness to more closely examine and intervene in FDA decision-making where the decision appears to be the product of political forces rather than scientific or technical judgment.⁵⁴

In furtherance of a policy of judicial deference to agency judgment, courts have read the APA to limit review of agency decisions to "the administrative record compiled by that agency when it made the decision."⁵⁵ However, this limitation, known as the

However, under the FDCA, applicants whose NDAs were denied or withdrawn may, following opportunity for a hearing, appeal such a decision in the U.S. Court of Appeals, subject to a standard of review that requires that such actions be supported by "substantial evidence." 21 U.S.C. § 355(h) (2012). While this standard of review is different and less deferential than the "arbitrary and capricious" standard, it is also relatively deferential to agency decision-making. *Universal Camera Corp. v. Nat'l Labor Relations Bd.*, 340 U.S. 474, 477 (1951) ("[S]ubstantial evidence is more than a mere scintilla. It means such relevant evidence as a reasonable mind might accept as adequate to support a conclusion" (quoting *Consol. Edison Co. v. Nat'l Labor Relations Bd.*, 305 U.S. 197, 229 (1938))); *Dickinson v. Zurko*, 527 U.S. 150, 161–65 (1999); *Allentown Mack Sales & Serv. v. Nat'l Labor Relations Bd.*, 522 U.S. 359, 377 (1998) ("The 'substantial evidence' test *itself* already gives the agency the benefit of the doubt, since it requires not the degree of evidence which satisfies the *court* that the requisite fact exists, but merely the degree which *could* satisfy a reasonable factfinder." (emphasis original)).

53. Metzger, *Abortion and Regulation*, *supra* note 47, at 899–900.

54. Metzger, *Separation of Powers*, *supra* note 10, at 445 ("[J]udicial review of agency actions often appears to turn on judges' perceptions of the role politics played in decisionmaking by agency officials."); *see, e.g., Tummino v. Torti*, 603 F. Supp. 2d 519, 523, 550 (E.D.N.Y. 2009) (holding that the FDA decision to restrict the over-the-counter sale of the contraceptive, Plan B, to patients ages 18 and older was the product of political influence, and was, therefore, arbitrary and capricious); *State Farm*, 463 U.S. at 43–57 (holding that National Highway Safety Administration's decision to rescind safety regulation that was promulgated under a previous administration was arbitrary and capricious); *see also O'Reilly*, *supra* note 48, at 953–55, 973–76 (explaining how the perception of increased politicization of the FDA under George W. Bush led to decreased judicial deference to FDA discretion).

55. *Nat'l Audobon Soc'y v. Hoffman*, 132 F.3d 7, 14 (2d Cir. 1997); Susannah T. French, *Judicial Review of the Administrative Record in NEPA Litigation*, 81 CAL. L. REV. 929, 933 (1993); Carmel Shachar, *Ending the Charade: Revising the Ban on Political Influence in FDA Decision Making in Light of Tummino v. Torti* 11 (Apr. 2010) (unpublished term paper, Harvard Law School) (on file at DASH at Harvard University), <http://nrs.harvard.edu/urn3:HUL.InstRepos:8822168>.

“record rule,” is subject to important exceptions.⁵⁶ For instance, courts will expand the scope of discovery “[i]f the record before the agency does not support the agency action, if the agency has not considered all relevant factors, or if the reviewing court simply cannot evaluate the challenged agency action on the basis of the record before it”⁵⁷ Courts may also expand the scope of discovery beyond the administrative record upon “a strong showing of bad faith or improper behavior”⁵⁸ Thus, where there is strong reason for the court to believe that political motives have compromised the “integrity of the FDA’s decision-making,”⁵⁹ “the court’s consideration of evidence outside the agency’s ‘administrative record’ is not only warranted, but necessary to a meaningful judicial review of the agency’s action.”⁶⁰

Taken together, policies of non-absolute deference to agency discretion mean that courts are reluctant to intervene in agency decision-making absent a strong reason to believe that the agency action at issue was the product of improper motives, such as undue political influence.⁶¹ While judicial deference to agency discretion is, in many instances, appropriate, in affording deference only when agency decisions appear to be appropriately expert, these policies also put pressure on agencies to justify their decisions as entirely scientifically founded, even where they may be the product of mixed scientific and political motives.⁶²

56. Shachar, *supra* note 55, at 11–12.

57. *Florida Power & Light Co. v. Lorion*, 470 U.S. 729, 744 (1984); French, *supra* note 55, at 942–45.

58. *Torti*, 603 F. Supp. 2d at 543 (quoting *Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 420 (1971)).

59. *Tummino v. von Eschenbach*, 427 F. Supp. 2d 212, 234 (E.D.N.Y. 2006).

60. *Torti*, 603 F. Supp. 2d at 543 (citations omitted).

61. Shachar, *supra* note 55, at 20; Metzger, *Abortion Regulation*, *supra* note 47, at 903–04 (“[A]dministrative law also puts strong emphasis on deferring to agency expertise and policy choices, an emphasis reflected (among other ways) in ostensibly deferential standards of review”).

62. Shachar, *supra* note 55, at 27; *see also* Metzger, *Abortion Regulation*, *supra* note 47, at 906 (arguing that standards of judicial review under both constitutional and administrative law incentivize agencies to emphasize “the health focus” of administrative regulation of abortions in order to reinforce “the appropriateness of deferential scrutiny.”); Sidney Shapiro, *OMB and the Politicization of Risk Assessment*, 37 ENVTL. L. 1083, 1087–92 (2007) (discussing how agencies may manipulate scientific uncertainty and available scientific information to veil political actions as founded in science).

C. FDA Advisory Committees

Since the 1960s, the FDA has made use of expert advisory panels to perform the highly technical risk-benefit analysis required to permit a drug to enter or remain on the market.⁶³ While the role of advisory committees has changed over time, today's FDA advisory committees are standing bodies of independent experts that advise the Commissioner "on the safety and effectiveness . . . of human prescription drugs . . . and on the scientific standards appropriate for a determination of safety and effectiveness . . . of drugs."⁶⁴ FDA advisory committees not only provide important expert guidance, but, in doing so, also serve to legitimize and lend credibility to the decisions of the agency as scientifically founded.⁶⁵

The Food and Drug Administration Modernization Act of 1997 amended Section 505 of the FDCA to formally require that the FDA convene expert panels "to provide scientific advice and recommendations to the Agency regarding the clinical investigation of drugs or the approval for marketing of drugs."⁶⁶ In light of this requirement, the FDA has issued draft guidance stating that advisory committee meetings need not be convened in all cases, but should be convened in controversial or close-call cases where the public could greatly benefit from the agency's obtaining expert advice in its decision-making process.⁶⁷

FDA advisory committees do not make binding decisions, but instead conduct a public hearing in which the risks and benefits of a given drug are debated and weighed. The advisory committee then votes on answers to questions posited about the safety or efficacy of the drug, as well as whether to recommend that the FDA take a

63. Glode, *supra* note 15, at 294–97 (2002) (detailing the gradual evolution of FDA Advisory Committees from external bodies convened for a limited purpose to internal, standing bodies). It should be noted that advisory committees are not only involved in the pre-market approval process, but also play an important role in the post-market surveillance of approved drugs.

64. 21 C.F.R. § 15.160(a) (2016); U.S. FOOD & DRUG ADMIN., ADVISORY COMMITTEES, <http://www.fda.gov/AdvisoryCommittees/> (last visited Feb. 11, 2017); Glode, *supra* note 15, at 1294–98.

65. Shapiro, *supra* note 10, at 189; Fox *supra* note 46, at 1161–62.

66. FDA SECTION 120 GUIDANCE, *supra* note 2, at 1.

67. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR THE PUBLIC AND FDA STAFF ON CONVENING ADVISORY COMMITTEE MEETINGS 4 (2008) [hereinafter FDA CONVENING COMMITTEE MEETINGS GUIDANCE]; Fox, *supra* note 46, at 1161.

certain action.⁶⁸ However, with regard to the approval of new drugs, the FDA nearly always follows the recommendation of the relevant advisory committee(s).⁶⁹ Furthermore, although there is no statutory requirement that NDAs be reviewed by an advisory committee, such review is almost always afforded for important new drugs.⁷⁰ As a result, NDA review by an advisory committee “represents the best opportunity that the applicant has to address the agency and the public about the evidence of safety and effectiveness and the importance of the drug to public health.”⁷¹ Many drug sponsors, therefore, expend large amounts of money and time in organizing strategic campaigns designed to secure positive recommendations from an advisory committee.⁷²

1. The Federal Advisory Committee Act: Fair Balance and Transparency

In 1972, Congress passed the Federal Advisory Committee Act (FACA).⁷³ In FACA, Congress recognized that advisory committees were “useful and beneficial means of furnishing expert advice, ideas, and diverse opinions to the Federal Government,” but, in light of the proliferation of advisory committees in federal agencies, expressed a need to promote public accountability of advisory committees and reduce bias in advisory committee decision-making.⁷⁴

68. Peter Barton Hutt, *The Regulation of Drug Products in the United States Food and Drug Administration*, in *FOOD AND DRUG LAW*, *supra* note 11, at 723–24 [hereinafter Hutt, *Regulation of Drugs*]; 21 CFR §§ 14.5, 14.22 (2016).

69. PHILIP MA ET AL., MCKINSEY CENTER FOR GOVERNMENT, MCKINSEY & CO., *FDA ADVISORY COMMITTEE OUTCOMES 2–3* (2013) (“[T]he FDA’s approval decisions have been broadly consistent with the recommendations of its advisory committees. The FDA approved 88% of the original NDAs or BLAs that were endorsed by its advisory committees, and did not approve 86% of those that the committees did not endorse.”).

70. Hutt, *Regulation of Drugs*, *supra* note 68, at 723–24. However, where a new drug contains no previously approved active ingredients, Section 505(s) of the FDCA provides that the “FDA must either refer that drug to an advisory committee or provide in the action letter for the drug a summary of the reasons why FDA did not refer the drug to an advisory committee before approval.” FDA, *CONVENING COMMITTEE MEETING GUIDANCE*, *supra* note 67, at 4.

71. Hutt, *Regulation of Drugs*, *supra* note 68, at 724.

72. *Id.*

73. Fox, *supra* note 46, at 1162. Federal Advisory Committee Act, 5 U.S.C. app. § 2 (2012).

74. 5 U.S.C. app. § 2 (2012); Shapiro, *supra* note 10, at 193; Daniel Walters, *The Justiciability of Fair Balance Under the Federal Advisory Committee Act: Toward a Deliberative Process Approach*, 11 MICH. L. REV. 677, 679–80 (2012).

Accordingly, FACA provides for several measures aimed at increasing public accountability of advisory committees:

Two of the most important requirements establish qualifications for membership on an advisory committee and create a “paper trail” of documents to explain a committee’s decision. . . . [M]embership must be “fairly balanced in terms of the points of view represented and the functions to be performed by the advisory committee” and appropriate precautions must be taken to ensure that committees are not influenced by “any special interest.” . . . In addition, FACA requires agencies to give prior notice of meetings, to hold open meetings in most cases, to keep “detailed minutes of each meeting, and to give the public access to most committee records, transcripts, minutes and other documents.”⁷⁵

i. The Fair Balance Requirement

Both the courts and the FDA have drawn a distinction between technical/scientific and substantive/policy advisory committee functions, and, with respect to technical or scientific advisory committees, have interpreted the requirement that advisory committees be “fairly balanced” not to mean that all interested parties must necessarily be afforded representation. Rather, “fairly balanced” requires that technical/scientific advisory committees be comprised of experts whose educational and professional backgrounds reflect a balance of expertise with regard to the subject matter to be considered by that committee.⁷⁶ Consistent with this approach, the FDA classifies advisory committees that evaluate the safety and

75. Shapiro, *supra* note 10, at 189 (quoting 5 U.S.C. app. §§ 5(b)(2)-(3), 10 (2012)).

76. 21 C.F.R. § 14.80(b)(1)(i) (2016); *Nat’l Hunger Coal. v. Exec. Comm. of the President’s Private Sector Survey on Cost Control*, 557 F. Supp. 524, 528 (D.D.C. 1983), *amended by*, 566 F. Supp. 1515 (D.D.C. 1983) (“Congress implicitly recognized the unworkability of such a requirement when it described balanced in terms of the functions to be performed by the advisory committee.”); Walters, *supra* note 74, at 686, 692 (distinguishing between “functional” and “point-of-view” balance, stating, “function-based approaches resolve the problem of representational balance by limiting the scope of a committee’s mandate to a narrow, technical task”); *Cargill, Inc. v. United States*, 173 F.3d 323, 337 (5th Cir. 1999) (“The task of the committee—providing scientific peer review—is politically neutral and technocratic, so there is no need for representatives from the management . . . to serve on the committee.”).

effectiveness of human prescription drugs as technical.⁷⁷ By law, voting membership on those advisory committees is limited to individuals with scientific expertise in the pharmacologic class covered by the committee such that “the committee will reflect a balanced composition of sufficient scientific expertise to handle the problems that come before it.”⁷⁸

By designating advisory committees for human prescription drugs as technical advisory committees and limiting voting membership of human prescription drug advisory committees to individuals with applicable scientific expertise, the FDA implicitly assumes that the safety and effectiveness analysis to be performed by these advisory committees is fundamentally scientific in nature, and therefore does not require a balance of political or policy expertise in voting capacities.⁷⁹

However, the FDA does recognize that technical advisory committee analysis will implicate more than purely scientific concerns.⁸⁰ In order to afford affected interests a fair voice in the decision-making process, FDA regulation provides for non-expert, special-interest representatives to serve on advisory committees in a nonvoting capacity.⁸¹ Given FACA’s requirement that, in order to be fairly balanced, an advisory committee may not be inappropriately influenced by special interests in its decision-making, the remaining regulatory effort to further the fair balance requirement has focused on minimizing and disclosing voting member conflicts of interest.⁸²

77. 21 C.F.R. § 14.160 (2016).

78. 21 C.F.R. § 14.80(b)(1)(i) (2016); 21 C.F.R. § 14.160 (2016).

79. Shapiro, *supra* note 10, at 197; *see* 21 C.F.R. § 14.160 (2016); 21 C.F.R. § 14.80(b)(1)(i) (2016); *see also* Pub. Citizen v. Nat’l Advisory Comm. on Microbiological Criteria for Foods, 886 F.2d 419, 423 (D.C. Cir. 1989) (Friedman, J., concurring) (“Since the Committee’s function in this case involves highly technical and scientific studies and recommendations, a ‘fair balance’ of viewpoints can be achieved even though the committee does not have any members who are consumer advocates or proponents of consumer interests”).

80. Shapiro, *supra* note 10, at 197–98.

81. *Id.*; 21 C.F.R. § 14.80(b)(2) (2016).

82. 5 U.S.C. app. § 15 (2012); 21 C.F.R. § 14.33 (2016); U.S. FOOD & DRUG ADMIN., GUIDANCE FOR THE PUBLIC, FDA ADVISORY COMMITTEE MEMBERS, AND FDA STAFF ON PROCEDURES FOR DETERMINING CONFLICT OF INTEREST AND ELIGIBILITY FOR PARTICIPATION IN FDA ADVISORY COMMITTEES (2008) [hereinafter FDA MEETING PARTICIPATION GUIDANCE]; Glode, *supra* note 15, at 299–304.

ii. Transparency, Participation, and Open Discussion Requirements

The open meeting and disclosure requirements of FACA take important steps towards promoting transparency and public accountability.⁸³ The FDA has complied with these requirements by opening advisory committee meetings to the public, making transcripts of advisory committee meetings publicly available, and, to the extent such information is not subject to Freedom of Information Act exemptions, making information provided to advisory committee members in connection with meetings publicly available, among other things.⁸⁴

Beyond simply requiring that advisory committee meetings be open to the public, FACA further requires that “interested persons . . . be permitted to attend, appear before, or file statements with any advisory committee, subject to such reasonable rules or regulations as the Administrator may prescribe.”⁸⁵ The FDA, recognizing that public meetings serve to “facilitate public discussion of important topics and provide a means for the public to provide comments to the agency,”⁸⁶ has acted on this requirement by issuing a regulation requiring that at least one hour of every advisory committee meeting be dedicated to an open public hearing (OPH) “during which interested persons may present relevant information or views orally or in writing.”⁸⁷ FDA guidance elaborating on OPH procedures states that the “FDA may decline a request to speak at an OPH if the person wishes to address a matter that is unrelated to the

83. See Shapiro, *supra* note 10, at 199.

84. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY ADVISORY COMMITTEE MEETINGS—PREPARATION AND PUBLIC AVAILABILITY OF INFORMATION GIVEN TO ADVISORY COMMITTEE MEMBERS 5 (2008).

85. 5 U.S.C. app. § 10(a)(3) (2012). The General Services Administration has issued regulations implementing FACA, stating that “[t]he head of each agency that establishes or utilizes one or more advisory committees must . . . [p]rovide the opportunity for reasonable participation by the public in advisory committee activities, subject to § 102–3.140 and the agency’s guidelines.” 41 C.F.R. § 102-3.105(j) (2016). Section 102-3.140 provides, in relevant part, that “[t]he agency head . . . must ensure that . . . [a]ny member of the public may speak to or otherwise address the advisory committee if the agency’s guidelines so permit” 41 C.F.R. § 102-3.140(d) (2016).

86. FDA CONVENING COMMITTEE MEETINGS GUIDANCE, *supra* note 67, at 3.

87. 21 C.F.R. § 14.25(a) (2016); 21 C.F.R. § 14.29(a) (2016).

advisory committee's work."⁸⁸ However, neither regulation nor FDA guidance articulate how relevant to the advisory committee's deliberation testimony must be in order for a speaker to be entitled to testify at an OPH.⁸⁹

Encouraging such transparency and open discussion has not come without costs to the expert deliberative process. OPHs have come under criticism for being politicized and inflammatory, and advisory committee members have accused FDA officials of asking "loaded" questions that further the Agency's agenda.⁹⁰ Furthermore, advisory committee members have expressed displeasure and even resentment over having their complex, scientific analysis scrutinized by an uninformed public, raising concerns that subjecting advisory committee decision-making to direct public scrutiny may cause advisory committee members to shy away from truly open, scientific debate.⁹¹ Nonetheless, "[a]llowing the public to observe the workings of advisory committees (despite committee members' discomfort) and requiring that documents relating to advisory committee decisionmaking be available for public scrutiny are critical concessions if [the] FDA is to defend the integrity of its advisory processes."⁹²

II. THE PROBLEM

Despite the FDA's efforts to maintain the scientific integrity of the new drug approval process, the FDA's decision-making with regard to women's health products has, historically, been plagued by problems of social and political influences infiltrating scientific risk-benefit analyses.⁹³ This infiltration occurs, in varying degrees, in a combination of two ways: (1) it may occur when paternalistic views

88. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR THE PUBLIC, FDA ADVISORY COMMITTEE MEMBERS, AND FDA STAFF: THE OPEN PUBLIC HEARING AT FDA ADVISORY COMMITTEE MEETINGS 5 (2013) [hereinafter FDA OPEN PUBLIC HEARING GUIDANCE].

89. 21 C.F.R. § 14.25 (2016); 21 C.F.R. § 14.29 (2016); FDA OPEN PUBLIC HEARING GUIDANCE, *supra* note 88, at 2.

90. Glode, *supra* note 15, at 299; DIV. OF HEALTH CARE POLICY, INST. OF MED., FOOD AND DRUG ADMINISTRATION ADVISORY COMMITTEES 180 (Richard A. Rettig et al. eds., 1992).

91. Glode, *supra* note 15, at 299.

92. *Id.*

93. *See infra* notes 98–100 in support of the proposition that the FDA has, historically, been vulnerable to sociopolitical influences in the context of women's health.

about women's health cause the FDA to either underestimate the morbidity treated by a women's health product or overestimate the risks posed by the drug; or (2) it may occur when FDA decisions are motivated by social views about what sexual behavior is or is not appropriate for women rather than by the balance of clinical risks and benefits of the drug.⁹⁴ Given courts' deference to administrative decisions that are perceived as purely technical or scientific, such inclusion of social and political factors in FDA risk-benefit analysis is especially problematic when social and political factors are veiled as scientific, frustrating judicial oversight and broader public accountability.⁹⁵

While social and political factors that distort FDA risk-benefit analysis of women's health products come from many sources, the recent path through which flibanserin, a drug for the treatment of Hypoactive Sexual Desire Disorder in women, gained FDA approval demonstrates that industry and public interest groups have become adept at exploiting the FDA's vulnerability to sociopolitical influences to pressure the FDA to take certain actions with respect to women's health products. Specifically, a review of the transcript of the advisory committee meeting at which the advisory committee recommended approval of flibanserin reveals that the drug's manufacturer, Sprout Pharmaceuticals, skillfully utilized the OPH portion of the advisory committee meeting to build on a public campaign for approval and pressured advisory committee members to act based on concerns about gender bias rather than a scientific analysis of the risks and benefits of the drug.⁹⁶ In the advisory committee's analysis of flibanserin, sociopolitical and scientific factors were so conflated as to render the role of each nearly inextricable.⁹⁷ Such conflation of scientific and political factors, in turn, reduced transparency, potentially thwarting public accountability and judicial oversight.

94. See *infra* pp. 168–169, arguing that the distortion of FDA risk-benefit analysis unique to women's health products falls into two categories: paternalistic distortion of individual risks and benefits and/or the overriding of scientific risk-benefit factors by concerns about compliance with sexual norms.

95. Shapiro, *supra* note 10, at 190–94.

96. See *infra* pp. 173–190 for a full discussion of flibanserin and its path to market approval, with a special focus on the advisory committee's review of its risks and benefits immediately preceding approval.

97. See *infra* pp. 185–192 for a full analysis of the transcript of the advisory committee's risk-benefit analysis of flibanserin.

A. Women's Health and the Politicization of FDA Decision-Making

Historically, the FDA has been particularly vulnerable to sociopolitical influences in the field of women's health.⁹⁸ In the NDA process specifically, FDA decision-making on women's health issues has, on occasion, been tainted by sociopolitical influence in two overlapping ways. First, gender bias has distorted risk-benefit analysis, causing experts to overestimate risks posed to women or to undervalue the morbidity treated by a drug, and thus, undervalue the drug's benefit.⁹⁹ ¹⁰⁰ Second, social norms regarding women's sexual

98. See, e.g., Metzger, *Abortion Regulation*, *supra* note 47, at 901–02 (discussing the state and federal use of administrative regulation to control access to abortion); Francine Stulac, *RU 486: The Politics of Choice*, 1 HEALTH MATRIX 77 (1991) (discussing the role of politics in the FDA's unusual treatment of the contraceptive, RU 486); Lars Noah, *A Miscarriage in the Drug Approval Process?: Mifepristone Embroils FDA in Abortion Politics*, 36 WAKE FOREST L. REV. 571 (2001) (same); John Fielder, *Ethics and FDA*, 61 FOOD & DRUG L.J. 809 (2009) (accusing the FDA of replacing health standards with moral standards in matters of women's reproductive health); R. Alta Charo, *Protecting Us to Death: Women, Pregnancy, and Clinical Research Trials*, 38 ST. LOUIS U. L.J. 135 (1993) (discussing how perceptions of the female body and patronizing social norms have resulted in the historical exclusion of fertile women from clinical trials by the FDA to the detriment of women's health generally); Anne Bloom, *Rupture, Leakage, and Reconstruction: The Body as a Site for the Enforcement and Reproduction of Sex-Based Legal Norms in the Breast Implant Controversy*, 14 COLUM. J. GENDER & L. 85 (2005) (arguing that, in acting on a perception of breast implants as more beneficial for post-mastectomy patients than transsexual patients, the FDA was “echoing and reproducing the socio-cultural norms about gender and sexuality”). *But see* Daniel Carpenter et al., *Reputation and Precedent in the Bevacizumab Decision*, NEW ENG. J. MED., July 2011, at e3(1) (applauding the FDA for prioritizing a scientific risk-benefit assessment over pressure from groups accusing the FDA of bias in a decision not to approve a breast cancer drug).

99. One example of such a distortion occurred in a controversy over silicone breast implants in the early 1990s, in which the FDA Commissioner imposed a moratorium on silicone breast implants following accusations that the silicone caused a host of adverse side effects. Henry Miller, *The Sad Saga of Silicone Breast Implants*, FORBES (Mar. 4, 2015), <http://www.forbes.com/sites/henrymiller/2015/03/04/infuriating-titbits-about-silicone-breast-implants/#2715e4857a0b6aeafec18d6>. Given that clinical studies have failed to show a significant link between silicone breast implants and the side effects claimed, the Commissioner has been accused of buckling under public pressure, myopically undervaluing breast implants as a pure vanity, and patronizingly reacting too quickly to anecdotal evidence of harms to unsuspecting women. See, e.g., Bloom, *supra* note 98, at 105–06 (arguing that the FDA's differential treatment of silicone breast implants between different classes of patients was the result of social norms that caused the FDA to undervalue the importance of breast implants to certain classes of patients); MARCIA ANGELL, SCIENCE ON TRIAL: THE CLASH OF MEDICAL EVIDENCE AND LAW IN THE BREAST IMPLANT CASE (1997) (arguing, in part, that, by basing

activity impact FDA decision-making with regard to certain drugs, especially contraceptives. The FDA's decision to approve or reject a drug in these cases has been both a reflection and an enforcement of social norms regarding women's sexuality, rather than an action based purely on the scientific risk-benefit profile of those drugs.¹⁰¹ While such sociopolitical distortions can enter the FDA's decision-making processes in many ways, by liberally entertaining public comment, the FDA Advisory Committee creates one vehicle

decisions on political pressures and public perceptions the FDA contributed to a massive controversy over silicone breast implants); Rebecca Dresser et al., *Breast Implants Revisited: Beyond Science On Trial*, 1997 WIS. L. REV. 705 (1997) (chastising the FDA for being "too submissive to political and consumer pressures" rather than relying on good science in the early stages of the silicone breast implant controversy); JACK FISCHER, *SILICONE ON TRIAL: BREAST IMPLANTS AND THE POLITICS OF RISK* (2015) (accusing the government, especially the FDA, of reacting to politics and not sound science in actions regarding silicone breast-implants).

100. The FDA's treatment of the contraceptive injection, Depo-Provera, has also generated quite a bit of controversy. Despite international acceptance of the contraceptive, the FDA took nearly 20 years to approve the drug due to concerns about its safety. While some commentators have applauded the FDA for their rigorous scientific analysis of the risks and benefits of the drugs, others have argued that the FDA's repeated decisions to withhold approval were politically driven reactions to overblown and unconfirmed risks, and others have even expressed concern that Depo-Provera was approved in response to highly political calls for contraceptive options for women, despite otherwise unacceptable health risks. See Rachel Benson Gold & Peters D. Willson, *Depo-Provera: New Developments in a Decade-Old Controversy*, 13(1) FAM. PLANNING PERSP. 35 (1981) (giving an overview of the controversy surrounding the then not-yet-FDA-approved Depo-Provera); Sidney Shapiro, *Scientific Issues and the Function of Hearing Procedures: Evaluating the FDA's Public Board of Inquiry*, 1986 DUKE L.J 288, 313-17 (1986) (concluding that, in recommending that Depo-Provera not be approved in 1983, the FDA Public Board of Inquiry reacted appropriately to scientifically founded concerns about the risks of cancer associated with Depo-Provera); Warren E. Leary, *U.S. Approves Injectable Drug as Birth Control*, N.Y. TIMES (Oct. 30, 1992), <http://www.nytimes.com/1992/10/30/us/us-approves-injectable-drug-as-birth-control.html> (documenting varying reactions to the eventual FDA approval of Depo-Provera).

101. Metzger, *Abortion Regulation*, *supra* note 47, at 866; Fielder, *supra* note 98, at 810; see also *Tummino v. Torti*, 603 F. Supp. 2d 519, 548 (E.D.N.Y. 2009) (finding that the FDA Commissioner's decision to restrict over-the-counter sale of the contraceptive, Plan B, to patients 18 years of age and older was the result of political, not scientific, considerations); Ilyssa Hollander, *Viagra's Rise Above Women's Health Issues: An Analysis of the Social and Political Influences on Drug Approvals in the United States and Japan*, 62 SOC. SCI. & MED. 683 (2006) (arguing that gendered social norms regarding sex and sexual pleasure have caused the FDA to unnecessarily impose harsher restrictions on contraceptives than Viagra).

through which industry or special interest groups can exercise sociopolitical influence over FDA action with respect to women's health products.

Many scholars have expressed broad concern over executive influence resulting in the politicization of agency decision-making, particularly during the George W. Bush administration.¹⁰² However, new grounds for concern about the politicization of the FDA have surfaced: interest groups, whether industry or public-interest driven, have become adept at utilizing sociopolitical influences to seize on existing biases within the FDA and distort the scientific risk-benefit analyses performed by FDA advisory committees with regard to women's health products.¹⁰³ Such politicization of the advisory committee process is especially problematic because it allows for normative judgments about women's sexuality and health to be veiled as scientifically founded.¹⁰⁴ This conflation of scientific and normative

102. Metzger, *Separation of Powers*, *supra* note 10, at 423–24 (“[T]he instances in which the Bush Administration appeared to evade and perhaps violate internal constraints on administrative decisionmaking can largely be grouped under the heading of politicization of administration.”); Henry A. Waxman, *Remarks at FDLI’s 46th Annual Educational Conference*, 58 FOOD & DRUG L.J. 205, 209 (2003) (inviting the public to join Waxman in his fight against the “trend towards the politicization of health science”); Stulac, *supra* note 98, at 80–87, 89–97 (wrestling with the extent to which abortion politics distorted the FDA’s evaluation of the drug, RU 486); Adrian Vermeule, *The Parliament of Experts*, 58 DUKE L.J. 2231, 2233 (2009) (noting the “politicization of science under the Bush administration”); Fielder, *supra* note 98, at 810 (accusing the George W. Bush administration of attempting “to hijack the FDA approval process and use it for their own ethical views and political goals”); Michael R. Taylor, *Protecting the FDA’s Ability to Protect Public Health*, 61 FOOD & DRUG L.J. 805 (2006) (expressing concern over the infiltration of value judgments in FDA risk-benefit analysis); Jody Freeman & Adriane Vermeule, *Massachusetts v. EPA: From Politics to Expertise*, 2007 SUP. CT. REV. 51, 52 (2007) (discussing increasing judicial concern over the politicization of the Environmental Protection Agency under the George W. Bush administration).

103. To be sure, the FDA is not unique in its vulnerability to political manipulation by industry interests. The EPA, for instance, has fallen victim to public campaigns initiated by energy-industry actors to discredit good environmental science and force non-scientifically founded environmental regulation (or lack thereof). *See generally* UNION OF CONCERNED SCIENTISTS, INTERFERENCE AT THE EPA: SCIENCE AND POLITICS AT THE U.S. ENVIRONMENTAL AGENCY (2008) (detailing interference by political forces in EPA expert decision-making during the George W. Bush administration).

104. Shapiro, *supra* note 10, at 191–92 (“Members of scientific or technical advisory committees often do not admit, and may not even recognize, when they exceed their expertise and based recommendations on policy values. This result not only obscures the distinction between science and policy decisions, but it can

judgments, in turn, damages public accountability with regard to FDA decision-making by misinforming the public about the scientific risk-benefit profile of the drugs available to them.¹⁰⁵

Given the significant deference afforded to agency scientific decision-making, courts also may rely on advisory committee findings to provide the necessary scientific backdrop for judicial oversight of FDA action.¹⁰⁶ Thus, when sociopolitical factors are veiled as scientific in an advisory committee's risk benefit analysis, effective judicial

also impede the agency's decision making process."); Sidney A. Shapiro, *OMB and the Politicization of Risk Assessment*, 37 ENVTL. L. 1083, 1087, 1090–92 (2007) (discussing how agencies may fall prey to politicization when political actors take advantage of scientific uncertainty or public misunderstanding to distort a risk-benefit analysis at the expense of sound science).

105. Shapiro, *supra* note 10, at 192 (“[A]s long as the policy aspect of a science/policy question is not immediately apparent to the public, a decision maker can use the advisory committee to shield himself or herself from criticism for policy choices by maintaining that the decision was made in accordance with the neutral advice of an independent scientific advisory committee.”); Waxman, *supra* note 102, at 206 (arguing that the infiltration of political ideology into the FDA advisory committee process has the potential to damage the public health).

106. Shapiro, *supra* note 10, at 189–90 (discussing how, when advisory committees function properly, they form an important backdrop for judicial oversight, but, when advisory committees fail to confine their deliberations to scientific judgments, they may frustrate judicial oversight). In *Tummino v. Torti*, a federal court ruled that the FDA's decision to restrict over-the-counter (OTC) sales of the emergency contraceptive, Plan B, to patients eighteen years and older was arbitrary and capricious because it was the product of political influence rather than scientific judgment. *Tummino v. Torti*, 603 F. Supp. 2d 519, 544–50 (E.D.N.Y. 2009). Central to the court's ability to differentiate between scientific judgment and purely political motives was the FDA Commissioner's unusual deviation from the recommendation of the advisory committees that reviewed the OTC application. *Id.* at 529, 545–49. In determining the extent to which the Commissioner's actions were the product of politics rather than science, the court was able to contrast scientific risk-benefit analysis of the advisory committees with the Commissioner's justifications for the ultimate FDA decision. *Id.* By providing a scientific judgment of the risk-benefit profile of the drug, the advisory committees that reviewed the Plan B OTC application thus served the important roles of not only facilitating appropriate and effective judicial oversight, but also of promoting agency accountability more generally by making clear to the public that the FDA had afforded unusual treatment to the Plan B OTC application. See Metzger, *Abortion Regulation*, *supra* note 47, at 900–02 (doubting the power of judicial review to check politicization of women's reproductive health regulation generally, but noting the power of internal processes such as advisory committee review to foster FDA accountability). For an in-depth discussion of the FDA's unusual treatment of the Plan B OTC application, see U.S. GOV'T ACCOUNTABILITY OFF., GAO-06-109, FOOD AND DRUG ADMINISTRATION: DECISION PROCESS TO DENY INITIAL APPLICATION FOR OVER-THE-COUNTER MARKETING OF THE EMERGENCY CONTRACEPTIVE DRUG PLAN B WAS UNUSUAL (2005).

oversight of the FDA's final decision may be thwarted, absent extensive inquiry into the scientific merits of the Advisory Committee's risk-benefit analysis, which would extend far beyond the expertise and appropriate reach of the courts.¹⁰⁷ Furthermore, to the extent that the infiltration of value judgments into advisory committees' scientific analyses results in the approval of drugs that should not be on the market or the denial of drugs that should be available to patients, such infiltration has the potential to undermine public confidence in FDA decision-making, reducing the power of FDA actions and recommendations to improve the public health.¹⁰⁸

The process by which the FDA came to approve flibanserin, a drug for female sexual dysfunction, is a recent example of a pharmaceutical company's manipulation of the advisory committee process to exploit FDA vulnerabilities on women's health issues.¹⁰⁹ Given the recentness of the approval and the complexity of the issues surrounding the drug's risk-benefit profile, it is unclear whether the drug truly should or should not have been approved as a matter of public health.¹¹⁰ What is clear, however, is that the current FDA advisory committee procedures, especially those related to the Open Public Hearing (OPH) portion of advisory committee meetings, are inadequate to ensure transparency and accountability in the face of

107. Metzger, *Separation of Powers*, *supra* note 10, at 438–40 (discussing limitations on judicial review of agency decision-making); Metzger, *Abortion Regulation*, *supra* note 47, at 884–85, 898–902, 906 (discussing how characterizations of FDA regulations of abortion and contraception as health-based exacerbate hurdles to judicial review of FDA action); Shapiro, *supra* note 10, at 190.

108. Carpenter et al., *supra* note 98, at e3(2)–e3(3) (“The agency’s reputation for using science to guide regulatory decisions in the public interest is its most critical institutional asset.”); Taylor, *supra* note 102, at 807 (“[K]eeping social impacts and other ‘political’ considerations out of decision-making helps ensure *the timeliness and transparency* of the decisionmaking process.”) (emphasis in original).

109. Moynihan, *supra* note 8.

110. Sabrina Tavernise & Andrew Pollack, *Aid to Women or Bottom Line?: Advocates Split on Libido Pill*, N.Y. TIMES, June 13, 2015, at A1; Anne Skmorkowsky, *Five Studies: Does Flibanserin Provide Real Sexual Benefits for Women?*, PAC. STANDARD (Sept. 30, 2015), <http://www.psmag.com/health-and-behavior/is-flibanserin-the-real-deal-or-a-pharmaceutical-ploy>; Cari Romm, *Why Flibanserin Is not the ‘Female Viagra’*, ATLANTIC (Aug. 19, 2015), <http://www.theatlantic.com/health/archive/2015/08/why-flibanserin-is-not-the-female-viagra/401789/>; Honor Whiteman, *‘Female Viagra’ Approved by FDA*, MED. NEWS TODAY (Aug. 19, 2015), <http://www.medicalnewstoday.com/articles/298349.php>; Peggy Barksdale, Letter to the Editor, *Libido Drug for Women*, N.Y. TIMES, June 23, 2015, at A22.

highly politicized efforts to hijack advisory committees' risk-benefit analyses.

B. The Case of Flibanserin: The Public Journey to FDA Approval for a Woman's Libido Drug

On June 4, 2015, a joint meeting of the Bone, Reproductive, and Urologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee (together the "Advisory Committee") was convened to discuss the safety and efficacy of the drug flibanserin.¹¹¹ Flibanserin, now marketed under the trade name Addyi, is a non-hormonal medication aimed at increasing sexual desire in women who suffer from pre-menopausal Hypoactive Sexual Desire Disorder (HSDD).¹¹² Flibanserin had come before FDA advisory committees on two previous occasions, and was rejected both times for failure to show that the drug was effective amidst concerns of severe and under-tested risks.¹¹³ At the June 4, 2015 meeting, the Advisory Committee voted 18 to 6 to recommend approval of the drug, provided that the drug's manufacturer, Sprout Pharmaceuticals, comply with certain Risk Evaluation and Mitigation Strategies

111. U.S. FOOD & DRUG ADMIN., JOINT MEETING OF THE BONE, REPRODUCTIVE AND UROLOGIC DRUGS ADVISORY COMMITTEE (BRUDAC) AND THE DRUG SAFETY AND RISK MANAGEMENT (DSARM) ADVISORY COMMITTEE QUESTIONS (2015), <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM452154.pdf>.

112. Hanae Armitage, *How Does the New 'Female Viagra' Work?*, SCI. MAG. (Aug. 24, 2015), <http://news.sciencemag.org/health/2015/08/how-does-new-female-viagra-work>; Stephen M. Stahl et al., *Multifunctional Pharmacology of Flibanserin: Possible Mechanism of Therapeutic Action in Hypoactive Sexual Desire Disorder*, 8 J. OF SEXUAL MED. 15, 16 (2011). "HSDD is no longer a stand-alone diagnosis in the current edition of the DSM (DSM-5), which was published in May 2013. DSM-5 describes a new condition, female sexual interest/arousal disorder (FSIAD), which combines features of both HSDD and another condition from DSM-IV known as female sexual arousal disorder." U.S. FOOD & DRUG ADMIN., BRIEFING DOCUMENT: JOINT MEETING OF THE BONE, REPRODUCTIVE AND UROLOGIC DRUGS ADVISORY COMMITTEE (BRUDAC) AND THE DRUG SAFETY AND RISK MANAGEMENT (DSARM) ADVISORY COMMITTEE 2 (2015) [hereinafter ADVISORY COMMITTEE BRIEFING DOCUMENT].

113. Bob Roehr, *FDA Committee Recommends Approval for "Female Viagra,"* BMJ (June 5, 2015), <http://www.bmj.com/content/350/bmj.h3097>; Walid F. Gellad et al., *Evaluation of Flibanserin: Science and Advocacy at the FDA*, 314 J. OF THE AM. MED. ASS'N. 869, 869 (2015).

(REMS).¹¹⁴ On August 18, 2015, following the recommendation of the Advisory Committee, the FDA approved flibanserin to treat HSDD in premenopausal women.¹¹⁵ As a part of its approval, the FDA required that Sprout comply with specific REMS, including certification requirements for pharmacists and physicians who wish to dispense or prescribe the drug and required boxed warnings highlighting the risks associated with taking flibanserin.¹¹⁶ Flibanserin is now the first and only FDA approved drug to treat sexual desire disorders in pre-menopausal women.¹¹⁷

Flibanserin was originally developed by Boehringer Ingelheim in the early 2000s as an antidepressant.¹¹⁸ However, Boehringer Ingelheim shifted its focus towards female sexual dysfunction when the drug, which had failed to demonstrate efficacy as an antidepressant, “was more effective than placebo in terms of study participants’ responses to the question ‘How strong is your sex drive?’”¹¹⁹ Following a unanimous vote by the Advisory Committee in 2010 not to approve the drug, the FDA rejected Boehringer Ingelheim’s application to market flibanserin.¹²⁰ Boehringer Ingelheim then sold the drug to Sprout Pharmaceuticals in 2011.¹²¹ In 2013, the FDA rejected Sprout’s application to market the drug.¹²² Sprout’s subsequent appeal of the 2013 rejection was denied by the FDA on the grounds that the rejection was “sound and did not deviate from precedent.”¹²³ Sprout then resubmitted its application for

114. Gellad, *supra* note 113, at 869–70. The Advisory Committee recommended REMS, including potentially requiring that pharmacies and physicians be certified before they can dispense and prescribe flibanserin. *Id.*

115. Press Release, U.S. Food & Drug Admin., FDA Approves First Treatment for Sexual Desire Disorder (Aug. 18, 2015).

116. *Id.* Much of the FDA required REMS focus on the potential risk of negative interactions with alcohol. *Id.*

117. *Id.*; Sindhu Sundar, *FDA Adviser’s Back Sprout’s Drug to Boost Female Sex Drive*, LAW360 (June 4, 2015, 7:54 PM), www.law360.com/articles/663843/fda-advisers-back-sprout-s-drug-to-boost-female-sex-drive.

118. Moynihan, *supra* note 8.

119. Gellad, *supra* note 113, at 869.

120. Moynihan, *supra* note 8.

121. Antonie Meixel et al., *Hypoactive Sexual Desire Disorder: Inventing a Disease to Sell Low Libido*, 41 J. OF MED. ETHICS 859, 860 (2015).

122. *Id.*

123. Hylton V. Joffe, M.D., Director, Division of Bone and Urological Products, Ctr. For Drug Evaluation and Research, U.S. Food & Drug Admin., Flibanserin New Drug Application Opening Remarks (June 4, 2015), <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM452159.pdf> [hereinafter Joffe Presentation to the Advisory Committee].

approval, and flibanserin was scheduled for reconsideration by the Advisory Committee in June of 2015.¹²⁴

1. The Public Campaign for FDA Approval of Flibanserin

In addition to appealing the FDA's second rejection, Sprout moved quickly to launch a highly political campaign, attacking the FDA for the imbalance between approved treatments for male sexual dysfunction and those for female sexual dysfunction.¹²⁵ Central to this campaign was an advocacy group, Even the Score, that was created after Sprout approached long-time women's rights advocate, Susan Scanlan, in 2013 about gender inequities in available sexual health pharmaceuticals.¹²⁶ Even the Score boasts a broad range of support from well-known health, women's rights, and consumer advocacy groups, but also lists the backing of various pharmaceutical companies, including Sprout and for-profit sexual health groups.¹²⁷

With Even the Score at the helm, the extended public relations campaign utilized the language of the feminist movement to push broadly for "women's sexual equity" in the treatment of sexual dysfunction.¹²⁸ Central to Even the Score's rhetoric was the claim that there were twenty-six FDA approved drugs available to treat male sexual dysfunction, but none available to treat female sexual

124. Meixel, *supra* note 121, at 860.

125. Roehr, *supra* note 113; *see generally* Moynihan, *supra* note 8 (arguing that organizations backed by Sprout are, "bullying the FDA to approve flibanserin."); *FDA Vulnerability Revealed: A Politically Charged Advisory Committee Meeting May have Tipped the Scales in Favour of a Mildly Effective Female Libido Drug*, 524 NATURE 387 (2015) [hereinafter *FDA Vulnerability Revealed*] (noting that the FDA is facing a "trend of increased pressures from targeted campaigns" in the new drug approval process); Tavernise & Pollack, *supra* note 110 (discussing a split among feminist advocates in the extent to which such advocates support or oppose the Sprout-initiated campaign).

126. Moynihan, *supra* note 8; *FDA Vulnerability Revealed*, *supra* note 125.

127. *About Us*, EVEN THE SCORE, <http://eventhescore.org/about-us/> (last visited Feb. 11, 2017) [hereinafter *About Us*, EVEN THE SCORE].

128. *FDA Vulnerability Revealed*, *supra* note 125 (stating that critics "blame[d] . . . Even The Score . . . for leading a campaign that made approval an issue of gender equality"); Roehr, *supra* note 113 (describing Sprout's rhetoric as "feminist"); Joe Van Acker, *FDA Must Handle Politics Over Female Libido Drug, Docs Say*, LAW360 (July 7, 2015, 5:59 PM), www.law360.com/articles/676480/fda-must-handle-politics-over-female-libido-drug-docs-say; *see also* *About Us*, EVEN THE SCORE, *supra* note 127 (describing Even the Score as "[a] campaign for women's sexual health equity [that] was created to serve as a voice for American women who believe that it's time to level the playing field when it comes to the treatment of women's sexual dysfunction").

dysfunction.¹²⁹ This claim is, at best, misleading. While it is true that flibanserin is the first FDA approved drug to treat low sexual desire in women, nearly all of the drugs for male sexual dysfunction treat difficulty achieving or maintaining an erection, a medical problem that is not only inapplicable to women, but is also noticeably biologically different from chronic low-libido.¹³⁰ Furthermore, the FDA has approved medications to treat pain with intercourse in women.¹³¹ Equally important to the campaign's rhetoric was legitimizing HSDD and demonstrating both its severity and prevalence.¹³² Even the Score also mobilized numerous prominent individuals and institutions to write to the FDA, heavily stressing the need to remedy the lack of available treatments for HSDD as a matter of gender fairness and feminism. While some writers overtly urged the FDA to approve flibanserin, others simply wrote to stress the reality and prevalence of HSDD.¹³³

The FDA was acutely aware of the perception of gender bias that was generated by Sprout's public relations campaign. In its briefing document for the June 4, 2015 Advisory Committee meeting, the FDA cautioned:

Panel members may be aware of the extensive publicity surrounding flibanserin and treatments for female sexual dysfunction. Some have alleged that there is gender bias at the FDA, stating that there are many medications approved for treating male sexual dysfunction but none for treating female sexual

129. *FDA Vulnerability Revealed*, *supra* note 125; Moynihan, *supra* note 8; *see also Get the Facts*, EVEN THE SCORE, <http://eventhescore.org/get-the-facts/> (last visited Oct. 22, 2016) [hereinafter *Get the Facts*, EVEN THE SCORE] (now displaying the statistic that the ratio of drugs available to treat sexual dysfunction for men to that for women is 26:1).

130. Joffe Presentation to the Advisory Committee, *supra* note 123, at 26.

131. *Id.*

132. *See Get the Facts*, EVEN THE SCORE, *supra* note 129 (noting that 1 in 10 women suffer from HSDD, and that more women than men suffer from sexual dysfunction); Moynihan, *supra* note 8 (portraying Even the Score's campaign to educate the public about HSDD as propagating a pathologized and hysterical view of variations in female sexual desire that may be explained by a number of different factors); Adrian Fugh-Berman et al., *Hypoactive Sexual Desire Disorder: Inventing a Disease to Sell Low Libido*, 41 J. OF MED. ETHICS 859 (2015) (accusing Sprout of creating a campaign to market an invented epidemic in lieu of FDA approval to market a treatment for said epidemic).

133. *Get the Facts*, EVEN THE SCORE, *supra* note 129 (displaying a selection of letters written by various advocates and organizations).

dysfunction, and that the FDA is holding drugs intended to treat female sexual dysfunction to more stringent standards of approval. These claims are misleading and inaccurate. The FDA rejects claims of gender bias. The FDA's regulatory decision for each product is based on an assessment of whether the benefits outweigh the risks, and does not take gender into consideration. The flibanserin NDA raises challenging scientific issues. The FDA welcomes science-based recommendations from the Advisory Committee panel as to whether the available data support a positive benefit/risk assessment for flibanserin.¹³⁴

The FDA's opening presentation at the June 4, 2015 Advisory Committee meeting further reflected these concerns, reiterating that the FDA rejected accusations of gender bias, and that the FDA's concern for unmet medical needs was not gender-contingent.¹³⁵

2. Sprout's Use of the Open Public Hearing to Infiltrate the Advisory Committee Process

Sprout's campaign, through Even the Score, extended beyond a mere public relations and education initiative and into the FDA approval process itself.¹³⁶ Specifically, Sprout adeptly utilized the OPH portion of the June 4, 2015 Advisory Committee meeting to bring the pressure of Even the Score and its allies to bear on the FDA.¹³⁷

At the OPH, thirty-three individuals testified in support of FDA approval of flibanserin.¹³⁸ Speakers included not only healthcare

134. ADVISORY COMMITTEE BRIEFING DOCUMENT, *supra* note 112, at 6.

135. Joffe Presentation to the Advisory Committee, *supra* note 123, at 28.

136. Roehr, *supra* note 113.

137. *Id.*

138. See CTR. FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD & DRUG ADMIN., SUMMARY OF MINUTES OF THE JOINT MEETING OF BONE, REPRODUCTIVE AND UROLOGIC DRUGS ADVISORY COMMITTEE AND THE DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE MEETING 3-4 (2015) [hereinafter SUMMARY OF MINUTES]; CTR. FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD & DRUG ADMIN., TRANSCRIPT OF THE JUNE 4, 2015 JOINT MEETING OF THE BONE, REPRODUCTIVE AND UROLOGIC DRUGS ADVISORY COMMITTEE (BRUDAC) AND THE DRUG SAFETY AND RISK MANAGEMENT (DSARM) ADVISORY COMMITTEE 231-340, <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials>

professionals and researchers, but also individuals who had been diagnosed with HSDD and advocates for women's rights generally.¹³⁹ Table 1 presents the individuals who spoke in favor of approval of flibanserin at the OPH. For the purpose of comparison, Table 2 presents the speakers at the OPH for ximelgatran, a controversial oral anticoagulant that had the potential to be the "first oral alternative to warfarin."¹⁴⁰ An initial comparison of the tables demonstrates the unusual extent to which laypeople, non-medical professionals, and medical professionals without experience with flibanserin dominated the flibanserin OPH.¹⁴¹

Table 1: Open Public Hearing Speakers at the June 4, 2015 Joint Meeting of the Bone, Reproductive and Urologic Drugs Advisory Committee (BRUDAC) and the Drug Safety and Risk Management (DSaRM) Advisory Committee Meeting.¹⁴²

Speakers in Favor of Approval

| Speaker | Interest/Stake | Summary of Opinion |
|--|---|--|
| Lisa Larkin, MD, FACP, NCMP UC Women's Health Center | None Noted | Flibanserin should be approved given that the risks of harm are outweighed by the need for a treatment for HSDD. |
| Irwin Goldstein, MD, IF San Diego Sexual Medicine Sue W. Goldstein, CCRC, IF Sexual Educator San Diego Sexual Medicine | Member of Sprout's Advisory Board Diagnosed with HSDD | Many women suffer from HSDD. They do not have the same treatment options as men with sexual dysfunction. HSDD can be very harmful to women, especially in the context of their relationships. |

/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM459503.pdf
[hereinafter MEETING TRANSCRIPT].

139. SUMMARY OF MINUTES, *supra* note 138, at 3–4; MEETING TRANSCRIPT, *supra* note 138, at 231–340. See Table 1, *infra*, for a full list of speakers.

140. Pol F. Boudes, *The Challenges of New Drugs Benefits and Risks Analysis: Lessons from the Ximelgatran FDA Cardiovascular Advisory Committee*, 27 CONTEMP. CLINICAL TRIALS 432, 432 (2006).

141. See *infra* Table 1, Table 2.

142. MEETING TRANSCRIPT, *supra* note 138, at 231–340.

| | | |
|--|--|--|
| Sally Greenberg Executive Director National Consumers League | None Noted | Flibanserin should be approved because women who suffer from HSDD, lacking better alternatives, will turn to harmful, snake-oil solutions. |
| Lori Weinstein CEO/Executive Director Jewish Women International | None Noted | There is a need for a drug to treat women's sexual dysfunction. Doctors and patients are capable of assessing and managing the risks of flibanserin. |
| Susan Scanlan Chair Even the Score | Receives a Consulting Fee From Sprout | The FDA should respect a woman's right to make her own medical decisions, especially with regard to matters of sexual intimacy. |
| Michael L. Krychman, MD, MPH Executive Director Southern California Center for Sexual Health and Survivorship Medicine, Inc. | None Noted | Played video. Contents not in transcript. |
| Wayne C. Shields President and CEO Association of Reproductive Health Professionals | None Noted | Health professionals belonging to Mr. Shields's organization support the approval of flibanserin, and, as a feminist, Mr. Shields personally supports its approval. |
| Anita H. Clayton, MD Professor and Interim Chair University of Virginia Department of Psychiatry and Neurobehavioral Sciences | Sprout Consultant, Researched Flibanserin | Flibanserin is adequately safe and effective. As a result of gender bias, the FDA has been moving the "goal posts" for approval. Given this, a vote against approval by the Advisory Committee would signal that it did not believe that HSDD was a legitimate health issue. |

| | | |
|--|--|--|
| Beth Battaglini, RN CEO and President HealthyWomen | None Noted | HSDD is distressing and disruptive to many women's romantic relationships and women should have access to an FDA approved medical treatment. |
| Amanda Parrish Participant and Her Husband | Flibanserin Clinical Trial | Flibanserin saved the Parrishs' marriage. Without flibanserin, Ms. Parrish would be tempted to turn to snake-oil solutions, and insinuations that she would not be capable of making appropriate decisions regarding her use of flibanserin with her doctor are offensive. |
| Katherine Campbell | Travel Expenses Paid by Sprout; HSDD Patient | HSDD is a serious, harmful disorder that "smart, modern" women should be able to choose to treat with FDA approved options. |
| Lynn Barclay President & CEO Health Policy, American Sexual Health Association | None Noted | Sexual health is part of overall health. Therefore, women need options to treat sexual dysfunction. |
| Judith Reid-Haff | Travel Expenses Paid by Sprout; HSDD Patient | Following treatment for breast cancer, Ms. Reid-Haff's struggle with low libido has hurt her deeply. Women should have access to treatment for HSDD. |
| Barbara Gattuso | HSDD Patient treated by Dr. Irwin Goldstein; Flibanserin Trial Participant | HSDD was very harmful to Ms. Gattuso's marriage, but flibanserin helped greatly. |
| Vicki Lofthus | HSDD Patient treated by Dr. Irwin Goldstein | HSDD has been very harmful to Ms. Lofthus's marriage. Ms. Lofthus tried testosterone treatment and suffered negative side-effects. Women should have access to an approved medicine. |

| | | |
|--|--|---|
| Greg Gattuso | Barbara Gattuso's Husband; Travel Expenses Paid by Sprout | Ms. Gattuso's HSDD has been very harmful to the Gattusos' marriage. Mr. Gattuso has many available, effective options to treat his sexual dysfunction, but Ms. Gattuso has none. |
| Gay Johnson CEO National Association of Nurse Practitioners in Women's Health | None Noted | The healthcare community is beginning to give women's sexual health the attention it deserves, and it has become clear that HSDD is a large, unmet medical need. |
| Kelli Stoup | HSDD Patient | HSDD is a real problem that has damaged Ms. Stoup's marriage. Ms. Stoup has tried other treatments, none of which were effective. Women deserve an FDA approved option. |
| Lauren F. Streicher, MD Clinical Associate Professor of Obstetrics and Gynecology Northwestern University Feinberg School of Medicine | None Noted | Female sexual dysfunction is a real medical condition that doctors are capable of accurately diagnosing. Flibanserin is an appropriate treatment for women who suffer from HSDD. |
| Derek Haff | Judith Reid-Haff's Husband; Travel Expenses Paid by Sprout | Because of their role in the family, women have great social influence. Therefore, women's sexual health needs, which are a part of their broader wellbeing, should be taken seriously. |
| Alyse Kelly-Jones, MD Mintview Women's Care | None Noted | HSDD is real and detrimental to women. Whether women receive treatment for HSDD is in the hands of the FDA. |

| | | |
|---|--|--|
| Maureen Whelihan, MD Center for Sexual Health and Education | None Noted | Women are capable of addressing the risks of medication with their doctors. The medical community accepts much greater risks than those discussed at the Advisory Committee meeting. |
| Ashley H. Tapscott, DO Carolina Urology Partners | None Noted | Flibanserin should be approved because it is safe and effective, and because men have many treatment options for sexual dysfunction and women have none. Ms. Tapscott states that it is “time to end the silence, to change history to herstory.” |
| Erica Palim | HSDD Patient (post-surgical menopause) | HSDD is real, and it is hypocritical of society to encourage depictions of casual, sometimes harmful, sex but not take medical treatment for women’s sexual dysfunction seriously. |
| Julianne Adams Birt, MD, FACOG President Radiant Women’s Health Chief Department of Women’s Services, Rockdale Medical Center | None Noted | HSDD is a real medical condition, and it is unfair to women that it is largely ignored by the medical community. |
| Jan Erickson Director of Government Relations National Organization for Women | None Noted | Sexual health is a fundamental human right, and the difference in available treatments for male and female sexual dysfunction is a matter of gender equality. Because Flibanserin is safe and effective, it should be approved. If it is not, resources will not be invested in remedying female sexual dysfunction. |

| | | |
|--|---|--|
| <p>James A. Simon, MD, CCD, NCMP, IF, FACOG Clinical Professor George Washington University President & Medical Director Women's Health & Research Consultants®</p> | <p>Conducted Clinical Trials on Flibanserin</p> | <p>Flibanserin is safe and effective. Should flibanserin not be approved, women who suffer from HSDD will turn to harmful, snake-oil treatments. Mr. Simon asks the panel, "will you be on the right side of history or not?"</p> |
| <p>Beverly J. Wiesen Apex Executive Search, LLC</p> | <p>HSDD Patient (post- menopause); Travel Expenses Paid by Sprout</p> | <p>The FDA approves drugs with much worse side effects than those discussed at the Advisory Committee Meeting. FDA approval would permit women to get necessary healthcare. Ms. Wiesen asks the men on the panel what they would do if their wives suffered from HSDD.</p> |
| <p>Marta Hill Gray Red Hot Mammias</p> | <p>None Noted</p> | <p>It is unfair that there are more treatment options for male sexual dysfunction than for female sexual dysfunction. Women are capable of making medical decisions with their doctors.</p> |
| <p>Sharon J. Parish, MD, IF, NCMP Professor of Medicine in Clinical Psychiatry & Professor of Clinical Medicine Weill Cornell Medical College President International Society for the Study of Women's Sexual Health</p> | <p>None Noted</p> | <p>Physicians are competent to diagnose HSDD, but currently do not have any effective treatment options to offer their patients.</p> |

| | | |
|---|------------|--|
| Vikki Pedigo, MSN, WHNP-BD Nurse Practitioner Women's Institute for Sexual Health Brooke Faught, MSN, WHNP-BC, IF Nurse Practitioner/Clinical Director Women's Institute for Sexual Health | None Noted | The benefits of flibanserin outweigh the risks, especially given the risks accepted in other medications and the fact the HSDD is an unmet medical need. |
|---|------------|--|

Furthermore, while a few speakers at the flibanserin OPH addressed concerns regarding the safety and efficacy of the drug, much of the testimony supporting flibanserin's approval addressed either the reality and severity of HSDD or the inequity of the lack of available treatments for female sexual dysfunction, often without mentioning flibanserin at all.¹⁴³ Women and couples testified to the damage that HSDD had done to their romantic lives, focusing on the importance of a healthy sexual life in the context of marriage,¹⁴⁴ and healthcare providers testified to the number of patients they had seen suffer from HSDD and the frustrations of not being able to provide those patients with effective treatments.¹⁴⁵ These speakers often spoke in the language of the women's reproductive rights movement, stressing a woman's right to sexual autonomy and implying that a rejection of flibanserin would be an intolerable imposition of patronizing sexual norms in a treatment decision that should be made privately between a patient and her doctor.¹⁴⁶

143. See *supra* Table 1; MEETING TRANSCRIPT, *supra* note 138, at 231–340.

144. For a selection of testimony from the flibanserin OPH regarding the effects of HSDD on women and their marriages, see MEETING TRANSCRIPT, *supra* note 138, at 256–60, 265–71, 275–78, 295–97, 328–29.

145. For a selection of OPH testimony by healthcare providers from the flibanserin OPH, discussing lack of available treatments for their patients who suffer from HSDD, see *id.* at 297–99, 303–05, 308–11, 333–36.

146. See, e.g., *id.* at 243 (“[T]he apparent insistence that female sexual dysfunction has neither a place nor a remedy on the same shelf as male dysfunction reminds us that there is yet another arena where women are voiceless.”); *id.* at 247 (“Progress in this case comes down to respecting a woman's right to make her own decision as to the best path for achieving her best sexual

Notably, while a few of the HSDD patients who testified had participated in flibanserin clinical trials, the vast majority had no experience with the drug and were testifying only to the legitimacy of HSDD as a diagnosis and the severity of their symptoms.¹⁴⁷ At least two of the women who testified suffered from post-menopausal sexual desire disorders, a condition that flibanserin neither treats nor claims to treat.¹⁴⁸ Furthermore, of the few healthcare professionals who addressed the FDA's safety concerns regarding flibanserin, many focused not on the safety of the flibanserin itself, but on the risk of women with HSDD, lacking FDA approved treatment options, turning to snake-oil or other harmful remedies.¹⁴⁹

In sum, testimony in favor of flibanserin's approval concentrated on the legitimacy of HSDD as a diagnosis, a women's right to sexual enjoyment within the context of marriage, and the imbalance of available treatments for sexual dysfunction between women and men.¹⁵⁰ To a lesser, albeit noticeable extent, testimony stressed the ability of women and their doctors to make appropriate treatment decisions together. Little of the testimony addressed flibanserin directly, and even less dealt with the clinically tested risks and benefits of the drug.¹⁵¹

self. . . . Let's call it the pursuit of happiness; a pretty longstanding right in the United States of America."); *id.* at 251–52 ("I'm also a feminist. . . . I support concepts like choice; and I support individual rights; and I support the strength of individuals being able to make decisions. . . ."); *id.* at 261 ("These are smart, modern women who are a hundred percent capable of knowing their own bodies and making good decisions."); *id.* at 308 ("[I]t is time to leave behind the outdated, insulting perception of women as immature and incapable of responsibly managing their own sexual health, and acknowledge that a healthy sex life is an important part of any person's overall wellbeing, men and women alike."); *id.* at 318 ("The World Health Organization has adopted a working definition about a fundamental human right to sexual health that recognizes the need for gender equality, and the need for recognition of the value of sexual pleasure. . . .").

147. *See supra* Table 1.

148. *Id.*

149. For testimony by healthcare providers regarding the risk of women using harmful treatment options in the absence of better treatments for HSDD, see MEETING TRANSCRIPT, *supra* note 138, at 240–41, 303–04, 324–37, 339–40.

150. *See supra* Table 1; MEETING TRANSCRIPT, *supra* note 138, at 231–340.

151. *See supra* Table 1; MEETING TRANSCRIPT, *supra* note 138, at 231–340.

Table 2: Open Public Hearing Speakers at the 2004 FDA Cardiovascular and Renal Drug Advisory Committee (CRAC) meeting to review ximelagatran.¹⁵²

| Public Hearing speaker | Opinion |
|---|---|
| Messmore H, MD, FACP; Dr. Wahí, Thrombosis Hemostasis Unit of Loyola University, Stritch School of Medicine | Concerned about lack of comparison with LMWH in high risk orthopedic patients Concerned about liver toxicity in AF patients and for secondary prophylaxis of VTE |
| Baranski J, CEO and Executive Director, National Stroke Association Ansell J, Hematologist and Professor of Medicine, Boston University Medical center, Founder and Chair of the Anticoagulation forum | Emphasize hurdles of warfarin use Emphasize hurdles of warfarin narrow therapeutic range, also a common cause of malpractice litigation Recommend access to ximelagatran |
| Lurie P, MD, Public Citizen Health Research group | No convincing evidence of effectiveness for TKR and AF populations For long-term secondary prevention, the liver toxicity RMP is inadequate Request for strict liver monitoring in ximelagatran label |
| Lodwick A, Pharmacist, certified anticoagulation care provider, owner of warfarinfo.com Colgan K, Pharmacist, Vice President for Outcome Research at EPI-Q, Inc, member of the board of director of the American society of Health-System Pharmacists; Tapson V, Professor of Medicine, Duke University School of Medicine for the National Anticoagulation Benchmark and Outcomes Report (NABOR) Steering Committee | Concerned by both non-treatment and sub-optimal treatment of patients at risk of stroke and VTE in the US Recommend access to ximelagatran |

The OPH testimony in favor of flibanserin, therefore, can be viewed as targeting the major points of FDA vulnerability on women's health issues: the speakers implied both that the FDA had patronizingly over-assessed risks that women were capable of evaluating with their doctors, and also undervalued the problem of female sexual dysfunction.¹⁵³ The OPH speakers also heavily implied that unequal access to sexual dysfunction treatments between men and women was an articulation of social norms that valued male sexual enjoyment much more than female sexual enjoyment, and, conversely, that modern society required parity between available treatments for male and female sexual dysfunction.¹⁵⁴

152. Boudes, *supra* note 140, at 434.

153. See MEETING TRANSCRIPT, *supra* note 138, at 245, 252, 259, 261–62, 271, 274, 301–02, 307–08, 328–29, 333 (providing selected OPH testimony in which speakers discuss the ability of women to assess the risks associated with flibanserin within the context of a doctor-patient relationship); *id.* at 253–54, 260–62, 264, 274, 281–83, 300, 305, 310–11, 320 (providing selected OPH testimony in which speakers discuss underestimation of the seriousness of HSDD as a morbidity).

154. See *id.* at 243, 253, 271–73, 303–04, 310, 318, 331 (providing selected OPH testimony in which speakers discuss the discrepancy in available treatments for sexual dysfunction between men and women, often citing social norms regarding women's sexuality as the cause of this disparity). It is notable that, for all of Sprout's feminist rhetoric, Sprout was careful to make clear to the Advisory Committee that the average HSDD patient who would be treated with flibanserin

In contrast, as presented in Table 3, only eight individuals spoke at the OPH against the approval of flibanserin.¹⁵⁵ Two of the speakers were women's health advocates, and the remaining six were either medical doctors or researchers in related healthcare/pharmaceutical fields.¹⁵⁶ However, even the roster of doctors and researchers speaking against the approval of flibanserin was not without noteworthy, though less direct, conflicts of interest. Dr. Adrian Fugh-Berman, for instance, is the director of PharmedOut, an organization dedicated to reducing the influence of pharmaceutical marketing in prescribing practices, and is a paid expert witness in "litigation regarding pharmaceutical marketing practices."¹⁵⁷ Another speaker who testified to caution against approval, Dr. Sidney Wolfe, is the cofounder of a prominent consumer advocacy group that has led the charge against numerous FDA drug approvals.¹⁵⁸

is a woman in a stable, heterosexual, monogamous relationship, cautiously complying with social norms that reject female sexual enjoyment in an extramarital context. Sheryl Kingsberg, Chief of Div. of Behavioral Med., MacDonald Women's Hosp., Overview and Impact of HSDD at the Joint Meeting of the Bone, Reproductive and Urologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee, slide 16 (June 4, 2015), <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM452160.pdf>; see also MEETING TRANSCRIPT, *supra* note 138, at 238–39, 259, 267, 271, 277 (discussing how HSDD is detrimental to sexual health in the context of marriage and other long-term, stable relationships).

155. MEETING TRANSCRIPT, *supra* note 138, at 231–340. See *infra* Table 3 (listing speakers who testified against approval of flibanserin at the June 4, 2015 OPH).

156. MEETING TRANSCRIPT, *supra* note 138, at 231–340; SUMMARY OF MINUTES, *supra* note 139, at 3–4; see also *infra* Table 3.

157. MEETING TRANSCRIPT, *supra* note 138, at 284; see *About Us*, PHARMEDOUT, <http://www.pharmedout.org/aboutus.html> (last visited Feb. 11, 2017).

158. MEETING TRANSCRIPT, *supra* note 138, at 288; Gardiner Harris, *Drug Industry's Longtime Critic Says 'I Told You So'*, N.Y. TIMES (Feb. 15, 2005), <http://www.nytimes.com/2005/02/15/health/policy/drug-industrys-longtime-critic-says-i-told-you-so.html>; See *Health Research Group Publications*, PUBLIC CITIZEN, <http://www.citizen.org/Page.aspx?pid=1260> (last visited Feb. 11, 2017).

Table 3: Open Public Hearing Speakers at the June 4, 2015 Joint Meeting of the Bone, Reproductive and Urologic Drugs Advisory Committee (BRUDAC) and the Drug Safety and Risk Management (DSaRM) Advisory Committee Meeting

Speakers Against Approval

| Speaker | Interest/Stake | Summary of Opinion |
|---|---|---|
| Cindy Pearson Executive Director National Women's Health Network | None Noted | HSDD is a real problem, and women are capable of making intelligent decisions. However, we do not know enough about the potential harms of flibanserin to be able to say that it is an appropriate treatment. |
| Alessandra Hirsch, MD Project Manager PharmedOut, Georgetown University Medical Center Adriane Fugh-Berman, MD Director PharmedOut, Georgetown University Medical Center | None Noted | Flibanserin is unsafe and ineffective. Drugs for women should be held to the same safety and efficacy standards as those for men. |
| Sidney M. Wolfe, MD Founder, Senior Advisor Health Research Group of Public Citizens | None Noted (has spoken at OPH's during past review cycles, advocating against approval) | Clinical trials of flibanserin indicate that the risks of the drug outweigh its benefits. |
| Christina Silcox, PhD Senior Fellow National Center for Health Research | None Noted | Clinical trials of flibanserin indicate that the risks of the drug outweigh its benefits, especially given the high level of unknowns regarding its risks. |
| Karen M. Hicks | None Noted (started advocacy group to demand justice for | Clinical trials addressing the risks of flibanserin, like those for the Dalkon Shield, were poorly designed. Clinical trials failed to |

| | | |
|--|--|---|
| | Dalkon Shield victims) | address key comorbidities and also failed to address why participants left the trials early. Ms. Hicks also noted that she has had a hysterectomy, so she understands the pain suffered by those with HSDD. |
| Leonore Tiefer, PhD The New Campaign | None Noted | Sprout has utilized Even the Score to initiate a misinformation campaign that relies on “deception to mobilize women with real sexual concerns to lobby for their questionable product.” |
| Liz Canner Director Astrea Media, Inc. | Created a documentary called <i>Orgasm, Inc.</i> after working with pharmaceutical companies to try to develop a ‘female Viagra’ | Ms. Canner is sympathetic to the pain felt by HSDD patients, but flibanserin poses serious safety concerns. Even the Score’s campaign is an unprecedented hijacking of the feminist movement. |

Testimony against the approval of flibanserin largely focused on the high risks and low efficacy of the drug, stressing that key risks, such as the interaction of flibanserin and alcohol, had not been adequately tested.¹⁵⁹ Two speakers were more overtly critical of Sprout and Even the Score, accusing them of an unprecedented misinformation campaign that hijacked the feminist movement to pressure the FDA to approve a risky drug for a diagnosis of dubious legitimacy.¹⁶⁰ However, a majority of those speaking against the

159. MEETING TRANSCRIPT, *supra* note 138, at 278–80, 283–95, 311–17, 321–24.

160. *Id.* at 317 (“Sprout has used deception to mobilize women with real sexual concerns to lobby for their questionable product. They’ve tried to distract the public, bully the FDA, and they have hampered real sex research.”); *id.* at 322 (“I’ve never seen anything like the Even the Score campaign, funded in part by Sprout Pharmaceuticals. It’s an attempt to hijack feminist language of equity and convince women that the lack of drugs for them is an issue of sexism, when it’s not It is a devious way to use non-profits as a cover for a marketing and lobbying campaign.”).

approval of flibanserin were conspicuously careful to clarify that they did not doubt the legitimacy of HSDD as a diagnosis, the pain of those suffering from HSDD, nor the ability of women to make their own medical choices.¹⁶¹

3. The Advisory Committee's Risk-Benefit Analysis: What Changed?

In flibanserin's first cycle of review in 2010, the Advisory Committee voted against approval of the drug due to the insufficiency of evidence of the drug's efficacy and concerns about its safety.¹⁶² Among the concerns expressed in its response letter, the 2010 Advisory Committee noted that clinical trials of flibanserin had been overly restrictive in their entry criteria and therefore were not adequately generalizable to the population of patients who would take flibanserin.¹⁶³ The Advisory Committee further noted the need for clinical studies addressing the interaction of flibanserin with other medications and substances, especially alcohol.¹⁶⁴ The Advisory Committee's response letter did not state that flibanserin was definitively impermissibly risky or ineffective, but instead recommended that the drug's manufacturer conduct additional, less restrictive studies to better assess the drug's efficacy and safety risks in the population of patients who would be likely to take the drug if approved.¹⁶⁵

In flibanserin's second cycle of review in 2013, the Advisory Committee again voted against recommending approval.¹⁶⁶ In its 2013 response letter, the Advisory Committee continued to express concerns regarding the efficacy of the drug: specifically, a treatment benefit that the Advisory Committee viewed as only very marginal,

161. *Id.* at 278 (“[W]e also recognize that lack of sexual desire can be a distressing problem for women”); *id.* at 312 (“I feel the pain of the women in this room who I can identify with from a great deal of lived angst like they also have had.”); *id.* at 321 (“I want to start by saying that I have real sympathy for the women who presented today who clearly have a lot of pain from their sexual desire issues.”).

162. Joffe Presentation to the Advisory Committee, *supra* note 123, at 6–7 (recapping that 10 of 11 committee members voted that evidence of efficacy was insufficient); Fugh-Berman, *supra* note 132, at 860; Joffe, *supra* note 9, at 101–02.

163. Joffe Presentation to the Advisory Committee, *supra* note 123, at 7; ADVISORY COMMITTEE BRIEFING DOCUMENT, *supra* note 112, at 3.

164. Joffe Presentation to the Advisory Committee, *supra* note 123, at 7.; ADVISORY COMMITTEE BRIEFING DOCUMENT, *supra* note 112, at 3.

165. ADVISORY COMMITTEE BRIEFING DOCUMENT, *supra* note 112, at 3.

166. Joffe, *supra* note 9, at 102.

and concerns regarding the dependability of the self-reporting mechanism for measuring treatment outcomes.¹⁶⁷ The Advisory Committee also repeated its concerns regarding the safety of the drug, especially the potential negative interactions with alcohol and with certain drugs.¹⁶⁸

On June 4, 2015, the Advisory Committee again met to review flibanserin.¹⁶⁹ The stated objective of the meeting was to “obtain independent expert advice from a multidisciplinary advisory committee on whether the benefits of flibanserin outweigh its risks.”¹⁷⁰ Immediately following the OPH, the Advisory Committee discussed questions aimed at determining whether the benefits of flibanserin outweighed its risks.¹⁷¹ In clinical trials, flibanserin treatment had the placebo-corrected effect of a median increase of 0.5–1.0 satisfying sexual events per month from a baseline of 2–3 satisfying sexual events.¹⁷² While this was a statistically significant

167. ADVISORY COMMITTEE BRIEFING DOCUMENT, *supra* note 112, at 3–4; Joffe Presentation to the Advisory Committee, *supra* note 123, at 9–10.

168. ADVISORY COMMITTEE BRIEFING DOCUMENT, *supra* note 112, at 4; Joffe Presentation to the Advisory Committee, *supra* note 123, at 9–10, 14 (citing concerns regarding risks of hypotension, syncope, and central nervous system depression, and concerns that such risks would be exacerbated if flibanserin was taken with alcohol or CYP3A4 inhibitors).

169. SUMMARY OF MINUTES, *supra* note 138, at 1.

170. MEETING TRANSCRIPT, *supra* note 138, at 28.

171. Three discussion points were posed to the Advisory Committee: (1) “Comment on the clinical significance of the observed placebo corrected treatment effects of flibanserin in satisfying sexual events, sexual desire, and related distress”; (2) “Take into account the generalizability of the clinical studies to the population of premenopausal women who would likely use flibanserin, if approved. Then, discuss your level of concern with the risks of hypotension and syncope when flibanserin is used alone and when flibanserin is used with alcohol”; (3) “Take into account the generalizability of the clinical studies to the population of premenopausal women who would likely use flibanserin, if approved. Then, discuss your level of concern with any other safety findings.” SUMMARY OF MINUTES, *supra* note 138, at 6–8 (sub-questions omitted).

172. *FDA Vulnerability Revealed*, *supra* note 125, at 387; Joffe Presentation to the Advisory Committee, *supra* note 123, at 13. Satisfying sexual events were measured based on patients’ responses to the yes or no questions in a daily eDiary: (1) “Did you have a sexual event?” and (2) “Was the sex satisfying for you?” Ashley F. Slagle, Office of New Drugs, Food and Drug Admin., NDA 022526 Flibanserin Outcome Assessments, Presentation at the June 4, 2015 Joint Meeting of the Bone, Reprod. and Urologic Drugs Advisory Comm. (BRUDAC) and the Drug Safety and Risk Mgmt. (DSaRM) Advisory Comm. Meeting (June 4, 2015), at slide 3–4. Clinical trials also showed an increase on the FSFI Desire Scale (scale 1.2–6.0) of 0.3,–0.4 and a decrease in distress (scale 0–4) of 0.3–0.4 in

increase in satisfying sexual events,¹⁷³ major safety concerns remained, such as incidents of hypotension, syncope, and central nervous system depression, all of which may be exacerbated by negative interactions with alcohol or moderate and strong CYP3A4 inhibitors.¹⁷⁴

It is important to note that despite the Advisory Committee's explicit statement that low efficacy remained a concern at the end of the second review cycle,¹⁷⁵ Sprout submitted no new efficacy data in flibanserin's third review cycle.¹⁷⁶ Regarding the efficacy of flibanserin, Sprout instead sought to clarify the meaningfulness and reliability of clinical trial outcomes and the severity of HSDD as a diagnosis.¹⁷⁷ As with past review cycles, the Committee wrestled with the statistical and clinical meaning of reported outcomes, expressing concern over the lack of a benchmark for what would be a meaningful improvement for HSDD patients and the lack of standardization in self-reporting of outcomes.¹⁷⁸ Some Committee members expressed discomfort and frustration about the Committee's admittedly unusual analysis of the clinical meaningfulness of the trial outcomes (as opposed to simply assessing the appropriateness of endpoints and statistical significance of data).¹⁷⁹ One member even challenged, "[H]as anyone ever asked these women who suffer from this how much they would think would be a meaningful improvement? . . . I hear you that from your clinical perspective, you say it is meaningful,

patients treated with flibanserin. Joffe Presentation to the Advisory Committee, *supra* note 123, at 13.

173. Joffe Presentation to the Advisory Committee, *supra* note 123, at 13.

174. *Id.* at slide 14; Olivia Easley, Div. of Bone, Reprod. and Urologic Drugs, Food and Drug Admin., NDA 022526 Flibanserin: Safety, Presentation for the June 4, 2015 Joint Meeting of the Bone, Reprod. and Urologic Drugs Advisory Comm. (BRUDAC) and the Drug Safety and Risk Mgmt. (DSaRM) Advisory Comm. Meeting (June 4, 2015), at slide 3.

175. ADVISORY COMMITTEE BRIEFING DOCUMENT, *supra* note 112, at 4.

176. *Id.*; Gellad, *supra* note 113, at 869. For a review of clinical trials of flibanserin, see CLINICALTRIALS.GOV, <https://clinicaltrials.gov/ct2/results?term=flibanserin&Search=Search> (last visited Feb. 12, 2017).

177. Josephine Torrente, Exec. Vice President of Corp. and Regulatory Affairs, Sprout Pharm., Inc., Presentation at the June 4, 2015 Joint Meeting of the Bone, Reprod. and Urologic Drugs Advisory Comm. and the Drug Safety and Risk Mgmt. Advisory Comm. (June 4, 2015), at slides 14–21, 23–29, 44–63 (slideshow of presentation of file at <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM452160.pdf>).

178. MEETING TRANSCRIPT, *supra* note 138, at 347–53.

179. *Id.* at 351.

but what do the women have to say?”¹⁸⁰ Ultimately, the Advisory Committee concluded that the clinical trials demonstrated a clinically meaningful, albeit numerically small, improvement in HSDD symptoms for patients treated with flibanserin, and that, while after placebo correction around 10% of patients saw improvements attributable to flibanserin, improvements were valuable for those patients.¹⁸¹

With regard to the safety of flibanserin, the Advisory Committee echoed the concerns expressed in flibanserin’s first and second review cycles. The Advisory Committee discussed risks of hypotension and syncope, incidents of which may have gone unreported in clinical trials.¹⁸² However, their primary concern appeared to be flibanserin’s interaction with alcohol.¹⁸³ While Sprout had conducted an alcohol interaction study, the study consisted of twenty-three men and only two women, a gender distribution that is especially concerning given the fact that men and women metabolize alcohol very differently.¹⁸⁴ Furthermore, Committee members expressed concerns that the study did not adequately assess the risk of negative interactions between flibanserin and alcohol for individuals who are not drinking to the point of intoxication, but are, instead, casual, social drinkers.¹⁸⁵

The Advisory Committee considered the potential for REMS to reduce the risks of alcohol-flibanserin interactions, but noted that

180. *Id.* at 352.

181. *Id.* at 348–49, 353–55; SUMMARY OF MINUTES, *supra* note 138, at 6; David Portman, Dir., Columbus Ctr. for Women’s Health Research, Presentation at the June 4, 2015 Joint Meeting of the Bone, Reprod. and Urologic Drugs Advisory Comm. and the Drug Safety and Risk Mgmt. Advisory Comm. (June 4, 2015) (slideshow of presentation on file at <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM452160.pdf>). There is no clear threshold for how effective a drug must be to be approved. Instead the relevant advisory committee makes a case-by-case judgment of whether the benefits of the drug outweighs the risks in light of a variety of factors, including the ability to control the risks using mitigation strategies and the availability of alternative treatments on the market). *See supra* pp. 8–9.

182. MEETING TRANSCRIPT, *supra* note 138, at 381–83, 419.

183. *Id.* at 355–78.

184. *Id.* at 365, 371, 376–78; *FDA Vulnerability Revealed*, *supra* note 125, at 387. A committee member did note, however, that numerous other FDA approved drugs interact negatively with alcohol, and that the FDA had not consistently required alcohol-interaction studies in order to approve those drugs. MEETING TRANSCRIPT, *supra* note 138, at 369.

185. MEETING TRANSCRIPT, *supra* note 138, at 367–69.

there was no available data on whether REMS were actually an effective means of reducing patient alcohol consumption or otherwise mitigating risks.¹⁸⁶ Furthermore, the Advisory Committee again expressed concerns that entry criteria for clinical trials of flibanserin were overly restrictive, and therefore were not adequately generalizable to the broader population of individuals who would likely be treated with flibanserin.¹⁸⁷

While the Advisory Committee expressed further concerns regarding the lack of adequate studies on numerous other risks associated with flibanserin,¹⁸⁸ Committee members were openly sensitive to accusations that first and second review cycle rejections of flibanserin were the result of gender-bias.¹⁸⁹ These members were careful to make clear that their concerns regarding the risks of flibanserin were not unfair given that the drug had shown only a marginal benefit and that the public had misunderstood the Advisory Committee's motives as sexist and patronizing.¹⁹⁰

Ultimately, the Committee members' discussion and explanation of their votes displayed a pervasive sentiment that Sprout's data had failed to resolve nearly all of the risk concerns articulated during flibanserin's previous review cycles.¹⁹¹ Furthermore, not only did Sprout present no new efficacy data, but

186. *Id.* at 360–61.

187. MEETING TRANSCRIPT, *supra* note 138, at 357, 408–15. The Advisory Committee was also concerned that the clinical trials were not generalizable because they were relatively short-term, whereas HSDD is chronic, and so the average patient would take flibanserin over the long-term. *Id.* at 408.

188. SUMMARY OF MINUTES, *supra* note 138, at 8.

189. MEETING TRANSCRIPT, *supra* note 138, at 394–95 (“But it’s sort of trending toward like we need to put all these extra controls on this drug, and I think that’s what’s giving the public the flavor that we think there’s something about women that they need more control than other people do.”); *id.* at 409 (“I want to just end my comment by saying I have a little confusion about the gender bias and sexism . . .”); *see also* Joffe Presentation to the Advisory Committee, *supra* note 123, at 28 (noting, in opening remarks to the Advisory Committee, that the FDA had been accused of gender bias due to the imbalance in available treatments for sexual dysfunction between men and women, and that “the FDA rejects this assertion”).

190. MEETING TRANSCRIPT, *supra* note 138, at 394–95, 409.

191. *See* ADVISORY COMMITTEE BRIEFING DOCUMENT, *supra* note 112, at 4–5 (summarizing the remaining safety concerns associated with flibanserin); *id.* at 36–44 (summarizing the safety concerns noted in the Advisory Committee's 2013 response letter); *see also* MEETING TRANSCRIPT, *supra* note 138, at 431, 438, 440–41, 444–47, 455–56 (discussing remaining uncertainties and concerns regarding the risks posed by flibanserin).

the Advisory Committee clearly felt that issues regarding the restrictiveness and generalizability of clinical trials remained.¹⁹² Despite this, the Advisory Committee voted 18 to 6 to recommend approval of flibanserin, provided that Sprout comply with certain REMS.¹⁹³ As such, it appears that the Advisory Committee's change in stance between the second and third review cycles was not motivated by a better understanding of the risks associated with flibanserin, but instead by an acceptance of the positive effects of flibanserin treatment as clinically meaningful (though numerically marginal) and a sense of urgency to resolve the unmet medical needs of HSDD patients.¹⁹⁴ Notably, the Advisory Committee's approval came with quite a bit of reservation regarding the risks associated with flibanserin and the ability of the REMS relied upon by Sprout to control those risks.¹⁹⁵

4. The Trouble with the Flibanserin Advisory Committee Meeting

A review of the meeting in which the Advisory Committee discussed flibanserin reveals a troubling distortion of FDA expert risk-benefit analysis. While approval of the drug may very well have been appropriate,¹⁹⁶ interest groups successfully hijacked the Advisory Committee's analysis of the risk-benefit profile of the drug through a combination of public campaigns and involvement in the OPH portion of the Advisory Committee's meeting. Such interest group infiltration of the advisory committee process is evident in the extent to which it is nearly impossible to discern whether an improved understanding of the risks and benefits of flibanserin motivated the Advisory Committee to recommend approval, or

192. MEETING TRANSCRIPT, *supra* note 138, at 357–58, 362, 399, 410, 414–15. *See also id.* at 444–45 (“[T]he generalizability of the results was another issue where there was very little evidence that this small effect size would replicate itself in a more general population.”).

193. Joffe, *supra* note 9, at 102.

194. Joffe Presentation to the Advisory Committee, *supra* note 123, at 21; Joffe, *supra* note 9, at 102 (“By a vote of 18 to 6, the committee recommended approval, though some members said it was a difficult decision. In general, those recommending approval acknowledged the small treatment effects and substantial safety concerns but considered the unmet medical need.”).

195. MEETING TRANSCRIPT, *supra* note 138, at 360–61 (“I think the answer is clear that we don't know the degree to which REMS will be effective.”); *id.* at 379, 390–93, 397–89, 444–49.

196. *See* Joffe, *supra* note 9, at 104 (arguing that FDA approval of flibanserin was appropriate).

whether the Advisory Committee did not see a meaningful change in the scientific risk-benefit profile of the drug between its second and third review cycles, but instead felt that it would be unfair to leave women without a treatment for HSDD when men had many available treatment for sexual dysfunction (despite the notable biological differences between male sexual dysfunctions, such as erectile dysfunction, and HSDD).¹⁹⁷

In this way, the Advisory Committee may have veiled a normative concern for superficial gender equity as a scientific factor by articulating the factor as “an unmet medical need,” thus overvaluing the efficacy of the drug.¹⁹⁸ Furthermore, a review of the transcript of the meeting reveals distinct concern over public perception of the Advisory Committee’s recommendation. Specifically, the transcript demonstrates concern among the members of the Advisory Committee that the public would perceive the Advisory Committee as underestimating HSDD as a morbidity or patronizingly overestimating risks that could be addressed within the doctor-patient relationship.¹⁹⁹ In the case of flibanserin, therefore, the Advisory Committee meeting did not serve to promote scientific decision-making and agency transparency, but instead reduced public accountability by pulling sociopolitical factors under the broad umbrella of health concerns, rendering normative/political value judgments inextricable from scientific analysis.

197. See MEETING TRANSCRIPT, *supra* note 138, at 459 (expressing the Acting Chairperson of the Advisory Committee’s view that he has never seen such striking similarities between the rationale of Committee members voting for and against approval).

198. See, e.g., MEETING TRANSCRIPT, *supra* note 138, at 448 (“I voted B, but somewhat a conflicted and still uncomfortable B. There was minimal effect of unclear clinical significance, and I agree with Dr. Orza’s comments that women suffering from HSDD deserve better than this.”); *id.* at 435 (“I took under serious consideration the fact that it’s another first drug—the seventh drug, let’s say, for this disorder, but it’s the first drug ever.”); *id.* at 450 (“I think it’s exciting that we’ll have a drug in the armamentarium for the treatment of HSDD, although I think we all wish that it was a drug that was a better one”); *id.* at 451 (“The reason to vote B and not C is that there is clearly an unmet need”).

199. For a non-exhaustive sampling of points during the meeting at which the Advisory Committee felt the need to address concerns of gender-bias, see MEETING TRANSCRIPT, *supra* note 138, at 39–41, 409.

III. SOLUTION

As noted above, one of the primary reasons that the FDA includes an OPH in every advisory committee meeting is to promote transparency and public accountability.²⁰⁰ Additionally, the FDA's requirement that advisory committee meetings include an OPH can be seen, in many cases, as an implicit recognition that bias is inherent to any human exercise of discretion, no matter how expert, and therefore balanced decision-making requires that members of the public be permitted to counter bias by advocating for their own interest.²⁰¹

However, the manner in which the flibanserin OPH proceeded did not simply fail to promote transparency and non-biased decision-making, it actively obscured the Advisory Committee's risk-benefit analysis and potentially greatly biased the Advisory Committee.²⁰² It is important to recognize that some of the OPH testimony was relevant to the extent that it aimed to educate the Advisory Committee on flibanserin and to reduce bias against women's sexual pleasure that could have resulted in an undervaluing of the morbidity treated by flibanserin. However, the majority of the testimony appeared to be, at best, little more than anecdotal evidence cherry-picked by an organization with an agenda, and, at worst, irrelevant testimony aimed at derailing scientific analysis with social and political pressure.

This is not to say that social agendas belong nowhere in FDA policy. Often times, social agendas aim to counter biases that may have become entrenched in regulation and agency decision-making.²⁰³

200. For a discussion of the roles of advisory committees, see *supra* pp. 8–10; see also Shapiro, *supra* note 10 (discussing the features of advisory committees that promote public accountability).

201. See FDA OPEN PUBLIC HEARING GUIDANCE, *supra* note 88, at 1–2 (“Advisory committees enhance FDA’s ability to protect and promote public health by ensuring FDA has access to . . . [independent expert] advice through the public hearing process as provided in existing laws and regulations FDA encourages participation from all public stakeholders in its decision-making processes.”); The language of 21 CFR § 14.29(a) also suggests a broad purpose of OPH’s to facilitate the provision of expert advice to promote the public health; see also Azebu, *supra* note 25, at 94–95 (“Indeed, the risk/benefit assessment allows for much subjectivity, with some arguing that the decision is purely impressionistic and judgmental.”).

202. Ironically, such bias was achieved, in large part, by accusing the Advisory Committee of gender bias.

203. For instance, in the late 1980s and early 1990s, advocates were able to bring social and political pressure to bear on the FDA to successfully counter

By addressing such biases, social advocacy may improve the integrity of the FDA and its ability to pursue its mandate of protecting the public health.²⁰⁴ However, FDA advisory committees serve the narrow and important function of providing independent expert risk-benefit analysis.²⁰⁵ Advisory committee risk-benefit analysis not only serves to advise the FDA on the appropriate action to take with respect to the drug at issue, but also sets the groundwork for public accountability and effective judicial review.²⁰⁶ As such, it is of the utmost importance that, in articulating the outcome of its analysis, an advisory committee not conflate sociopolitical and scientific factors.²⁰⁷

Given the pharmaceutical industry's proven adeptness at utilizing the OPH portion of advisory committee meetings to exploit the FDA's vulnerability to political pressure, the FDA should introduce more rigorous guidelines regarding who may speak at OPHs and for what purpose. While the advisory committee meetings should remain open to the public, the OPH portion of the meetings need not be "open" in the sense that anyone who wishes to speak may do so. Instead, the function of the advisory committee meetings would be better served by allowing only those speakers who can address, from direct experience or scientific expertise, one of the questions laid out in the meeting agenda. Testimony beyond that which is relevant

social bias within the FDA that had caused the FDA to limit access to important, experimental treatments for patients with HIV/AIDS. For a discussion of the role of social advocates in bringing about important changes to the FDA's stance on treatment for HIV/AIDS, see Lisa Terrizzi, *The Need for Improved Access to Experimental Drug Therapy: AIDS Activists and Their Call for a Parallel Track Policy*, 4 ADMIN. L.J. 589, 589-90 (1991); Steven R. Salbu, *Regulation of Drug Treatments for HIV and AIDS: A Contractarian Model of Access*, 11 YALE J. ON REG. 401, 410 (1994); Fielder, *supra* note 98, at 809.

204. See Fielder, *supra* note 98, at 809-10 (noting that "[n]ew developments will naturally raise ethical questions not adequately covered by the existing regulatory framework").

205. See *supra* Part I.C (discussing the role of Advisory Committees and the statutes, regulations, and guidance governing their role in the NDA process).

206. Shapiro, *supra* note 10, at 189-91 (discussing how, when advisory committees function properly, they provide the necessary scientific backdrop against which to evaluate agency decisions, but, when scientific or technical advisory committees fail to confine their deliberations to scientific judgments, they may frustrate public accountability).

207. See *id.* at 192 ("Members of scientific or technical advisory committees often do not admit, and may not even recognize, when they exceed their expertise and based recommendations on policy values. This result not only obscures the distinction between science and policy decisions, but it can also impede the agency's decision making process.").

to the narrow scientific risk-benefit determination at issue should be limited to statements that address pre-identified gaps in the advisory committee's knowledge or understanding. Such topics may include elements of the risk-benefit analysis that the panel members feel are not adequately addressed through data from clinical trials or other topics that the panel members feel require further clarification, but should be directly related to the data that is the subject of the advisory committee's analysis (i.e., the risks and benefits of the drug as demonstrated through clinical trials or lack thereof). What would not be permitted, however, are unsolicited anecdotes from individuals who have not participated in clinical trials, statements from professional social advocates, especially those in non-healthcare fields, and purely political statements not grounded in scientific expertise. Such testimony may be excluded on the grounds that it is not relevant to the technical risk-benefit determination of the advisory committee.²⁰⁸

With such restraints on advisory committees in mind, it is important to note that, on a fundamental level, no scientific endeavor is free of value judgments or social implications.²⁰⁹ Politics and personal bias will always be an element of FDA decision-making, no matter how expert.²¹⁰ As a result, individuals and advocates must be able to inform the FDA when its internal biases are operating to the detriment of the public health. Such advocacy, however, is most beneficial, when it is distinct from the expert risk-benefit analysis performed by an advisory committee and can be viewed independently of the scientific risk-benefit profile of the drug as articulated by that advisory committee. As such, this content is best aired before the Commissioner, and not the advisory committee.

208. See 21 C.F.R. § 14.25(a) (2016) (requiring that OPHs be open to all relevant information).

209. See A.C. Molewijk et al., *Implicit Normativity in Evidence Based Medicine: A Plea for Integrated Empirical Ethics Research*, 11 HEALTH CARE ANALYSIS 69, 70 (2003) (arguing that the manner in which scientific facts are collected and articulated is often founded on and reinforces social precepts about healthcare); Daniel Strech & John Tilburt, *Value Judgments in the Analysis and Synthesis of Evidence*, 61 J. OF CLINICAL EPIDEMIOLOGY 521, 521 (2008) (discussing how value judgments can infiltrate the manner in which scientific data is interpreted and the conclusions drawn are applied).

210. See Azebu, *supra* note 25, at 95 (recognizing that subjective judgments and reactions to public pressure are inherent to the FDA's risk-benefit calculus); see also Elena Kagan, *Presidential Administration*, 114 HARV. L. REV. 2245, 2383–84 (2001) (discussing executive political influence over agency decision making, and arguing that such influence is neither entirely detrimental, inappropriate, nor contrary to law).

Indeed, since the passage of FACA in 1972, Congress's view of the extent to which the FDA should rely on advisory committee recommendations has fluctuated.²¹¹ However, at no point has Congress felt that advisory committee recommendations should be per se dispositive.²¹² Instead, Congress has made clear that advisory committees serve the narrow function of filling gaps in FDA technical expertise by providing independent, expert, scientific insight, and that the FDA should retain at least some level of internal discretion as to whether or not an advisory committee's recommendation should be decisive in a given case.²¹³ As such, it is neither inappropriate nor contrary to law to establish a system in which advisory committee scientific risk-benefit analysis is a compelling factor in FDA decision-making, but not the sole consideration. In fact, creating a bifurcated system in which the Commissioner may deviate from the recommendation of advisory committees may serve to allow for social advocacy to correct biases internal to an advisory committee in a way that is more readily judicially reviewable, simply by nature of the fact that the Commissioner's reasoning for doing so must be articulated as distinct from the risk-benefit analysis itself.²¹⁴

Bifurcation of the scientific risk-benefit and public comment portions of the NDA process also has multiple benefits.²¹⁵ First, it

211. See DIVISION OF HEALTH CARE POLICY, *supra* note 19, at 101–08.

212. See *id.*

213. See *id.*; Federal Advisory Committee Act, Pub. L. No. 92-463, § 2, 86 Stat. 770, 770 (1972). The FDA has enacted regulation that supports such a view. 21 C.F.R. §§ 14.1(a)(1), 14.1(b)(6)(i), 14.174 (2016).

214. For a discussion of *Tummino v. Torti*, in which the Commissioner's deviation from the advisory committee recommendation enabled judicial review of the ultimate FDA decision at issue because it allowed the court to distinguish between the scientific risk-benefit factors as analyzed by the advisory committee and factors external to the risk-benefit analysis that motivated the Commissioner's deviation, see *supra* note 106. For a discussion of an important instance in which social advocacy was appropriately utilized to correct internal FDA biases, see *supra* note 203.

215. There are existing examples of processes that bifurcate this kind of analysis. Under Medicare Part D, pharmacy and therapeutics (P&T) committees are tasked with creating drug formularies to guide drug prescription and reimbursement decisions. Because of the mixed financial and scientific nature of the healthcare analysis required to manage formularies, CMS guidance requires that P&T committees perform distinct risk-benefit and pharmacoeconomic analyses in evaluating drugs for inclusion in formularies. Such bifurcation seeks to ensure that financial considerations do not distort the scientific risk-benefit analysis of drugs. AM. SOC'Y FOR HEALTH-SYSTEM PHARMACISTS, ASHP GUIDELINES ON THE PHARMACY AND THERAPEUTICS COMM. AND THE FORMULARY SYS. 178–85 (2008); CTR. FOR MEDICARE AND MEDICAID SERVS., CMS STRATEGY

promotes public accountability by forcing a clearer articulation of what factors drove the FDA's final decision. Similarly, by providing a channel for independent and distinct articulation of sociopolitical concerns, bifurcation would help ensure that adjustments that occur on account of social advocacy efforts are appropriate and proportional: if, as in the case of flibanserin, for instance, there are reasonable allegations that an advisory committee undervalued the morbidity treated by a drug out of gender bias, bifurcation allows for the FDA to appropriately adjust its understanding of the benefits of the drug, without surrendering meaningful judgment of the risks posed by the drug. Bifurcation also allows the Commissioner, if she wishes to deviate from an advisory committee's recommendation, to clearly articulate why concerns of bias or other social considerations merit discounting the advisory committee's recommendation. Finally, by preserving the clarity and integrity of advisory committee risk-benefit analysis, bifurcation allows for appropriate and effective levels of judicial oversight, as it makes clearer when the FDA has deviated from scientific judgment, and for what reasons, without extensive judicial inquiry into the agency's expert processes and judgment.

CONCLUSION

An analysis of the Advisory Committee's review process of flibanserin demonstrates how pharmaceutical companies and special interest groups have become adept at exploiting the FDA's vulnerability to sociopolitical influences on issues of women's health. While non-scientific factors may infiltrate FDA decision-making in many ways, such infiltration of the advisory committee process is especially problematic because it distorts the scientific risk-benefit analysis that serves as an important backdrop for public accountability and appropriate judicial oversight, rendering appropriate scientific and technical considerations inextricable from inappropriate political influence and social pressure.

FOR AFFORDABLE ACCESS TO COMPREHENSIVE DRUG COVERAGE: GUIDELINES FOR REVIEWING PRESCRIPTION DRUG PLAN FORMULARIES AND PROCEDURES; ACAD. OF MANAGED CARE PHARMACY, FORMULARY MGMT. (2009); HEALTH PARTNERS, PHARMACY AND THERAPEUTICS COMM. POLICIES AND PROCEDURES (2016); CTR. FOR MEDICARE AND MEDICAID SERVS., MEDICARE PRESCRIPTION DRUG BENEFITS MANUAL, CHAPTER 6: PART D DRUGS AND FORMULARY REQUIREMENTS art. 30 (2016).

In order to promote transparency, accountability, and balanced decision-making, the FDA should issue guidance that better manages the OPH portion of advisory committee meetings, restricting testimony to only those speakers who can directly and credibly address the risk-benefit profile of the drug at issue. Such guidance would not be aimed at removing social advocacy and industry voices from the NDA process altogether, but instead at insulating expert scientific risk-benefit analysis from sociopolitical influences to promote integrity and clarity in the reasoning behind the FDA's ultimate decisions.