PRESCRIPTION FOR A CURE: DOES THE FDA’S DRAFT GUIDANCE ADEQUATELY MANAGE ADVISORY COMMITTEE MEMBERS’ CONFLICTS OF INTEREST?

Ian J. Kellogg*

INTRODUCTION

On November 16, 1999, the Gastrointestinal Drugs Advisory Committee of the Food and Drug Administration (FDA) recommended prompt approval of the drug Lotronex, used to treat women with irritable bowel syndrome.1 Among the participants on the advisory committee was a paid consultant of the drug manufacturer, Glaxo, who had participated in the investigation of the drug for the company.2 At the meeting, he acknowledged concerns about evidence that the drug caused some people to develop ischemic colitis,3 but rather than delay approval of the drug he suggested “monitor[ing] it very carefully,” with

---

* J.D., Stanford Law School, 2007. The author would like to thank Alan Morrison for his inspiration and patient direction in writing this article and the editing team of Rajat Rana at SLPR for helping to prepare it for publication. The views (and any errors) contained in the piece are the author’s and the author’s alone; they should not be attributed to any other individual or institution.


2. See Willman, supra note 1; GASTROINTESTINAL DRUGS ADVISORY COMMITTEE MEETING, supra note 1, at 6.

3. GASTROINTESTINAL DRUGS ADVISORY COMMITTEE MEETING, supra note 1, at 194-95, 202-03. Ischemic colitis is defined by the National Library of Medicine at the National Institutes of Health as “inflammation (irritation and swelling) caused by interference with the blood flow to the colon . . . .” Medline Plus, Ischemic Colitis, http://www.nlm.nih.gov/medlineplus/ency/article/000258.htm (last visited Apr. 10, 2008).
the expectation that complications would not prove too injurious.\(^4\) The commit-
tee ultimately recommended approving the drug without further testing, and the
FDA followed the committee’s advice and formally approved Lotronex in Feb-
ruary 2000.\(^5\) Just nine months later, Glaxo withdrew the drug from the U.S.
market after forty-nine patients taking Lotronex developed ischemic colitis and
five died.\(^6\) These and other similar events led to criticism of the FDA’s han-
dling of conflicts of interest from many fronts.\(^7\)

On Friday, March 23, 2007, the FDA sought public comment on new
guidelines for determining conflicts of interest and eligibility for participation in
FDA Advisory Committee meetings.\(^8\) Part I.A of this Note gives a brief his-
tory of the factual and legal background that led the FDA to propose the new
guidelines, focusing on the FDA’s own rationale—a recognized inconsistency
and lack of determinable standards under which waivers were granted in the
past. The new guidelines, the salient features of which are summarized in Part

\(^4\) *Gastrointestinal Drugs Advisory Committee Meeting*, supra note 1, at 203.

\(^5\) Willman, *supra* note 1. While we can, of course, never know definitively that the
consultant’s comments influenced the committee’s unanimous decision to approve the drug
without awaiting further testing, it is interesting to note that the consultant was the only
committee member to respond directly to the question of “whether more safety studies
should be performed prior to approval, or after approval?” See supra note 1.

\(^6\) Id.; Cnn.com, Drug for Irritable Bowel Pulled off U.S. Market (Nov. 29, 2000),

\(^7\) See, e.g., NIH Ethics Concerns: Consulting Arrangements and Outside Awards :
Hearings Before the H. Comm. on Energy and Commerce, 108th Cong. (2004); Elizabeth R.
Glodé, *Advising Under the Influence? : Conflicts of Interest Among FDA Advisory Commit-
tee Members*, 57 Food & Drug L. J. 293 (2002); Peter Lurie et al., *Financial Conflict of In-
terest Disclosure and Voting Patterns at Food and Drug Administration Drug Advisory
Committee Meetings*, 295 J. Am. Med. 1921, 1924 (2006); Peter Lurie & Allison Zieve,
*Sometimes the Silence Can Be Like the Thunder : Access to Pharmaceutical Data at the
FDA*, 69 Law & Contemp. Probs. 85 (2006); Sheila R. Shulman & Andrea Kuetel, *Drug
Development and the Public Health Mission: Challenges at the FDA, NIH, and Academic
Medical Centers*, 53 Buff. L. Rev. 663 (2005); Dennis Cauchon, FDA Advisers Tied to In-
dustry, USA Today, Sept. 25, 2000, at A1; David Willman, Scientists Who Judge Pill Safety
Received Fees, L.A. Times, Oct. 29, 1999, at A22; DIANA M. ZUCKERMAN, FDA ADVISORY
COMMITTEES: DOES APPROVAL MEAN SAFETY?, NAT’L RESEARCH CTR. FOR WOMEN &

\(^8\) Draft 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, 72 Fed. Reg. 13805 (proposed Mar. 23, 2007) [hereinafter Notice of
Draft Guidelines]; FDA, *Draft Guidance for the Public, FDA Advisory Committee
Members, and FDA Staff on Procedures for Determining Conflict of Interest and
Guidelines]. This Note will refer exclusively to committees convened to review new drugs,
but it applies equally to the review of medical devices, as well. See, e.g., FDA, *Policies and
Procedures for Handling Conflicts of Interest with FDA Advisory Committee
Members, Consultants, and Experts*, http://www.fda.gov/oc/advisory/conflictofinterest/
policies.html (last visited Mar. 21, 2008) (noting that the FDA oversees both drugs and de-
vices, as well as foods and biologies).
I.B, purport to set forth “a more stringent approach for considering eligibility for participation . . . .”9 Their official purposes are “to [1] simplify and streamline the process by which FDA considers meeting participation, [2] increase the transparency, clarity, and consistency of the process, and [3] enhance public trust in this important function.”10 Part I.A assesses the guidelines’ effectiveness and potential impact and concludes that disqualifying conflicted committee members as the rule, and granting non-voting waivers as the rare exception,11 make great strides in effectuating the guidelines’ purposes. In spite of these steps toward conflict-free advice, Part II.B discusses a number of lingering concerns about undue influence from committee members with financial conflicts under the terms of the Draft Guidelines: namely, that their language leaves sufficient loopholes that their purposes can be avoided. While this Note focuses on the FDA, the principles and suggestions about ways to eliminate or minimize potential conflicts are applicable to any agency that employs advisory committees to assist in product-specific analysis.12

I. THE FDA’S 2007 DRAFT GUIDELINES

A. Background

The FDA is required to approve new drugs prior to sale.13 The agency was created by the Food, Drug, and Cosmetic Act, which was passed following the deaths of over one hundred children caused by a widely marketed “elixir” for “strep” infections made by dissolving the curative sulfanilamide in diethylene glycol, a poisonous chemical used as antifreeze.14 The current iteration of the Act requires a demonstration of “safety” and “efficacy,” necessitating a long, complex, and expensive approval process.15

The FDA is one of eleven health agencies that comprise the Department of Health and Human Services (DHHS), the cabinet-level department concerned

10. Id.
11. See DRAFT GUIDELINES, supra note 8, at 7.
with public health issues. The FDA is tasked with evaluating applications submitted by pharmaceutical companies and determining, based on a review of scientific evidence pertaining to safety and efficacy, whether their drugs can be sold in the United States and under what terms. This review process is handled in the first instance by an FDA sub-entity, the Center for Drug Evaluation and Research (CDER). Often, the CDER will seek a recommendation from a federal advisory committee. Advisory committees range in size from three to fifteen persons and include members of the public, industry representatives, and scientific experts in the specific field in which the new drug is introduced. While not binding on the FDA, those recommendations are widely followed.

The scientific experts retained by the CDER to serve on federal advisory committees and to make recommendations on whether to approve or deny a new drug are often “Special Government Employees” (SGEs), part-time government employees, who are regularly employed elsewhere. These experts are often pharmaceutical researchers employed by research institutions, including universities and pharmaceutical companies, with significant (and highly specialized) expertise in the relevant area. The product-specific determina-


tions made by these advisory committee members can have significant financial impacts on both the sponsoring (developing) company and its competitors. Depending on their personal, familial, or university affiliations, even the FDA recognizes that individual committee members might have serious conflicts of interest in some cases and that these conflicts can lead members to vote with their pocketbooks, or at least the appearance of such.24 This Note focuses on potential financial conflicts of interest among SGEs on Federal Advisory Committees making recommendations to the FDA about whether to approve drugs for sale in the United States.

The conflicts of interest of SGEs serving in advisory capacities to federal agencies exist at the intersection of four bodies of law: (1) the Federal Advisory Committee Act (FACA); 25 (2) federal conflict of interest laws and the regulations promulgated thereunder by the Office of Government Ethics (OGE); (3) the organic statutes creating (some) federal agencies and supplemental regulations promulgated thereunder; as well as, in some situations, (4) ethical specifications in the statutes or regulations under which a particular committee was convened.26 In spite of this tangle of laws and regulations, many conflicts have slipped through the cracks. The FDA describes its own process for reviewing potential conflicts of interest as “complex and . . . poorly understood.”27

The FDA adopted new conflict and waiver guidelines in 2000, 28 but the

who serve FDA are often pre-eminent scientists in their field. They are typically active researchers on the cutting edge of science. As such, they and their organizations are often sought out by regulated industry to assist in product development. Indeed, studies have shown that academic biomedical research in the United States increasingly is supported by industry. For that reason, the FDA’s outside experts and the research centers where they work frequently have research grants from, and contracts with, regulated industry.

24. See id. (“This situation can give rise to potential conflicts of interest or appearances of a lack of impartiality.”).

25. 5 U.S.C. app. 2, §§ 1 et seq. (2007) (governing committees established to advise officers and agencies in the executive branch). FACA does not have separate conflict of interest standards, per se, insisting only that “the membership of the advisory committee to be fairly balanced in terms of the points of view represented and the functions to be performed by the advisory committee.” Id. § 5(b)(2).

26. This formulation comes from Richard Berg. See Richard K. Berg, Conflict-of-Interest Requirements for Members of Federal Advisory Committees, Report to the Administrative Conference of the U.S., 37 FED. BAR NEWS & J. 396, 396 (1990) (“The problem of conflict of interest requirements for federal advisory committee members involves the interaction of three distinct bodies of law—the Federal Advisory Committee Act (FACA), the conflict of interest laws, . . . and the federal personnel statutes and regulations.”). Because some organic statutes under the auspices of which agencies were created contain additional conflict provisions, as can the specific statutes whose mandates SGEs are implementing, my numerical formulation is slightly different. The point, however, is the same : personnel in this position are governed by numerous laws, regulations, and guidelines, between which—in spite of their number—there may exist some gaps.

27. DRAFT GUIDELINES, supra note 8, at 5

criteria were complicated and discretionary, leading to complaints of inconsistency.29 Both before and after the 2000 guidelines were adopted, there continued to be demands for change in the way that the FDA handled conflicts of interest.30 Various studies found both that committee members continued to be conflicted and that their conflicts were routinely waived. For example, USA Today reported in 2000 that fifty-four percent of supposedly independent experts “have a direct financial interest in the drug or topic they are asked to evaluate.”31 Even at meetings where the fates of specific drugs were discussed, USA Today found that thirty-three percent of advisory committee members had conflicts.32 More recently, a Public Citizen study concluded that “at least 1 conflict was declared for at least 1 advisory committee member or voting consultant . . . [at] 81% [of] product meetings. . . .”33 In the highly publicized recall of Vioxx, a private study commissioned by the New York Times found that twenty-seven of the thirty-two advisory committee members who debated the risks posed by COX-2 inhibitors had industry ties, including ten with recent ties to COX-2 manufacturers.34 According to USA Today, “the FDA ha[d] waived the restriction [on financial conflicts for experts] more than 800 times” between 1998 and September of 2000.35 Public Citizen agreed that conflicts of interest “rarely result in recusal of advisory committee members.”36

These examples are emblematic of the widespread criticism that the FDA has faced from the public, the press, and Congress.37 As one trade publication put it, the Draft Guidelines “come in response to proposed legislation in Congress that aims to prevent experts that either have financial interests in or receive funding from specific pharma[ceutical] companies from voting on the approval of these companies’ drugs or on competing products. . . . The new rules should be seen largely as a pre-emptive attempt by the FDA[ ] . . . to prevent political intervention in the agency’s approval process.”38 The FDA stated that it remains “committed to strictly adhering to the laws and regulations governing the process for selecting advisory committee members” and that it seeks

---

29. See Notice of Draft Guidelines, supra note 8, at 13,806 (acknowledging same).
30. See supra note 7 (citing sources).
32. Id.
33. Lurie et al., supra note 7, at 1924.
35. Cauchon, supra note 7.
36. Lurie et al., supra note 7, at 1924.
37. See supra note 7.
38. Milena Izmirlieva, Experts Who Receive Over US $50,000 in Company Funding Banned from FDA Advisory Committees, World Markets Research Centre, at In Brief (Mar. 22, 2007); see also Gardiner Harris, FDA Role Limits Role of Advisers Tied to Industry; N.Y. TIMES, Mar. 22, 2007, at A6 (“F.D.A. is trying to strike a balance here, . . . and they would rather strike it themselves than have it struck for them.” (quoting Daniel E. Troy, former FDA general counsel)).
to “simplify and streamline[]” that process through the proposal and adoption of the new guidelines. The guidelines—whether proposed to preempt Congressional action, curb public criticism, or otherwise—represent an attempt to synthesize applicable laws and regulations and to present a comprehensive, comprehensible, and unified approach to conflict of interest review by the FDA.

B. “Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees”

1. Purpose and Summary

Since before the adoption of the new guidelines, the FDA has purported to recognize the importance of conflict-free advice from its advisory committee members. The FDA says that “it is critical that the advice be free from conflict of interest and potential bias. If the advice FDA receives is biased or is seen as biased, it is of little value to the Agency.” The Draft Guidelines is an attempt to (at least appear publicly to) create policies to implement that goal.

According to the FDA, the guidelines “implement a more stringent policy for considering eligibility for participation than would be permitted under the current legal framework.” This new policy has four basic tenets: (1) individuals with financial conflicts above $50,000 are generally prohibited; (2) individuals with conflicts of $50,000 or less may participate only if the need for the individual’s services outweighs the potential conflict; (3) even where the need for services outweighs the potential conflict, participation is non-voting; and (4) non-voting participation will be limited in cases where there is a perceived conflict of interest, even if full participation would otherwise be permitted under law. The next Subpart analyzes the practical implementation of those four principles.

2. Step-By-Step Review

The proposed guidelines set forth a detailed six-step algorithm by which FDA staff members are to assess the potential conflicts of interest of members of their advisory committees on a meeting-by-meeting basis.

39. DRAFT GUIDELINES, supra note 8, at 4, 6.


41. DRAFT GUIDELINES, supra note 8, at 7.

42. Id. at 7-8.

43. “This guidance document is intended for use by FDA staff (‘you’) involved with advisory committee matters . . . [to determine] whether an advisory committee member has a conflict of interest and whether participation is appropriate.” Id. at 2-3. This Note will
a. Step One: Particular Matter?

Committee members with potential conflicts of interest are only prohibited from participating in meetings in which “particular matters” are involved. Particular matters are defined as those “that involve deliberation, decision, or action that is focused upon the interests of specific persons, or a discrete and identifiable class of persons.”

This includes all committee meetings regarding individual drugs, and the guidelines suggest that “most FDA advisory committee meeting topics will involve ‘particular matters.” Evaluators are required to prepare memoranda supporting their classification of a meeting as non-particular, and they must seek concurrence from the advisory committee oversight director. If the meeting is not concerned with a particular matter, all committee members may fully participate; if it is concerned with a particular matter, then the inquiry proceeds to Step Two.

b. Step Two: Direct and Predictable Effect?

An advisory committee member is prohibited from participating in a particular matter meeting that will have “a direct and predictable effect” on his financial interests. Existing regulations define a direct effect as one with a “close causal link between any decision or action to be taken in the matter and any expected effect of the matter on the financial interest.” A “predictable effect” is one in which “there is a real, as opposed to a speculative, possibility that the matter will affect the financial interest.” The FDA says that meetings affecting “legal rights or responsibilities . . . would ordinarily have a ‘direct and predictable effect’ on financial interests.” This would encompass “most potential advisory committee recommendations pertaining to marketing status, labeling, post-marketing requirements, and device classification or reclassification,” including recommendations as to whether to approve or deny a particular

refer to those staff personnel making determinations about potential conflicts of interest and participation as “Evaluators.” The FDA’s Algorithm is attached hereto, in an effort to provide a graphical overview of how these guidelines operate.

44. Id. at 8.
45. Id. (emphasis added).
46. Id. at 9. The oversight director heads the committee created to “ensure[] that all FDA committee management activities are consistent with the provisions of FACA, Departmental policies, and related regulations and statutes.” See FDA, ADVISORY COMMITTEE OVERSIGHT AND MANAGEMENT STAFF, http://www.fda.gov/oc/advisory/missionandstaff.html (last visited Mar. 21, 2008).
47. See DRAFT GUIDELINES, supra note 8, at 9 & n.1. “Full participation includes voting.” Id.
48. Id. at 9.
49. See id. at 9-10.
51. Id. § 2640.103(a)(3)(ii).
52. DRAFT GUIDELINES, supra note 8, at 10.
drug. If it is determined that the particular matter meeting in question will not have a direct and predictable effect on a member’s financial interests, then the member may participate. If a direct and predictable effect is likely, then the analysis proceeds to Step Three.

c. Step Three: Disqualifying Financial Interest?

Step Three examines all interests that may have financial consequences for the employee, either directly or through personal or business relationships, to determine whether they are “disqualifying.” A financial interest is “the potential for gain or loss to the employee . . . as a result of governmental action on the particular matter.” It includes the interests of the committee member, spouse, and minor children, as well as general partners, current or prospective employers, and organizations of which the member is an officer or director. Any such financial interests are deemed disqualifying. If there are no disqualifying interests, the analysis moves to Step Four (A) to determine whether there might be the appearance of a conflict for which the member should be excluded. If there are any disqualifying interests, then the analysis proceeds to Step Four (B), to determine their collective amount and whether there are exemptions that permit the member to avoid disqualification.

d. Step Four (A): Appearance of Conflict?

Where a member has no current disqualifying interests attributable to her, the new guidelines nevertheless direct an inquiry into the appearance of a conflict to enhance public trust in the process. Evaluators are directed to consider any financial interests held “within the preceding twelve months that would be a disqualifying financial interest if it were currently held . . . even though full participation would be permitted under [applicable law].” Members with past

53. Id. However, if a committee member is employed by a university that receives funding from, or has “a grant or contract with,” a drug company’s sponsor or its competitors “to conduct research on a product that is not the subject of the particular matter before the advisory committee,” the deliberations will ordinarily not be considered to have direct and predictable effects on this interest. Id. at 10 (citing 5 C.F.R. § 2640.103(a)(3) ex. 2 (2007)).

54. DRAFT GUIDELINES, supra note 8, at 10-11. The Reviewing Agent must then prepare a memorandum and “obtain [supervisory] concurrence.” Id.

55. 5 C.F.R. § 2640.103(b) (2007).

56. DRAFT GUIDELINES, supra note 8, at 11. A prospective employer is defined as “anyone with whom the [committee member] has any arrangement concerning future employment or with whom he/she is seeking or negotiating for employment.” Id. at 11 n.2.

57. See id. at 12.

58. See id. at 13.

59. See id.

60. Id. at 8, 12, 20.
financial interests greater than $50,000 are generally barred from participation, whereas members with past financial interests of $50,000 or less are able to participate in the meeting, but not to vote on the final dispensation. If a member has not held disqualifying interests in the past twelve months, then the member may fully participate in the meeting and the Evaluator is directed to prepare a memorandum outlining and supporting the conclusion and to seek supervisory concurrence from the advisory committee oversight director.

e. Step Four (B): Amount of Disqualifying Interest?

If Step Three leads to the conclusion that a committee member has disqualifying interests, Step Four (B) determines the value of those interests. Interests greater than $50,000 will (generally) prohibit a member from participating at all; whereas, members with interests less than this threshold may be allowed to participate in a non-voting capacity. The combined value of disqualifying interests is determined after applying specific exemptions.

The FDA’s proposed guidelines adopt “a simplified subset” of the exemptions issued by the Director of the OGE. The subset includes, but is not limited to, pension funds, diversified financial funds, de minimis funds concentrated in the committee’s area of review, de minimis securities that may be affected by the committee’s decision, and interests stemming from certain academic employment relationships. These interests are deemed “too remote or too inconsequential to affect the integrity of the services of the Government officers or employees to which such regulation applies.”

If, after applying all relevant exemptions, the committee member still has disqualifying interests greater than $50,000, she is then precluded from participa-

---

61. Id. at 12-13. In certain “limited” cases, the “FDA may determine that participation is appropriate even if the combined value of the non-current financial interests exceeds $50,000.” Id. at 13 n.3. Potential problems with this guideline are discussed infra Part III.B.2.

62. See id. at 13. For a critique of non-voting participation, see infra Part II.B.6.

63. In the case that no interests are found, the decision maker is nonetheless directed to consider “other applicable regulatory provisions such as [5 C.F.R. § 2635.502],” id., which discusses considerations regarding the appearance of potential conflicts of interest in personal and business relationships.

64. See id.

65. See id. at 13-15.

66. Id. at 14-15 (citing 5 C.F.R. §§ 2640.201-06 (2007)).

67. Id. at 15 (citing 5 C.F.R. § 2640.201(c) (2007)).

68. 5 C.F.R. § 2640.201(a) (2007); DRAFT GUIDELINES, supra note 8, at 15.

69. See 5 C.F.R. § 2640.201(b) & exs. 2 & 3 (2007); DRAFT GUIDELINES, supra note 8, at 15.

70. 5 C.F.R. § 2640.202(a) (2007); DRAFT GUIDELINES, supra note 8, at 15.

71. 5 C.F.R. § 2640.203(b)-(c) (2007); DRAFT GUIDELINES, supra note 8, at 15.

72. 18 U.S.C. § 208(b)(2) (2007); see also DRAFT GUIDELINES, supra note 8, at 14.
pating in the meeting. 73 While the committee member is banned from participa-

In "a large majority," 74 or "most cases," 75 the Evaluator may nonetheless seek a conflict of interest waiver, which will be reviewed directly by the Commissioner of the FDA. 76 If, after taking the exemptions into account, a commit-
tee member’s disqualifying interests do not exceed $50,000, the inquiry proceeds to Step Five to determine whether the member may participate in the committee meeting in a non-voting capacity. 77

f. Step Five: Need for the Member’s Services?

Step Five determines if an individual who has disqualifying interests of $50,000 or less should be barred from participation or if the analysis should proceed to Step Six concerning whether a waiver should be granted. The decision to recommend a waiver is to be made by balancing the individual’s unique ability to contribute to the committee against her financial conflicts. Waivers may be granted to SGEs serving on advisory committees if either of two separate standards is met: “the need for the individual’s services outweighs the potential for a conflict of interest created by the financial interest involved” 78 or “a waiver is ‘necessary’ to afford the committee ‘essential expertise.’” 79 To determine the “need” for the individual’s services, the FDA directs the Evaluator to consider four factors including the “uniqueness” of the member’s qualifications, how difficult it would be to find another similarly qualified individual, how essential the expertise is, and “[t]he nature and extent of the disqualifying

73. DRAFT GUIDELINES, supra note 8, at 13.
74. Id.
75. Id. at 14.
76. See id. at 13-14. The (lack of) criteria and process for granting a waiver at this stage is discussed infra at Part III.B.3.
77. DRAFT GUIDELINES, supra note 8, at 15-16.
78. 18 U.S.C. § 208(b)(3) (2006); see also DRAFT GUIDELINES, supra note 8, at 16. Although federal law establishes different waiver conditions for regular government employees and special government employees, this Note focuses on the latter. The standard for the former is “whether the member’s financial interest is not so substantial as to be deemed likely to affect the integrity of the services provided by that individual.” DRAFT GUIDELINES, supra note 8, at 16 (citing 18 U.S.C. § 208(b)(1) (2006)).
79. DRAFT GUIDELINES, supra note 8, at 16 (citing Food Drug & Cosmetic Act § 505(n)(4), 21 U.S.C. § 355(n)(4) (2006)). References to Section 355(n)(4) in this Note are to the statute in effect at the time the Draft Guidelines were issued. It has since been slightly amended, though the original is still cited (and its spirit embodied) in the guidelines. If one satisfies the standards set forth in Section 355(n)(4), voting participation is allowed unless the committee member’s own scientific research is involved, in which case voting participation is never allowed. 21 U.S.C. § 355(n)(4) (2006); DRAFT GUIDELINES, supra note 8, at 16 n.4. The Draft Guidelines do not separately address situations involving the evaluation of the member’s own scientific research, because the FDA “ha[s] decided, as a policy matter, to consider only non-voting participation when the individual has financial conflicts of interest.” Id. at 16 (emphasis added).
financial interest.”80 The second criterion is the most important, and the Evaluator is directed to document that a “reasonably thorough” search turned up no similarly qualified individuals with lesser conflicts.81 To determine whether the need “outweighs the potential for a conflict of interest created by the disqualifying financial interest,”82 the Draft Guidelines refer to seven criteria: (1) “[t]he type of interest”; (2) the holder of the interest and the relation of the holder to the member; (3) the “uniqueness of the individual’s qualifications”; (4) “[t]he difficulty of locating a similarly qualified individual”; (5) the relative value of the interest; (6) the potential change in that value of the interest; and (7) the directness of the effect on that interest.83 If, after weighing these factors, the need for the member’s services does not outweigh the potential for a conflict of interest, then the member should not participate.84 If the need does outweigh the potential for conflict, then the analysis proceeds to Step Six.85

g. Step Six: Participation? In What Capacity?

Step Six is the final inquiry to determine whether to grant participation on a non-voting basis, to recommend a waiver granting non-voting participation, or to disallow participation all together.86 The Evaluator is directed to apply additional statutory exemptions87—including a de minimis and a general-matter exemption—to determine the final value of the member’s past88 and current disqualifying interests.89 If these additional exemptions transform a committee member’s financial interests into non-disqualifying ones, then the member is allowed to participate in the committee meeting on a non-voting ba-

80. DRAFT GUIDELINES, supra note 8, at 18. Given that the last factor speaks to the potential conflict, and not the need for the individual’s participation, this information seems more appropriately considered in the next step of the analysis: balancing the need for participation with the potential for conflict.
81. Id.
82. 5 C.F.R. § 2640.302(b) (2007).
83. DRAFT GUIDELINES, supra note 8, at 17-18; 5 C.F.R. § 2640.302(b)(1)-(7).
84. See DRAFT GUIDELINES, supra note 8, at 18.
85. Id. at 18-19.
86. See id. at 19-21.
87. These are exemptions under applicable law not considered in Step Four (B). See id. at 19; see also supra Part II.B.2.e.
88. At this stage, the Evaluator is to look at whether there are “any financial interests held within the preceding 12 months that would be a disqualifying financial interest if they were currently held.” DRAFT GUIDELINES, supra note 8, at 22 (algorithm). While this same inquiry was undertaken in Step Four (A), a member whose evaluation has proceeded this far through the Algorithm would have skipped Step Four (A), because Step Three determined the member had disqualifying financial interests and the evaluation proceeded to Step Four (B), rather than Four (A). See id.
89. Id. at 19 (citing 5 C.F.R. § 2460.202(b)-(c) (2007)).
sis without waiver. 90 If, after applying the additional exemptions, a conflict of interest of $50,000 or less remains, then a waiver for non-voting participation can be recommended. Finally, participation should generally be barred where the interests are greater than $50,000. 91 In all instances, the Evaluator is directed to draft a memorandum in support of the conclusion and to obtain supervisory concurrence from the advisory committee oversight director. 92

II. ASSESSMENT OF DRAFT GUIDELINES

There are two ways to deal with conflicts: prevention and disclosure. Preventing conflicts is the best defense against potentially tainted recommendations. If a conflict is allowed to go forward, disclosing the conflict so that the FDA and the public can weigh the conflicted committee member’s record of participation accordingly, is the next best defense. The FDA’s proposed guidelines focus on disqualification, and Part II.A addresses the extent to which they succeed: They preclude conflicts greater than $50,000, and they encourage administrators to be vigorous in adhering to the guidelines. Where conflicts are waived, they are waived by the Commissioner, and participation is allowed only on a non-voting basis, thereby minimizing the potential influence a conflicted member might have on the committee’s recommendations. However, potential problems remain, which are detailed in Part II.B: The guidelines’ preventative measures are merely suggestions, which the FDA is not legally bound to follow. Moreover, even if the guidelines are followed, they provide substantial wiggle-room, so that their policy can be subverted. This wiggle-room is widened by the lack of clarity in a number of exemptions. Finally, even assuming these ambiguities are not exploited, the FDA still has not adequately justified the need for waivers for conflicted committee members. Thus, while the draft guidelines potentially address a number of concerns about conflicts of interest among advisory committee members, only an application of the guidelines that is faithful to both their letter and spirit, accompanied by robust disclosure, will truly resolve those concerns.

A. The Guidelines Address Many Concerns About Committee Members with Conflicts

After the FDA released its proposed guidelines, they received an endorsement from one of the FDA’s most vocal critics. Public Citizen’s Dr. Peter Lurie was quoted as saying that, “I think it’s likely to improve the quality of the recommendations, remove the taint of the recommendations and improve the

91. DRAFT GUIDELINES, supra note 8, at 20.
92. Id. at 21.
2008] PRESCRIPTION FOR A CURE 313

credibility of the recommendations.”93 Public Citizen is responsible for significant pressure on the FDA regarding conflicts and disclosure in advisory committees,94 and the guidelines seem to address many of the organization’s concerns: First, the guidelines provide incentives for the Commissioner’s designees to staff committees with conflict-free personnel in the first instance. Second, the guidelines’ initial response to any potential financial conflicts of interest—both actual and perceived—among committee members is disqualification. Third, any waivers for individuals with conflicts are to be reviewed by the FDA Commissioner personally. Finally, even where waivers are granted, they are to be non-voting.

Advisory committee members are initially selected by a designee of the FDA Commissioner.95 The new guidelines provide strong incentives for those filling committees to pick individuals who will be conflict-free (or at most minimally conflicted) in the large majority of cases.96 First, because conflicts have to be assessed on a meeting-by-meeting basis,97 simple administrative convenience will steer administrators toward scientists with minimal potential financial conflicts. Second, public accountability dictates that the designee will seek to fill the committees with members who can both participate and vote; to do otherwise would (publicly) undermine the very purpose of the advisory committee. Third, because waivers for conflicts are to be granted, if at all, by the FDA Commissioner personally, it is unlikely that a lower-level FDA employee will make committee selections that risk frequent escalation to the FDA’s top official.

Among sitting committee members, disqualifying financial interests are addressed, in the first instance, by precluding the advisory committee member who holds them from participating in the advisory committee meeting. If Steps

93. Gardiner Harris, FDALimits Role of Advisers Tied to Industry, N.Y. TIMES, Mar. 22, 2007, at A6 (quoting Dr. Peter Lurie, Deputy Director, Health Research Group, Public Citizen); see also FDA to Restrict Conflicts of Interest in Advisory Committee Members, 6 DRUG INDUSTRY DAILY 58 (2007) (“The restrictions [contained in the new guidelines] will motivate the FDA to find individuals ‘almost completely devoid of conflicts of interest.’” (quoting Dr. Peter Lurie, Deputy Director, Health Research Group, Public Citizen)).
95. See, e.g., FDA, Gastrointestinal Drugs Advisory Committee Charter (Feb. 27, 2006), available at http://www.fda.gov/cedr/audiences/acspage/Gastrointestinalcharter1.htm (last visited Mar. 21, 2008). While the power is technically designated to the “Commissioner or designee,” id., in practice, this is never undertaken directly by the Commissioner.
96. This idea is attributable to Dr. Peter Lurie of Public Citizen. See Telephone Interview with Dr. Peter Lurie, Deputy Director, Health Research Group, Public Citizen (Apr. 23, 2007) (notes on file with the author).
97. See supra Part II.B.2.a (describing Step One).
One and Two determine that the member has a financial interest on which the particular-matter meeting in question might have a “direct and predictable effect,” then Steps Three and Four default to disqualification. Even if the financial stake is in the past, but might give the appearance of a conflict, a member is precluded from participating if that interest is over $50,000. One of the main criticisms of past conflict criteria was the frequency with which waivers were granted.98 Making disqualification the general rule indicates a strong commitment to conflict-free advisory committee participation.99

For financial interests less than $50,000, the Evaluator can recommend a waiver, which must be reviewed by the FDA Commissioner personally. This, too, indicates a strong commitment to truly conflict-free recommendations. The CDER and the head of any sitting advisory committee have an interest in expedited review processes,100 and thus they may be less likely to perform an adequate search for other potentially well-qualified members before contemplating a waiver.101 The FDA Commissioner, on the other hand, has an interest in the appearance and actuality of conflict-free resolution. The negative fall-out from a drug recall is likely to be less severe if conflicts are not found among reviewing members. Moreover, the Commissioner is both the most visible and the most politically accountable member of the organization, and hence the Commissioner’s personal interest in conflict-free advisory committees aligns more closely with the public interest in the same.102

Even in the “limited cases”103 in which the Commissioner grants a waiver, participation is to be non-voting.104 While a member with minimal conflicts may be allowed to participate in the committee meeting, the member will not be allowed to vote. Thus, the member will not be allowed directly to affect the final outcome of a product-specific decision in which the member may have a financial interest. While limiting participation to non-voting might still allow

98. See, e.g., Lurie et al., supra note 7, at 1921 (concluding that conflicts of interest “rarely result in recusal of advisory committee members”); see also Dennis Cauchon, FDA Advisers Tied to Industry, USA TODAY, Sept. 25, 2000, at 1A.

99. Disqualifying a member from participating in the committee meeting at all implicitly acknowledges and lends credence to the criticisms leveled against granting waivers, even just for non-voting participation. See infra Part III.B.6 (arguing that any participation in the deliberative process, even on a non-voting basis, might taint the committee’s recommendation).

100. Cf. MANAGEMENT REVIEW, supra note 17, at ii (“Reviewers are under constant pressure to meet time goals.”).

101. See 5 C.F.R. § 2640.302(b)(4) (2007) (stating that “[t]he difficulty of locating a similarly qualified individual without a disqualifying financial interest” is one of the factors to be weighed in assessing whether or not the need for the member’s services outweighs her potential financial conflicts of interest).

102. Lower-level FDA officials are likely to be well aware of this interest and, like those making initial committee selections, are likely to limit their waiver recommendations accordingly.

103. DRAFT GUIDELINES, supra note 8, at 13 n.3.

104. See id. at 8, 14, 16, 16 n.4, 19, 20.
indirect influence, precluding voting participation by potentially conflicted members at the very least helps to avoid the appearance of impropriety, in keeping with the FDA’s goals in issuing these guidelines.

B. The Guidelines Leave Some Conflict of Interest Problems Unresolved and Could Create Others

In assessing the efficacy of these guidelines, one must determine, first, whether the Draft Guidelines will have any real effect. Because they are merely guidelines, the FDA is not bound to follow them. Second, if the guidelines are followed, one must evaluate whether they provide sufficiently strict parameters to prohibit any unduly conflicted committee member from influencing the committee’s recommendation. The question is whether, because the guidelines are full of noncommittal language and contain numerous exemptions, they permit Evaluators to evade the guidelines’ stated intent, allowing conflicted committee members to participate unnoticed and unannounced. Finally, even if the preclusionary spirit of the guidelines is followed and the public is fully informed, the FDA has not justified its need for even non-voting participation of conflicted committee members.

1. Do the Guidelines Mean Anything?

The positive analysis in Part II.A assumes that the FDA will follow its guidelines. However, the Draft Guidelines are not binding on the FDA, and they confer no legal rights. The guidelines make no secret of their status and prominently display the following caption: “This draft guidance . . . represents the Food and Drug Administration’s (FDA’s) current thinking on this topic. It does not create or confer any rights for or on any person . . . .” In issuing its guidelines, the FDA followed the attempt by the Office of Management and Budget (OMB) to clarify what guidance is allowed to be issued by federal agencies under the Administrative Procedure Act (APA). According to the OMB, a “guidance document” is “an agency statement of general appli-

---

105. See infra Part III.B.6 (questioning whether a potentially conflicted committee member should be allowed to participate in any of the committee’s deliberations, even if the member cannot vote).

106. See supra text accompanying note 10 (setting forth the stated purposes).

107. See DRAFT GUIDELINES, supra note 8, at 3.

108. Id. (emphases added).

 Capability and future effect ... that sets forth a policy on a statutory, regulatory, or technical issue or an interpretation of a statutory or regulatory issue.”

Guidance documents “include, but are not limited to, agency interpretations or policies that relate to ... compliance guides,” and the FDA issuance is explicitly titled a “Draft Guidance.” Among the purposes for which the OMB says a draft guidance may be used are “interpreting existing law ... or clarifying how [an agency] tentatively will treat or enforce a governing legal norm through a policy statement.”

Here, the FDA says that “[t]his guidance describes FDA’s policy in applying the statutory and regulatory requirements found in [applicable law].”

While the Draft Guidelines may describe the FDA’s policy, the FDA is under no legal obligation to follow them. This is reflected both in the OMB

110. OMB Bulletin, Final Bulletin for Agency Good Guidance Practices, 72 Fed. Reg. 3432, 3434 (Jan 25, 2007). The Bulletin further delineates “significant guidance documents” and “economically significant guidance documents.” See id. However, little seems to hinge on these definitions. They merely impose more stringent notice requirements, see id. at 3439-40, all of which the FDA has complied with in issuing the Draft Guidelines, up to and including a verbatim repetition of the suggested caption. Compare id. at 3437, with DRAFT GUIDELINES, supra note 8, at 3. In any case, no guidance documents are legally binding, which is the fact of utmost importance for this analysis.


112. DRAFT GUIDELINES, supra note 8, at 1; Notice of Draft Guidelines, supra note 8, at 13,805.


114. DRAFT GUIDELINES, supra note 8, at 3.

115. While beyond the scope of this Note, it is interesting to consider how courts would scrutinize FDA practices under the guidelines. The FDA has given notice and solicited comments, 72 Fed. Reg. 13,805, 13,805 (Mar. 23, 2007), which may alleviate fears about unanchored agency action. But see Robert A. Anthony, Interpretive Rules, Policy Statements, Guidelines, Manuals, and the Like—Should Federal Agencies Use Them To Bind the Public?, 41 DUKE L.J. 1311 (1992) (questioning the increased use of draft guidance by agencies as binding documents); Wilson, supra note 109. In addition to following procedures that would comply with Section 553 of the Administrative Procedure Act for notice and comment rulemaking, the FDA has arguably gone beyond a mere interpretive rule or policy statement by choosing “to implement a more stringent policy for considering eligibility for participation than would be permitted under the current legal framework.” DRAFT GUIDELINES, supra note 8, at 7 (emphasis added). In spite of this formality, which suggests binding rules, the draft guidelines are explicitly non-binding. It is unclear why the FDA would take the trouble to go through the notice and comment process (beyond simply following its own and the OMB’s “best practices”). Perhaps it is a political move, which the FDA thinks will silence and preempt its critics. If so, critics should take note of the great pains through which the FDA has gone not to bind itself, suggesting that it may intend to be bound even less than the exemptions and precatory language would otherwise allow. See infra Parts III.B.2, 5. Regardless of the niceties of such an administrative law inquiry, it is difficult to imagine who would mount a challenge to the guidelines. The groups most likely to file suit—a public interest group or a competitor whose business was harmed by the introduction of a new drug—would have a difficult time establishing standing and demonstrating
Bulletin, which does not intend “to inhibit the flexibility needed by agency officials to depart appropriately from significant guidance documents,” and the guidelines themselves, which permit Evaluators to “use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations.” The FDA specifically states that the guidance document “does not operate to bind FDA or the public.”

In spite of such explicit statements, the tone of the Draft Guidelines indicates that FDA Staff will be expected to follow them to the letter. The guidelines reflect the FDA’s current policy for determining committee member eligibility and its interpretation of the applicable conflict laws and regulations; the “FDA is committed to strictly adhering” thereto. The new guidelines were proposed “because of [the prior guidelines’] complexity and discretionary elements.” If these guidelines were adopted to minimize discretionary elements, one would expect that the new guidelines are to be less discretionary in their application. In fact, the FDA says that the new guidelines will alleviate the problems of discretion and public perception by “implement[ing] a more stringent approach for considering eligibility for participation in FDA advisory committee meetings.” The acting FDA deputy commissioner told the New York Times that a “significant number” of the agency’s present advisers would be affected by the new policy. Furthermore, incentives for Evaluators to find conflict-free committee members and the fact that waivers must be sought directly from the Commissioner are in keeping with the overall tone of strictness and address public concern about potential conflicts. Thus, although the guidelines are only a proposed “draft guidance,” this designation, and the disclaimers that the guidelines are non-binding, are in tension with the tone and purpose of the guidelines themselves.

It is unclear how that tension is resolved. But, perhaps some clarity is

---

117. DRAFT GUIDELINES, supra note 8, at 3.
118. Id.
120. Id. at 13,806 (emphasis added).
121. Id.
123. As discussed in the next Part, not much may hinge on its resolution, if the FDA is able to avoid the guidelines’ “strict” tone due to the absence of mandatory language. Of course, the refusal to propose mandatory language may simply be a way to deal with the OMB’s admonition that “guidance documents should not include mandatory language.” OMB Bulletin, Final Bulletin for Agency Good Guidance Practices, 72 Fed. Reg. 3432, 3436 (Jan. 25, 2007); see also Comm. Nutrition Inst. v. Young, 818 F.2d 943, 947 (D.C. Cir. 1987) (stating that “mandatory, definitive language is a powerful, even potentially dispositive, factor suggesting . . . substantive rules”). Perhaps anticipating pushback from pharma-
found in the following statement from the OMB: “[A] guidance document may explain how the agency believes a statute or regulation applies to certain regulated activities . . . . [W]hile a guidance document cannot legally bind, agencies can appropriately bind their employees to abide by agency policy as a matter of their supervisory powers over such employees without undertaking pre-adoption notice and comment rulemaking.”124 Because the FDA’s conflict review speaks to the FDA,125 the fact that it comes in guideline form may not hinder its effectiveness, if in fact the FDA staff and Commissioner follow it.

2. The Guidelines Contain Enough Gaps To Allow Their Recommendations To Be Effectively Avoided

Even assuming that the FDA will follow the letter of the guidelines, they contain enough wiggle room to allow Evaluators—should they so choose—to avoid the guidelines’ spirit. So, in actuality, little may turn on whether or not the guidelines are legally binding on the FDA. The guidelines repeatedly say that a member with certain financial interests “generally” will not participate,126 meaning that participation will not be warranted “in a large majority of cases.”127 In those “limited”128 situations in which the FDA Commissioner determines that participation is warranted in spite of conflicts of interest, the FDA “does not plan to consider voting participation,”129 so conflicted committee members “generally” will not vote.130 The implication of this language is clear: even if the FDA adheres to the guidelines’ terms, those terms give the FDA a way to circumvent their alleged purpose.131 For example, while members with

---

125. DRAFT GUIDELINES, supra note 8, at 3 (“This guidance document is intended for use by FDA staff (‘you’) involved with advisory committee matters.”).
126. DRAFT GUIDELINES, supra note 8, at 7 (emphasis added); id. at 12 (emphasis added).
127. Id. at 13 (emphasis added).
128. Id. at 13, 13 n.3, 20 n.5 (emphasis added).
129. Id. 16 n.4 (emphasis added).
130. Id. at 13 (“If the sum of those financial interests is less than or equal to $50,000, the member generally would participate but not vote.”) (emphasis added); id. at 19, 20 (emphasis added).
131. This problem is reflected not just in the provisional language but also in the Algorithm itself. Step Two asks the Evaluator to determine whether a meeting will have “a direct and predictable effect” on the member’s financial interests. DRAFT GUIDELINES, supra note 8, at 9. But, the OGE regulations define a direct effect as one with a “close causal link” and a predictable effect as one with “a real, as opposed to a speculative,” possibility of financial
financial conflicts may, in fact, “generally” not participate or vote, there is clearly the authority for them to do so.

3. No New Standards Are Given on Which To Base Waivers

Exacerbating the potential difficulty of the guidelines’ open-ended language is the fact that they contain no coherent standards on which to base waiver decisions. A major part of past criticism has been the inconsistencies with which waivers were granted.132 While the guidelines purport to provide consistency for recommending waivers, they do not add consistency to the process for granting waivers. One might assume that a well-taken recommendation would simply be granted, but this would obviate the need for recommendation and review in the first place; that is, if the Commissioner grants waivers on exactly the same basis on which the committee recommends them, then there is no role for the Commissioner to play. Presumably then, waivers would be granted based on the same individual interpretations of the same laws and regulations that led to prior complaints about inconsistencies.

Furthermore, no standards are given by which to consider waivers for those with interests over $50,000. After Step Four (B), if a member is determined to have attributable disqualifying financial interests greater than $50,000, the member is precluded from participating “in a large majority of cases.”133 However, the algorithm specifies only that “[i]n rare cases, you may wish to pursue whether a conflict of interest waiver is appropriate where the combined value of the disqualifying financial interests exceeds $50,000. In such cases, the Commissioner of FDA will review and make a determination on the appropriateness of a waiver.”134 However, no criteria to determine when such a waiver—for those who have financial conflicts greater than the precatory minimum—are specified. Under what criteria will the FDA Commissioner evaluate such conflicts? Will he use the same criteria as those set forth in Step Five for lesser conflicts? If so, what difference does the amount of disqualifying interests make? Or is one to presume—based on logic and the FDA’s repeated assurances that this is to be rare—that the criteria will be more stringent than those set forth for committee members with interests below the threshold? The guidelines offer no answers to these questions. Neither is it specified whether, in these “limited” instances, the committee member will be a voting or non-voting participant. One presumes the latter, since members with lesser conflicts are to be limited to non-voting participation, but, again, this is not stated. Given

132. See Notice of Draft Guidelines, supra note 8, at 13,806; Elizabeth R. Glodé, supra note 7, at 304-08.
133. DRAFT GUIDELINES, supra note 8, at 13.
134. Id. at App. I (Algorithm).
that the binding legal requirements allow for voting participation,\textsuperscript{135} the public could be faced with a situation under the FDA’s new guidelines in which those with conflicts of the greatest magnitude are afforded the greatest opportunity (voting participation) to affect the outcomes of the committees’ deliberations.\textsuperscript{136}

This problem is even more acute for those committee members for whom the staff “use[s] an alternative approach” to “satisf[y] the requirements of the applicable statutes and regulations.”\textsuperscript{137} In such cases, not only is there no consistency on the basis for granting a waiver, but there is no consistency on the basis for recommending a waiver. Evaluators are left on their own to interpret and apply the (morass of) conflict statutes and regulations—exactly the same situation that prompted severe criticisms and the FDA’s adoption of the prior and current guidelines on committee-member participation. In this situation, little seems to have been gained from the arduous and expensive process of giving notice of and seeking comment on the new guidelines.\textsuperscript{138}

4. Even If the FDA Follows the Draft Guidelines and Does Not Exploit Its Loopholes, How Will the Public Know?

There are two ways to handle conflicts of interest: disqualification and disclosure. Even assuming that the FDA is true to the letter of the Draft Guidelines and even assuming it does not exploit the loopholes in the text, the guidelines make no provisions for disclosure. While preventing conflicts is the first line of defense, disclosing them when they exist is necessary to ensure “transparency, clarity, and consistency of the advisory committee process and enhance public trust in this important function.”\textsuperscript{139} Disclosure—whether of recusal, waiver, or non-waiver determination—must be made in a timely manner, to allow the public and interested parties sufficient time to review the information prior to the affected committee meeting.

Great steps were made in the FDA’s disclosure of conflicts, largely as a result of the efforts of Public Citizen.\textsuperscript{140} However, many of those steps are the result of voluntary concessions by the FDA.\textsuperscript{141} It is troubling that there is no

\textsuperscript{135} 21 U.S.C. § 355(n)(4) (2006); see also supra notes 78 & 79 (discussing the statutory versus guideline allowances for voting participation).

\textsuperscript{136} Even under the code, a committee member is prohibited from voting where his own scientific work is involved. 21 U.S.C. § 355(n)(4) (2006); see also DRAFT GUIDELINES, supra note 8, at 16 n.4.

\textsuperscript{137} DRAFT GUIDELINES, supra note 8, at 3.

\textsuperscript{138} See Wilson, supra note 109, at 180 (discussing the agency “time and resources” expended in such an issuance).

\textsuperscript{139} DRAFT GUIDELINES, supra note 8, at 6 (giving the same as the intention of the FDA in adopting these guidelines).

\textsuperscript{140} See supra notes 7, 93, 94 (citing sources).

\textsuperscript{141} See, e.g., FDA, DRAFT GUIDANCE ON DISCLOSURE OF CONFLICTS OF INTEREST FOR SPECIAL GOVERNMENT EMPLOYEES PARTICIPATING IN FDA PRODUCT SPECIFIC ADVISORY
specific reference in the Draft Guidelines to a commitment to continue (and further) such disclosure. The FDA website indicates that the Draft Guidance on Disclosure represents the FDA’s current thinking on disclosure.\textsuperscript{142} The FDA further suggested that the Draft Guidelines “will be in concert with existing [disclosure] guidelines.”\textsuperscript{143} However, the FDA indicated that it is working on new draft guidance concerning disclosure,\textsuperscript{144} and a recent conversation confirms that this is still “in the works.”\textsuperscript{145}

In the case of waiver, the public is entitled to know what the conflict was (including its relative magnitude) and why it was waived;\textsuperscript{146} this should include the identity of the affiliated institution and whether it is the drug sponsor or a competitor.\textsuperscript{147} For public disclosure, speaking in terms of relative magnitude (as the 2002 Draft Guidance on Disclosure does\textsuperscript{148}) is perfectly acceptable, as long as the FDA is true to its word that conflicted members will generally not be allowed to participate and will never be allowed to vote.\textsuperscript{149} While

\textsuperscript{142} See \textit{Draft Guidance on Disclosure}, \textit{supra} note 141; accord Email from Heidi Rebello, Office of Public Affairs, Food & Drug Administration, to author (Apr. 24, 2007) (“[T]hese [guidelines] are in effect and are being followed.”) (on file with author).

\textsuperscript{143} \textit{Id}.

\textsuperscript{144} FDA News Release, FDA Announces Plan to Strengthen Advisory Committee Processes (July 24, 2006).

\textsuperscript{145} Telephone Interview with FDA Office of Policy Representative (Apr. 19, 2007) (notes on file with author).

\textsuperscript{146} Internal conflict disclosure should be both exact and complete. This Part refers only to public disclosure of this information.

\textsuperscript{147} The current Draft Guidance on Disclosure does not require the name of the competitor to be revealed. \textit{Draft Guidance on Disclosure}, \textit{supra} note 141, § V. Not specifically identifying the competitor company seems acceptable to protect privacy interests, but only if the possible effects of the committee’s deliberations on that competitor are described generally.

\textsuperscript{148} See \textit{Draft Guidance on Disclosure}, \textit{supra} note 141, § V.

\textsuperscript{149} Making public disclosures of relative magnitudes seems an adequate balance between privacy interests and the public’s right to be aware of conflicts. However, this absolutely depends on the near-uniform preclusion of members with disqualifying conflicts greater than $50,000. If, for example, the FDA was making its exceptions for hugely conflicted members (say, over $500,000 of direct financial interests), this should surely be disclosed. To that end, if the FDA grants a participatory waiver for individuals with conflicts over $50,000, then disclosure of the current magnitude of the waived interest, within a $100,000 range, ought to be disclosed. Currently, stock interests need to be disclosed only that they are “greater than $100,000.” \textit{Draft Guidance on Disclosure}, \textit{supra} note 141. For
disclosure of only relative magnitude seems an appropriate balance of the member’s privacy interest and the public’s interest in disclosure, the public has a right to know the exact type of interest that has been waived. For example, if no disqualifying interest was found based on a member’s de minimis stock exemption under Step Four (B) (less than $15,000), but the stock is held in an emerging pharmaceutical company and the value stands to go up ten-fold if the company’s new drug is approved, this will be of interest and concern and ought to be disclosed. Disclosure allows for closer public scrutiny and serves as a backstop to keep potentially conflicted members from voting with their pocket-books.

In cases where it is determined that no waiver is needed to allow for participation, the public is nonetheless entitled to know why this determination was made. At Steps Two and Three of the evaluation process, an Evaluator may determine that a committee member’s financial interest either will not be directly and predictably affected by the committee’s deliberations or that the financial interest is not disqualifying. In either case, the Evaluator is directed to draft a memorandum supporting the decision and to seek supervisory concurrence. The FDA indicated that it currently considers these determinations and the memoranda supporting them internal, deliberative documents, not to be disclosed to the public and not discoverable under the Freedom of Information Act. Assuming that the FDA follows the guidelines, it may well be that conflicts that are dismissed at this stage are worrisome. Nonetheless, if for no other reason than to avoid the appearance of impropriety, the FDA should consider large consulting arrangements, the only disclosure needed is that it is “greater than $50,000.” Finally, disclosure for large-magnitude contracts and grants needs to indicate only that the interest is “greater than $300,000 per year.” In each instance, disclosure needs to be sufficient (including on the high end) to allow public assessment of the conflicts’ relative magnitude and possible influence on the member’s record of participation.

150. Such disclosure is reflected in the current Draft Guidance on Disclosure, and should be adequate, as long as those guidelines are followed. But cf. supra Part III.B.1 (pointing out that guidelines are non-binding and will be effective in achieving their purposes only if they are followed).


152. See supra Parts II.B.2(b), (c).

153. Id.

voluntarily disclosing at least a summary of why certain conflicts were deemed unproblematic.

5. Will the “Exemptions” Swallow the Rule?

Just as the public has a right to know the relative magnitude of the exemptions granted, it also has the right to know what those exemptions are and why the interests they represent are waivable. Certain interests are considered “too remote or too inconsequential to affect the integrity of the services of the Government officers or employees to which such regulation applies.” However, a number of the exemptions contemplated in Step Four (B) are unclear; combined with the exception for university-funding in Step Two, they could lead to far greater conflicts being considered non-disqualifying than first appears.

The guidelines purport to be concerned with the “perception of [] conflict.” Given this concern, the “de minimis” exemption for security interests less than $15,000 that will be directly affected by the committee’s decision is untenable. While $15,000 may appear minimal to pharmaceutical companies and Washington bureaucrats and lawyers generally dealing with these guidelines, it is more than one-third the median household income. For seniors over age sixty-five, the group with the greatest health care needs and the most significant prescription drug costs, the de minimis exemption is more than half of the median income. When one considers the incredible amount of money at stake in the pharmaceutical industry and the effect that the FDA review process has on that pool, one meeting might have a significant impact.

156. Draft Guidelines, supra note 8, at 8.
157. 5 C.F.R. § 2640.202(a) & exs. 1-3 (2007); Draft Guidelines, supra note 8, at 15.
160. Census Report, supra note 158, at 4 (finding that the median household income for those over 65 was $24,509 in 2004).
162. See Cong. Budget Office, How Increased Competition From Generic Drugs Has Affected Prices and Returns from the Pharmaceutical Industry 49 (1998) (“[A]ccelerating the FDA review period by one year would have a much greater effect on the
on $15,000 worth of stock.

Second, one must question whether the $50,000 exemption for mutual funds that concentrate in the sector with regard to which the advisory committee is meeting makes sense. Even though the stock of the company whose drug is being reviewed may not be held by the fund, one would expect that the company’s competitors’ interests in the same industry (sector) are held. If the drugs are substitutes, the approval and availability of a new drug would decrease the demand for the drugs of its competitors, negatively affecting any interests held therein. Alternatively, the new drug could be a complement to an existing product, in which case a decision that increases the demand for the product being reviewed would be expected to increase demand for the complement and, consequently, the value of the committee member’s interests in the company that manufactures it. In either situation, the potential financial effect on the individual member’s financial interests is great.

Next, it is unclear how these exemptions interact with one another. For example, while the sector-specific mutual funds exemption does not apply to funds that “contain holdings that may be affected by the particular matter,” the de minimis exemption does apply to holdings that may be affected by the committee’s decision. May these exemptions be taken in conjunction with one another? The guidelines indicate that they can, directing the Evaluator to determine the amount of disqualifying interests after applying the (plural) “exemptions.” This would allow a committee member to have $50,000 worth of industry-specific mutual funds in the particular field at issue (presumably biotechnology) as well as $15,000 in stock in the company that manufactured the drug under review. This would exempt a single-meeting conflict for a single committee member well above the average median income of American families.

Finally, these exemptions must be considered in conjunction with Step Two’s exclusion of financial interests arising from university grants, and the present discounted value of the returns from marketing a new drug [than extending patent life by one year.”]. This is an amazing conclusion, given that a patent gives the holder a legal entitlement to a complete monopoly on the market for its drug, allowing sole use of the patented product and sole appropriation of monopoly rents. Viscusi et al., supra note 14, at 868-87, unless the patent-holder wishes to grant a license, in which case the company recoups licensing fees and royalties, id. at 868.

163. See 5 C.F.R. § 2640.201(b) & exs. 2, 3 (2007); Draft Guidelines, supra note 8, at 15.
165. See id. at 23.
166. 5 C.F.R. § 2640.201(b) & ex. 3. (2007).
167. Id. § 2640.202(a) & exs. 1-3(2006); Draft Guidelines, supra note 8, at 15.
168. See Draft Guidelines, supra note 8, at 13.
170. See Draft Guidelines, supra note 8, at 10.
combination threatens to undermine the efficacy of the guidelines. If a committee member is employed by a university that receives funding from, or has “a grant or contract with,” a drug company’s sponsor or its competitors “to conduct research on a product that is not the subject of the particular matter before the advisory committee,” the deliberations will ordinarily not be considered to have direct and predictable effects on this interest. But, while filtering corporate money through the university might decrease the appearance of conflict, it does not eliminate the potential for actual conflict. It is unreasonable to expect that a university researcher whose chair is endowed by and research funded by a corporate interest will not know who pays the bills, even if the university writes the checks. Making a decision adverse to the company’s financial interest might jeopardize funding for the researcher’s own livelihood, increasing the risk that the committee member would vote in line with the company’s interests, and the FDA should reconsider this exclusion. At the very least, such interest should not be categorically excluded at Step Two, and should be submitted to further scrutiny set forth in the algorithm. Such a change, along with resolution of the other uncertainties explored in this Part, would bolster the effectiveness (and credibility) of the FDA’s efforts to address conflicts among committee members.

6. The FDA Has Not Justified the Need for Non-Voting Participation by Conflicted Committee Members

Assuming that the guidelines are followed and its vagueries and exemptions are not allowed to defeat its purposes, the FDA has not justified its need for potentially conflicted committee members to participate, even on a non-voting basis. There is ample evidence that participation by a single individual in a group setting is enough to influence the outcome of the group’s decision. There are other options to obtain “essential expertise” and to achieve the FDA’s goal of appearing conflict-free.

The FDA can, and does, invite expert witnesses to present testimony or

---

171. Id. (citing 5 C.F.R. § 2640.103(a)(3) & ex. 2 (2007)).
172. The case for this complaint is made even stronger if the FDA does not follow its guidelines, or exploits their precatory language. In those instances, there is no indication of what sort of internal disclosures would be made—i.e., other committee members would not know that their fellow committee member was conflicted and would not be able to weigh the conflicted member’s contributions accordingly. Cf. infra note 181 (analogizing the participation of a conflicted expert to a jury’s determination of witness credibility).
173. See, e.g., DEBRA L. NELSON & JAMES CAMPBELL QUICK, ORGANIZATIONAL BEHAVIOR: FOUNDATIONS, REALITIES, AND CHALLENGES 334 (5th ed. 2006) (citing one disadvantage of group decision making as the possibility for “domination of the group by one forceful member . . . who may ramrod the decision”); ZUCKERMAN, supra note 7, at 2 (finding that a single “committee member[,] can have a disproportionate influence on approval recommendations” and describing “pressure to conform and to recommend approval”).
evidence to advisory committees. Just as these witnesses do not participate in internal committee deliberations on the recommendation to be made to the CDER, nor should conflicted committee members be able to do so. Allowing participation as an expert witness affords the committee access to the member’s “essential expertise” and “unique[]” qualifications without allowing the member to influence other members’ deliberations (beyond persuasiveness as a witness). Of course, the knowledge needed to approve a drug is highly technical and specialized, and industry insiders may be the only ones with sufficient direct experience to truly assess a drug’s effectiveness, but it is difficult to imagine any situations where participating as a non-deliberating, non-voting witness would be an insufficient to substitute for participation as a full, voting member. And, in those rare instances where this might occur, the guidelines suggest a formal process requiring assent directly from the FDA Commissioner. Presumably the FDA’s federal advisory committees are comprised of intelligent and competent people, generally well-versed enough in the specific science that they can understand the explanations of experts that are convened to explain clinical trials and results. By relegating financially conflicted members with “essential” expertise to the status of witnesses, the FDA can achieve its goals of “transparency, clarity, and consistency . . . and enhance[ing] public trust” while elevating fiduciary duty over financial inter-

175. FDA, Overview and General Information on Advisory Committee Membership, http://www.fda.gov/oc/advisory/vacancies/acvacfaq.html (last visited Apr. 23, 2007) (“Additional experts with special knowledge may be added for individual meetings as needed.”); cf. generally DRAFT GUIDELINES ON DISCLOSURE, supra note 141 (advising the SGEs serving as expert witnesses will generally be precluded from participating in advisory committee meetings).

176. There remains, of course, the possibility of a quid-pro-quo arrangement, as certain conflicted members are excluded while their colleagues, knowing of the excluded member’s interests, are allowed to participate and vote, with their roles likely to be reversed at a future meeting. One can only hope that the notion of civic virtue, which ought to be the cornerstone of public service will deter such an arrangement. While any evidence thereof could subject the members to criminal penalties, see 18 U.S.C. §§ 201 et seq. (2006), such an arrangement, especially a tacit one, would be difficult to prove.


179. The Public Citizen study cited above concluded that “there was no relationship between the conflict rate and voting outcome,” Lurie et al., supra note 7, at 1925, meaning that the committee would not have voted differently had the conflicted member been excluded from voting Id. at 1926. However, given the evidence of the potential for influence merely from participation, ZUCKERMAN, supra note 7, at 2, one should question whether Public Citizen’s conclusion would have been different if the conflicted committee members were precluded from participating in the deliberative process at all.


181. Like a jury they could then make a determination of the scientist’s credibility in presenting his results and make an independent determination about whether the potential benefits of the drug outweigh its risks based on the evidence presented.

182. DRAFT GUIDELINES, supra note 8, at 5-6.
CONCLUSION

The FDA has set forth a framework with the potential to alleviate many of the concerns about conflicts of interest among advisory committee members making recommendations concerning specific drugs. As a “rule,” members with financial conflicts may not participate in committee meetings implicating their own interests. The guidelines are poised to achieve the FDA’s stated goals of simplification, clarity, consistency, and enhanced public confidence. Nonetheless, the guidelines contain ample space within which FDA Evaluators may confound those purposes and maintain a practice of conflicted members participating in meetings, the outcome of which may affect their financial interest. Much will depend on how the FDA implements its guidelines—whether it follows both their letter and their spirit—as well as how the FDA integrates its forthcoming disclosure guidance. After all, the “policy” behind the Draft Guidelines is the same as that which led to the adoption of the prior guidelines. Waiting for the same ends—simplicity, clarity, consistency, and public confidence—to be effectuated by the adoption of the new Draft Guidelines is a little like waiting . . . for Godot.183

183. SAMUEL BECKETT, WAITING FOR GODOT: A TRAGICOMEDY IN TWO ACTS (1954).