Robert M.
La Follette School of Public Affairs
at the University of Wisconsin-Madison

Working Paper Series
La Follette School Working Paper No. 2009-022
http://www.lafollette.wisc.edu/publications/workingpapers

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August 12, 2009

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Information Costs, Policy Uncertainty, and Political Control: Federal Advisory Committees at the FDA

Draft. 08/12/09

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[1] We thank George Krause, Marc Ratkovic, and Susan Yackee for their helpful suggestions, and Britta Johnson and Karina Silver for their valuable research assistance. We also thank Daniel Carpenter for sharing his coding procedures.

Abstract

Federal agencies make extensive use of advisory committees. Committee consultation may provide agencies with policy expertise or help legitimize their policy positions. In addition, advisory committees may facilitate political accountability by making the agency decision-making process more transparent and by giving certain interests seats at the table. We investigate these functions by analyzing the use of advisory committees by the FDA in the approval of drugs and medical devices. Specifically, we consider both the choice to consult an advisory committee and the effect of votes within advisory committees on agency decisions. The analysis provides empirical support for existing models of FDA drug and device approval; reveals that committee consultation does not necessarily extend review times if it reduces the FDA's policy uncertainty sufficiently; and, in view of what we know about the role of legislative coalitions in defining committee memberships, suggests that FDA advisory committees likely serve a control function (although their potential to do so may have declined beginning in 2001). As a result, this study provides incremental gains in three disparate literatures and, most importantly, provides a rare statistical assessment of committee impact on agency decision-making, which is usually just assumed.

The Food and Drug Administration (FDA) may choose to consult advisory committees in the course of performing its regulatory functions. Most notably, the FDA regularly seeks advice from advisory committees when deciding whether or not to approve pharmaceutical drugs and medical devices for marketing. These committees are composed of private citizens with some expertise regarding the drug or device application at hand, including scientific and medical experts, and representatives of relevant industry, consumer, or patient groups. The FDA retains all formal decision-making power; committees merely offer recommendations. Indeed, news reports in recent years have accused a politicized FDA of ignoring "scientific" committee advice. Nevertheless, most popular and academic accounts suggest that committees wield influence over FDA decision-making.

The objective of our study is to elucidate the role of advisory committees with regard to the FDA's approval of pharmaceutical drugs and medical devices. In particular, our analysis explains when the FDA seeks committee advice, how it responds to that advice, and whether or not the role of advisory committees changed in 2001, as some popular accounts suggest. In the process, we test Carpenter's (2002) theory of FDA drug approval with more varied data, explore the implications of our results for theories of political accountability, and contribute to a literature that focuses on the relationship between administrative procedures and the time it takes government bureaus to accomplish their regulatory tasks. Perhaps most importantly, we provide a rare statistical analysis of the impact of committee advice a federal agency's decision-making.

Specifically, we analyze 1997-2006 drug and medical device approval data. We find that our measures of policy uncertainty correlate with the FDA's decision to consult advisory committees; that an increase in the proportion of committee members voting for drug approval increases the probability of FDA approval; and that an increase in the proportion of committee

members voting for approval reduces the time it takes for the FDA to approve a drug or device application. These results are consistent with the theory that drug and device approval is driven by the FDA's desire to reduce its policy uncertainty, and that the agency consults committees in order to decrease this uncertainty.

In addition, in view of the FDA's resource constraints, need for expertise, and statutorily mandated advisory committee memberships, as well as the transparency that committees bring to the agency's decision-making process, the results are consistent with the theory that advisory committees serve to control agency decision-making. Was control attenuated by FDA actions under the Bush administration? On the one hand, rates of committee referral declined significantly after 2001. On the other hand, there is no indication that the FDA places less weight on committee advice after 2001.

Finally, the results contradict some previous findings that advisory committee consultation introduces delay in the regulatory process (e.g., Balla & Wright 2003). Because it appears that the FDA consults committees in large part to gain expertise, committees may speed regulatory decision-making in those cases in which committees sufficiently decrease the agency's uncertainty.

In the sections that follow, we review the relevant literatures, present a reputational model of FDA decision-making, derive hypotheses, and test them using the data we collected. We conclude with a review of this study's implications for the literatures on which we focus.

FDA Drug and Device Approval

The FDA faces a "demanding and conflict-ridden environment" characterized by constant uncertainty (Quirk 1980, 206). The pharmaceutical and medical device industries and patient groups pressure the FDA to approve products for marketing quickly, but there also is substantial

political pressure for more stringent consumer protection. Unfortunately, "in order to make decisions with reasonable speed and accuracy, given the complexity and magnitude of its information-processing requirements, the FDA would need either a great deal of slack resources…, or a highly sophisticated management system," neither of which it is thought to possess (Quirk 1980, 207). FDA capacity for reviewing drugs has increased in recent years due to the Prescription Drugs User Fee Act of 1992 (Carpenter 2004a & 2004b), and the same may have happened for devices with the passage of the Medical Device User Fee and Modernization Act (MDUFMA) of 2002. Yet, agency capacity is unlikely ever to be sufficient to meet the demands of the most influential political groups (Carpenter 2004b). In sum, the FDA is an agency in constant need of information and information-processing capacity as it confronts a very demanding and variable political environment (Committee on the Assessment of the US Drug Safety System 2007).

Daniel P. Carpenter (2002) models FDA drug approval as an optimal stopping problem. The FDA's driving motivation is to protect its reputation. Drug approval presents a problem, however, because the agency is uncertain about the safety (and efficacy) of drugs under consideration. The FDA uses review time to collect and process information in order to reduce that uncertainty. In other words, delaying a decision is beneficial to the agency. Waiting is also costly, however, because drug sponsors and disease advocates wish to have drugs come to market as soon as possible. Moreover, the media has the power to magnify the pleas of disease advocates and sufferers. According to Carpenter, the agency will stop attempting to reduce its uncertainty and will approve a drug if the benefits of collecting more information are outweighed by the political costs of delay, i.e., when it finds it optimal to stop learning and to approve a drug.

Our analysis enables us to test the theory that Carpenter (2002) presents using data from different years and more varied types of drug applications. Basically, the data enable us to observe whether political or technical uncertainty about an application drives the FDA's decision to consult committees, and whether obtaining uncertainty-reducing information reduces approval times.[2] In addition, we test Carpenter's particular model by including political, media, and interest group variables, and by comparing drug and device results to determine whether his model applies to the approval of medical devices.

Political Control and Advisory Committees

There is substantial research in public administration and political science that focuses on the role of administrative procedures in facilitating various notions of agency accountability. A notable literature in political science, for example, anchored by Mathew D. McCubbins, Roger G. Noll, and Barry R. Weingast (1987), views administrative procedures, such as advisory committees, as devices that legislative principals employ to control the behavior of bureaucratic agents. According to these authors, federal advisory committees may render agency decisions more visible and therefore help political principals overcome informational deficits that prevent oversight, as meetings are advertised in the *Federal Register* and most are open to the public. In addition, committees may enable legislative coalitions to enfranchise favored groups in agency

[2] "Political uncertainty" refers to uncertainty about the political costs that various principals may impose on the agency for making a particular decision. "Technical uncertainty" refers to uncertainty as to whether or not a drug or device's benefits outweigh its risks—i.e., the type of uncertainty on which Carpenter (2002) focuses. The model we lay out later assumes that committee consultation may help alleviate both types of uncertainty; and it also incorporates the perspective that consulting a committee may shield an agency from political repercussions, as much of the literature claims (e.g., see Jasanoff 1990).

decision-making processes, as legislation often explicitly details the groups that must be represented on such committees (McCubbins et al. 1989).

Steven J. Balla and John R. Wright (2001) consider explicitly the control function that federal advisory committees may serve. They assert that the Environmental Protection Agency's National Drinking Water Advisory Council represents an attempt by Congress to reproduce the political environment under which the Safe Drinking Water Act Amendments were passed. Drawing directly from the deck-stacking theory of McCubbins, Noll, and Weingast (1987, 1989), their theory stipulates that exposing the EPA to a similar political environment would lead agency policymakers to make decisions that the enacting legislative coalition would have made. Specifically, they assert that the enacting coalition in Congress wants interest group representation on the council to mirror the interest group presence it faced when it passed the Safe Drinking Water Act Amendments. The council does not make binding decisions, but, according to the authors, by allocating membership rights to particular interest groups, Congress is able to control the information that influences agency decision-making.

Some scholars consider such rational-choice theories of institutional design to be simplistic and misguided (West 2005). Further, although there is evidence that legislative coalitions attempt to control bureaucratic discretion using administrative procedures, there is only modest empirical evidence that "deck stacking" benefits the interests it purportedly advantages—see Huber and Shipan (2007) for a review. Nevertheless, exploring the theory of control that McCubbins and colleagues offer helps us understand the role of advisory committees in promoting notions of accountability that require that agencies utilize committee advice. In particular, our analysis helps us understand whether there has been a change in terms of the accountability that FDA advisory committees promote.

FDA Advisory Committees and Political Control

Popular media accounts suggest that FDA advisory committees may facilitate the first type of control that McCubbins and colleagues (1987) present. Instances in which FDA actions contradict committee decisions often generate controversy and thereby facilitate oversight of bureaucratic decision-making (e.g., see GAO 2005). Indeed, as we mention below, legislative coalitions have encouraged the FDA to consult committees when it comes to controversial issues, which facilitates this type of oversight. Our statistical results also enable us to determine whether or not the FDA seeks out and responds to the information provided by advisory committees, which can help us understand whether or not FDA committees plausibly provide the "deck stacking" form of control. However, in order for our results to serve as evidence of such control, we first must establish that legislative coalitions have sought to determine the interests represented on advisory committees, and that they have made the FDA dependent on committee information by limiting its resources.

As of the passage of the Food and Drug Modernization Act in 1997, through public law, legislative coalitions had recommended or mandated that advisory committees be employed as sources of information in determining the safety, effectiveness, and manufacturing practices for drugs and devices; that committees be consulted if drugs under consideration were politically or scientifically controversial; that a certain number and type of experts be given membership; that industry, patient, and consumer representatives be more actively involved in committee meetings; and that records of committee action be better publicized, especially to drug applicants (Schulman et al. 2002). For example, drug committees on average have 11 voting members present at any given meeting, most of whom are scientific or medical experts. Membership must include one voting consumer representative and one non-voting industry representative, and

there may be one voting patient representative. Finally, there is reason to believe, because of Balla and Wright's study of the EPA, that bureaucrats keep the wishes of enacting coalitions in mind when recruiting committee members. Indeed, it appears that members often are nominated by or recruited from prominent groups and associations.[3]

Moreover, legislative coalitions have the power to determine whether the FDA relies on committees for information by determining their organizational resources. Susan L. Moffitt (2002) finds that the greater the technical uncertainty surrounding a drug, the lower the administrative capacity of agency divisions, and the better the academic reputation of a committee chairman, the more likely the FDA is to consult drug committees. In other words, keeping agency resources low increases the influence of the advice from drug and device committees. (Interestingly, it appears that the imposition of user fees and the subsequent increase in the number of agency staff may have contributed to a decline in committee consultations). We do not claim that the FDA's low organizational capacity is the result of legislative coalitions consciously trying to strengthen the control function of committees. However, there is a clear relationship between FDA capacity and committee consultation and, historically, the organizational resources at the FDA have been low relative to its tasks (Quirk 1980; Committee on the Assessment of the US Drug Safety System 2007).

It is clear, therefore, that legislative coalitions have sought to make the FDA dependent on committee information, and that they have sought to influence agency advice by dictating committee membership. What we do not know, but what our analysis tells us, is whether the FDA responds to the information it receives from committees. Our results reveal whether or not committee information influences FDA behavior, and therefore reveal whether or not committees

[3] For example, see "Overview and General Information on Advisory Committee Membership," available: http://www.fda.gov/oc/advisory/vacancies/acvacfaq.html (Accessed: 02/22/2009).

could be serving a control function. In addition, we include a measure capturing whether a drug or device application was filed during the Clinton administration or Bush administration, as well as a variable that interacts this measure with the committee vote. If the FDA's information-processing capabilities have increased during the years our data cover, or if the Bush administration indeed is more resistant to committee advice and outside control, then one should expect the FDA to consult committees, and act in accordance with committee advice, less frequently after 2001.

Administrative Procedures and the Speed of Bureaucratic Action

Lawmakers and the public have long expressed concern over the slow speed with which they perceive regulatory agencies take action. The time it takes agencies to issue rules and standards, or perform other regulatory tasks, may be costly to the organizations and individuals that regulatory actions affect, especially pharmaceutical companies and disease sufferers. Moreover, an increase in the time it takes to perform regulatory functions may translate to significant monetary costs for government (Balla & Wright 2003). Variations in the time it takes to accomplish regulatory tasks often is attributed to the complexity of the subject matter a regulatory action addresses, political influences, and the procedural complexity of undertaking regulatory action (Kerwin & Furlong 1992).[4] In addition, administrative procedures increase the visibility of agency action and involve more participants in the process, perhaps introducing costly delay. Administrative procedures such as those we discuss above, those meant to enhance some form of accountability into bureaucratic policymaking, are thought by many to extend the time it takes agencies to perform their regulatory functions.

[4] McCubbins, Noll, and Weingast (1987) assert that rules that introduce delay are meant to stack the deck in favor of groups for whom delay is advantageous, and to disadvantage groups for whom delay is costly.

Although the introduction of new administrative procedures often is thought to introduce delay in bureaucratic processes, certain procedures, such as consensual rulemaking procedures, are thought by some to reduce the time it takes agencies to accomplish their tasks. Consensual rulemaking procedures bring together stakeholders during the rulemaking process with the hope of making regulations more effective, timely, and responsive to changing stakeholder situations. Some suggest that procedures that breed consensus early on should increase the speed of regulatory action by limiting stakeholder challenges (see, e.g., Harter 1982; Susskind and McMahon 1985). Such procedures also should increase the speed of bureaucratic action if they enable agencies to gather up-to-date technical expertise that agencies are likely to lack (Weimer 2006).

Although by some standards FDA committee meetings are not held early in the approval process, the agency has at times welcomed the inclusion of various political constituencies on drug and device committees. According to the FDA, doing so may attenuate conflict between different interests and therefore decrease approval times, perhaps because the information meetings provide dispels some suspicions (Lewis 2000). Moreover, the technical information that drug and device committees yield may further reduce review times. Recall that Carpenter (2002) asserts that FDA policymakers wish to minimize the risk of reputation costs that come with approving what ultimately turn out to be dangerous drugs. His theory suggests that if the FDA is able to get such technical information more quickly, then review times should decrease, all else being equal.

Nevertheless, scholars have obtained mixed results regarding the effect of such procedures on the time it takes to develop and issue rules (Balla & Wright 2003; Coglianese 1997; Kerwin 1999; Kerwin & Furlong 1992). In addition, empirical studies of consensual

rulemaking have focused their attention on negotiated rulemaking committees and have largely neglected other examples of consensual regulatory procedures, such as federal advisory committees, despite the fact that federal advisory committees are far more prevalent than negotiated rulemaking committees. Balla and Wright (2003), to our knowledge, have published the only quantitative study to consider federal advisory committees as a means of reducing rulemaking times. The authors sample 170 major rules across 40 agencies between 1996 and 1999. They conclude that advisory committees may actually slow the rulemaking process.

Moffitt (2002) also considers the effect of FDA drug advisory committees on review times. She includes a committee-consultation indicator variable in a model similar to the duration model in Carpenter (2002). The results are weakly significant, but it appears that drug committees *reduce* review times. These results are not too surprising if review times are tied to the FDA's policy uncertainty, and if the FDA consults committees in order to reduce this uncertainty. Once it decides to consult committees, the FDA must schedule a meeting, make notice of that meeting, make various arrangements, and put together meeting materials. The procedures required to get that additional information introduce delay, just as scholars such as Cornelius M. Kerwin and Scott R. Furlong (1992) assert. Yet, it is plausible that committees reveal sufficient uncertainty-reducing information to compensate for this effect, thereby yielding a net reduction in review times. Our results enable us to explore whether or not this is the case.

Brief Overview of FDA Drug and Device Review

The responsibility for reviewing applications for the marketing of drugs and medical devices is divided between two centers at the FDA. The Center for Drug Evaluation and Research is responsible for conducting reviews of new drugs, generic drugs, and over-the-counter drugs, as well as undertaking various post drug-approval activities; while the Center for

Devices and Radiological Health regulates the marketing of medical devices and radiation-emitting products. Our study focuses on the review of New Drug Applications (NDAs) for brand-name drugs and on the review of applications for "class III" medical devices (PMAs), as they referred to committee in sufficiently high numbers. Devices classified as "class III" are those devices "that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury" (FDA Web site).

Consistent with earlier studies, our study focuses on original product applications (as opposed to supplemental applications for drugs or devices that already have been approved in some form) because they are referred to advisory committees at far greater rates and typically involve greater technical uncertainty and political stakes. The applications contain results from all required clinical studies, which the applicant typically conducts. Once the appropriate center accepts the application, it must determine whether or not a drug or device is "safe and effective." If the center determines that a product is safe and effective for its intended uses, then the FDA approves it for marketing.

Committees may assist the centers in their review of drug and device applications, help them establish general regulatory guidelines, or provide answers to any other questions that the centers may have. Our focus is on committee votes that assist the FDA in determining whether drugs and devices are "safe and effective." For our purposes, drug and device committees are similar (although the charters of device committees need not be renewed every two years). They are governed by the provisions of the Federal Advisory Committee Act (FACA) and the Freedom of Information Act (FOIA). For example, meeting materials must be made available to the public unless granted an exemption under FOIA, and FACA demands that committee

meetings be open to the public and that committee membership be "balanced" in terms of the interests represented. In addition to these general guidelines set for all federal advisory committees, as we note above, over the years Congress has included provisions in legislation that increasingly define the role, responsibilities, and membership of advisory committees at the FDA.

Theoretical Model of FDA Decision-making

The theories we review above emphasize informational and political factors that influence agency decision-making. The model of FDA decision-making that we present below, which focuses on the agency's decision to consult an advisory committee and approve or reject a drug or device application, takes into account these factors and generates some testable predictions. In addition, in view of the implications of our model and the theory that Carpenter (2002) offers, we hypothesize certain relationships between the time it takes to approve an application and the FDA's policy uncertainty and political concerns.

We employ a simple decision-theoretic framework with the following sequence of actions.[5] First, the FDA receives and files an application and estimates the benefits and costs associated with processing, and accepting or rejecting, that application. Second, using these estimates, the agency decides whether or not to consult a committee. Finally, after analyses are conducted in-house or with the help of an advisory committee, the FDA updates its estimates of

[5] The model involves numerous simplifying assumptions and does not formalize many aspects of the decision-making process (e.g., repeated interactions with firms regarding particular submissions). We generated this simple model to help us illustrate and keep clear how the different factors in the literature come to bear in our empirical analysis, and we leave it to future scholarship to incorporate these insights into formal theories of committee consultation.

benefits and costs and decides whether or not to approve the product application. We review each step in turn below.

First, the FDA estimates the product's benefits (b) and risks (r); the probability (p) that the medical benefits outweigh the risks [i.e., $\Pr(b/r > 1)$]; the organizational benefits (B) of approving (rejecting) when the medical benefits outweigh the risks (when the risks outweigh the benefits), i.e., the organizational benefits of making a "technically correct" decision; the information-processing costs (I) in terms of the resources and time the agency will need to identify the probability that a product's benefits outweigh its risks; the political costs (P) of deciding against the interests of organized political actors (especially firms, patient groups, and consumer groups); its uncertainty (u) about the political costs of making a given decision, i.e., its "political uncertainty"; and, finally, the political cover (t) that consulting an advisory committee may provide. For simplicity, we roll u and t into a function $\alpha(u,t)$, where $\partial\alpha/\partial \mathrm{u} > 0$ and $\partial\alpha/\partial t > 0$. All of the above parameters are strictly positive and $\alpha(u,t) > 1$.

The FDA then uses its estimates of the above parameters to decide whether or not to consult an advisory committee. To do so, it estimates with error the optimal action, approve (A) or reject (R), if it were to consult an advisory committee (C) and if it were not to consult (N). The FDA estimates and compares the four possible utilities (U_{AC}, U_{RC}, U_{AN}, and U_{RN}) with errors (ε_{AC}, ε_{RC}, ε_{AN}, and ε_{RN}) that are i.i.d. and standard-normal. The random utilities from each of the four possible choices appear below.

Committee Consultation

Approval: $U_{AC} + \varepsilon_{AC} = pB - P_A - I_C + \varepsilon_{AC}$

Rejection: $U_{RC} + \varepsilon_{RC} = (1-p)B - P_R - I_C + \varepsilon_{RC}$

No Committee Consultation

$$\text{Approval: } U_{AN} + \varepsilon_{AN} = pB - \alpha(t,u)P_A - I_N + \varepsilon_{AN}$$

$$\text{Rejection: } U_{RN} + \varepsilon_{RN} = (1-p)B - \alpha(t,u)P_R - I_N + \varepsilon_{RN}$$

In deciding whether or not to consult a committee, the agency compares the optimal estimated utility from consulting with the optimal estimated utility from evaluating the application without committee consultation.[6]

Finally, after the FDA has or has not consulted a committee and has expended time and resources (I) to research the benefits and risks of a product, it updates its belief about whether or not the benefits outweigh the risks, and decides whether to approve or reject the application. Again, we assume that the agency may make mistakes in deciding which of the two actions is optimal.

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[6] It may be optimal to make a different decision if it consults a committee than if it keeps the analysis in-house. For example, suppose that the FDA estimates that, if it were to evaluate an application in-house, its utility from approving an application would outweigh the utility it derives from rejecting it:

$$U_{AN} > U_{RN}$$

$$pB - \alpha P_A - I_N > (1-p)B - \alpha P_R - I_N$$

$$p > \frac{\alpha(P_A - P_R)}{2B} + \frac{1}{2}$$

Similarly, if it were to consult a committee, approval is the optimal decision if:

$$p > \frac{P_A - P_R}{2B} + \frac{1}{2}$$

Whether or not the two above conditions hold simultaneously depends on whether the agency estimates that $\alpha(P_A - P_R)/2B$ is greater than or less than $(P_A - P_R)/2B$, as the former may be more negative or more positive than the latter.

Note that, via $\alpha(u,t)$, which is greater than one, the model states that consulting an advisory committee reduces political uncertainty and attenuates political costs, as we assume $\partial\alpha/\partial \mathrm{u} > 0$ and $\partial\alpha/\partial t > 0$.[7] This feature captures the notion that consulting committees provides the FDA with political information (key interests enjoy membership rights and all principals are better able to observe and comment on agency decision-making) and that consultation potentially enhances the legitimacy of making a technically correct decision (e.g., see Jasanoff 1990). In other words, consulting a committee provides the FDA with political information (information about the preferences of political principals) in addition to technical information, and it makes it relatively more rewarding for the agency to make a technically correct decision [i.e., leads it to value $\Pr(b/r > 1)$ relatively more].

Another feature of the model worth emphasizing is that the political costs that organized interests impose in response to product approval (P_A) and rejection (P_R) are unrelated to the FDA's estimate of the probability (p) that the medical benefits of a product outweigh its risks. The agency's estimate of p takes into account all factors that an agency considers when determining the technical benefits and risks of a product, including the general political fallout from the public and top-level government officials that may come if a product ultimately results in greater patient harm than benefit. The more uncertain the agency is about whether or not the benefits outweigh the risks (i.e., as p approaches .5), the lower the expected political benefit of the optimal decision.

The political costs (P_A and P_R), on the other hand, are meant to capture the costs resulting from organized groups (e.g., firm lobbyists, disease sufferers, consumer groups, the

[7] Letting P depend on whether or not a committee is consulted, and subsequently incorporating uncertainty about the costs it represents, would make for a more precise and informative theoretical model. We incorporate these factors using the alpha term, however, in order to facilitate exposition and to more clearly motivate the statistical models.

president, etc.) pressuring the agency to reject or approve a drug regardless of p . Groups may impose costs via formal challenges to an agency decision in other formal venues, such as the courts, or by shaping public opinion in a manner that is detrimental to the agency's reputation. We assume that this is political pressure that is essentially unrelated to whether or not the FDA views the medical risks as outweighing the benefits because organized groups—especially firms and patient advocates—often have a very different conception from the agency (which has a broader constituency) of whether or not technical benefits outweigh risks. Committee consultation may provide political cover for the FDA in part because committee deliberations may help moderate the potentially extreme positions of organized groups that may have an incomplete understanding of the relative benefits and risks of a product prior to committee deliberations.

Consultation Decision

The model enables us to illustrate the impact of key factors emphasized in the theoretical literature. It reveals clear monotonic relationships between the comparative utility of consulting a committee ($U_C - U_N$) and information-processing costs (I_C, I_N), uncertainty about the preferences of political principals (u), and the political cover (t) that consulting an advisory committee may provide from the costs these principals may impose (making it relatively more beneficial for the agency to make a technically correct decision). Moreover, because the FDA is assumed to make utility calculations with error, the model reveals the impact of these factors on the probability that the agency will choose to consult an advisory committee, i.e.,

$\Pr(U_C - U_N > \varepsilon_N - \varepsilon_C)$.

The FDA's estimate of the probability that approval is the technically correct decision (p) and its estimate of the political costs (P_A, P_R) of displeasing political principals do not have

a monotonic influence on the estimated utility of committee consultation.[8] But we assume that the FDA is uncertain about the relative benefits and risks of a product before it processes application-related information (i.e., we assume that p is close to 0.5). This renders the benefits of making a technically correct decision essentially irrelevant in the consultation decision. In addition, the empirical portion of this study enables us to control for some political costs (P_A, P_R), which are independent of p by construction.

Comparing the four possible conditions under which consultation is optimal enables us to generate the following hypotheses. (See previous footnote for derivations.)

H1: The probability of committee consultation increases as the cost of processing information internally increases [$\partial \Pr(U_C - U_N > \varepsilon_N - \varepsilon_C)/\partial \mathrm{I_N} > 0$]. Conversely, the

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[8] In order to say something about the general impact of various factors on the probability that the FDA will choose to consult committees, one must evaluate the utilities of all four possible combinations of optimal actions.

A) $U_{RC} + \varepsilon_{RC} > U_{RN} + \varepsilon_{RN}$

$$(1-p)B - P_R - I_C + \varepsilon_{RC} > (1-p)B - \alpha P_R - I_N + \varepsilon_{RN}$$
$$\alpha P_R - P_R + I_N - I_C > \varepsilon_{RN} - \varepsilon_{RC}$$

B) $U_{AC} + \varepsilon_{AC} > U_{RN} + \varepsilon_{RN}$

$$pB - P_A - I_C + \varepsilon_{AC} > (1-p)B - \alpha P_R - I_N + \varepsilon_{RN}$$
$$B(2p-1) + \alpha P_R - P_A + I_N - I_C > \varepsilon_{RN} - \varepsilon_{AC}$$

C) $U_{RC} + \varepsilon_{RC} > U_{AN} + \varepsilon_{AN}$

$$(1-p)B - P_R - I_C + \varepsilon_{RC} > pB - \alpha P_A - I_N + \varepsilon_{AN}$$
$$B(1-2p) + \alpha P_A - P_R + I_N - I_C > \varepsilon_{AN} - \varepsilon_{RC}$$

D) $U_{AC} + \varepsilon_{AC} > U_{AN} + \varepsilon_{AN}$

$$pB - P_A - I_C + \varepsilon_{AC} > pB - \alpha P_A - I_N + \varepsilon_{AN}$$
$$\alpha P_A - P_A + I_N - I_C > \varepsilon_{AN} - \varepsilon_{AC}$$

The effects of p, P_A, and P_R are not monotonic across the four conditions. If we assume that p is close to 0.5, however, then B becomes largely irrelevant.

probability of committee consultation decreases as the cost of processing information with the help of a committee increases [$\partial \Pr(U_C - U_N > \varepsilon_N - \varepsilon_C)/\partial \mathrm{I_C} < 0$].

H2: The probability of committee consultation increases as a committee's ability to reduce an agency's uncertainty regarding the political cost of its decision increases [$\partial \Pr(U_C - U_N > \varepsilon_N - \varepsilon_C)/\partial \mathrm{u} > 0$]. (This is, because $\partial\alpha/\partial \mathrm{u} > 0$.)

H3: The probability of committee consultation increases as the relative political cover that it provides increases [$\partial \Pr(U_C - U_N > \varepsilon_N - \varepsilon_C)/\partial \mathrm{t} > 0$]. (This is, because $\partial\alpha/\partial t > 0$.)

Approval Decision

Our analysis of approval decisions focuses exclusively on the FDA's decision to approve or reject an application *after* it has consulted an advisory committee. The decision depends on the realization of all of the above parameters except those capturing information-processing costs, as those are sunk because they already would have been incurred. We assume that the committee vote reveals a probability that the benefit of a drug or device outweighs its risk, which the FDA uses in place of its previous estimate of this probability. In other words, the committee vote may be equated with the probability that a drug or device's benefits outweigh its risks [$p = \Pr(b/r > 1)$]. Specifically, the model suggests that the FDA will approve a drug if it believes that the probability that the benefits outweigh the risks is sufficiently high to compensate for the net political cost its decision may yield [$p > (1/2) + (P_A - P_R)/2B$]. Again, because the FDA makes this calculation with error, one can state hypotheses in terms of the probability that the FDA will come to this conclusion.[9]

[9] The derivation is as follows:

$$\Pr(U_A + \varepsilon_A > U_R + \varepsilon_R) =$$

H4: The probability of approving a drug or device application increases as the proportion of committee members voting for approval increases [$\partial \Pr(U_A - U_R > \varepsilon_R - \varepsilon_A)/\partial \mathrm{p} > 0$].

H5: The probability of approving a drug or device application decreases as the political cost of approval (typically imposed by consumer groups) increases [$\partial \Pr(U_A - U_R > \varepsilon_R - \varepsilon_A)/\partial \mathrm{P_A} < 0$].

H6: The probability of approving a drug or device application increases as the political cost of rejection (typically imposed by patient groups and firms) increases [$\partial \Pr(U_A - U_R > \varepsilon_R - \varepsilon_A)/\partial \mathrm{P_R} > 0$].

Review Time

According to H1, as the FDA's estimate of I_N increases or its estimate of I_C decreases, the probability that it will consult an advisory committee increases. If the cost associated with the time it takes to process an application indeed is the dominant information-processing cost that the FDA incurs (e.g., see Carpenter 2004a), then one may put forth the following hypothesis:

H7: Committee consultation does not extend review times, holding all other factors constant.

Existing theory suggests that the FDA will delay making a decision until it has sufficiently reduced its technical uncertainty (Carpenter 2002). Taken in conjunction with our model, one might say that uncertainty is greatest when $\Pr(b/r > 1) = 1/2$. (If the FDA places sufficient weight on technical certainty after committee consultation, or if the committee vote incorporates political information, as it appears to, then the political costs may safely be

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$$\Pr[pB - P_A + \varepsilon_A > (1-p)B - P_R + \varepsilon_R] = \Pr\left(p - \frac{1}{2} + \frac{P_R - P_A}{2B} > \frac{\varepsilon_R - \varepsilon_A}{2B}\right)$$

removed.) As in Carpenter's study, however, the data are censored in that we lack decision dates for rejections. Therefore, we posit that the FDA's level of policy certainty regarding approval increases as $\Pr(b/r > 1)$ gets close to 1, holding political factors constant.

H8: The time it takes the FDA to approve a drug or device application decreases as the proportion of committee members voting for approval approaches 1, holding political factors constant.

Statistical Models

Consultation Model

The independent and standard-normal errors in our random utility model lead us to a probit statistical model. Specifically, the probability of committee consultation is represented this way:

$$P_C = \Pr(U_C - U_N > \varepsilon_N - \varepsilon_C).$$

Our comparative static results and the linear combination of two independent random error terms allow us to express the statistical model this way:

$$P_C = \Pr(X_j \beta_j > \varepsilon).$$

Finally, because the errors are standard normal, we obtain the probit model to help us estimate the probability of committee consultation:

$$P_C = \Phi(X_j \beta_j).$$

The theoretical consultation model indicates that the probability that the FDA will consult an advisory committee is a function of three types of variables with monotonic effects: those that capture information-processing costs (I_C, I_N), those that capture the attenuating effects on political costs that consulting a committee may have (t), and those that capture the agency's uncertainty about political costs (u).The factors with non-monotonic effects, the FDA's estimate

of the political costs (P), enter as controls. (Recall that we assume that the FDA's initial estimate of p is sufficiently uninformative that we need not estimate it.) We account for all of these factors in the model for drug applications, while we are able to account for fewer factors in the device model.

Approval Model

The probit model for the approval decision is similarly derived. The factors that differentiate the utility of consultation from conducting the evaluation in-house no longer apply; but the probability that the benefits outweigh the risks (p) and the political costs (P) become relevant. We lack rejection data for drugs that were not referred to committee; and we have no rejection data for device applications. Therefore, we limit the analysis of the approval model to drug applications that were referred to committee. We seek to reduce selection bias using a Heckman (joint) probit model that includes the consultation factors in a selection equation.

Review Time Models

The hypotheses regarding review times are not explicitly derived from our theoretical model. The tentative hypothesis that committee consultation does not affect overall time-to-approval (H7) is an informal implication drawn from melding the implications of our consultation model with the formal implications of Carpenter's (2002) model of review times, and we employ a duration model similar to his to estimate the total time it takes the FDA to approve drug applications.[10] In particular, we estimate a Cox proportional-hazards model for drug applications and a lognormal model for medical devices. The drug survival data reveal no internal peaks, and none of the variables fails a proportionality test, so we do not need to specify

[10] Unfortunately, we have a random sample of only some of Carpenter's interest-group conflict and political salience variables.

a non-proportional hazard function as in Carpenter (2002). (However, some of our variables appear to be time dependent, so we estimate a model that allows the initial hazard to vary by year.) The Cox proportional-hazards model using device data fails the global proportionality test, so we estimate the model using the lognormal and Weibull survival functions. (We report the results of the lognormal model because it yields a higher likelihood ratio.)

The hypothesis regarding post-consultation approval times (H8) is a formal implication of Carpenter's (2002) theoretical model, and we again employ duration models similar to his to estimate the time-to-approval *after* a committee meeting has been held. Again, we estimate a Cox proportional-hazards model for the drug data and a lognormal survival model for the device data. We estimate the appropriate hazard function using the committee vote (which is our proxy for p) and some statistical controls for political factors. For the drug data, we include controls for interest-group presence and political salience to more closely replicate Carpenter's formulation.

Data

We collected data on the approval of original New Drug Applications and Pre-Market Device Applications between 1997 and 2006 as well as non-approvals for drug applications referred to committees. Ideally, one would like to have the full universe of applications, including non-approvals not referred to committees. However, the FDA does not release information on non-approvals so that a complete listing of applications is not available. Carpenter (2002) searched public sources to compile a list of non-approvals for a subset of applications. Moffitt (2002) estimated committee consultation models both with and without these non-approvals and found virtually identical results. This data limitation is not relevant to our analysis of approval times conditional on committee referral—we obtained information for

non-approvals after committee referral from our review of committee transcripts, which provides full set of relevant applications, and web searches to find non-approvals. However, it is relevant to our consultation model, which should therefore be interpreted with some caution. Whether or not greater transparency for FDA decisions about applications not referred to committee would be good public policy, it would certainly contribute to more confident research about pharmaceutical regulation.

For each application in our dataset, we have the application and approval dates, indicator variables for the various FDA programs and designations we review below, and the votes taken by the committees as a whole. When discernable, we also have data on the votes cast by consumer representatives. And, for all of the drugs referred to committee, and a sample of all approved drug applications, we have measures of interest group presence and media salience.[11]

All approval data for original drug and device applications are from databases made publicly available on the FDA's "Advisory Committees" webpage.[12] We tallied committee votes using committee transcripts available online.[13] We coded interest group presence and media salience variables for drug applications using the procedures from Carpenter (2002). We identified the disease each drug is meant to treat and used Boolean terms to search newspaper and interest group databases. We used the Gale's Association Database to record the number of

[11] Due to cost constraints, we employed only a sample of media and interest group variables to estimate consultation models. Their effects were not statistically significant.

[12] "Advisory Committees," *U.S. Food and Drug Administration*, Available: http://www.fda.gov/oc/advisory/default.htm (Accessed: 02/22/2009)

[13] There may be missing transcripts, and we discarded a few cases for which we could not identify with certainty the product under review.

national interest groups in existence concerned with the disease in question; and we used the *Washington Post* electronic archives to tally the number of articles in Section A that mention the disease in question. The article tallies include four years up to the application date, as per Carpenter (2002).

[Insert Table 1 and Table 2 about here.]

Table 1 and Table 2 describe the variables we employ in this analysis, as well as the theoretical parameters to which they correspond. The proportion of committee members voting for approval (Proportion Yes) roughly captures the information that a committee transmits about the probability that the benefits of the product outweigh its risks [$\Pr(b/r > 1)$]. For those inclined to make a distinction between political information (i.e., information on stakeholder preferences) and technical information (information on how to realize stakeholder preferences), the proportion of the committee voting for approval may be seen as capturing technical information because all but one or two of 11 voting committee members (on average) are scientific and medical experts (although, from our perspective, scientists also represent "interests" that legislative coalitions have enfranchised in the drug and device approval processes).

The new molecular entity (NME) variable captures technical uncertainty (i.e., relatively high in-house information-processing costs) and political uncertainty (i.e., uncertainty about the political costs that organized political actors will impose on the FDA) associated with a drug application, as new molecular entities typically involve more uncertainty than applications for other chemical classifications. NME applications are for drugs that represent significant changes to those currently on the market and likely entail greater information-processing costs. The unusual nature of an NME drug also makes it more difficult to anticipate the political costs

associated with approval or rejection, as political principals may be unsure of their preference for approval or rejection if they are unfamiliar with the drug. In terms of our model, an NME drug application involves higher values of I_N and u.

The Priority Review, Accelerated Approval, and Expedited Review variables represent programs meant to reduce review times. Reviewing applications with these designations may involve higher information-processing costs (I_N) because it must be done in a shorter period of time or with different evidentiary standards. In addition, these designations also may indicate that there will be high political costs to rejecting the application (P_R), as patient groups and drug sponsors eager to get innovative drugs and devices to market lobby to obtain such designations (Carpenter 2004b).

The Orphan Drug variable indicates a program that the FDA employs to help bring certain drugs to market and perhaps speed up the review process. Although this designation suggests that some of the traditional hurdles of bringing a drug to market have been removed, it also suggests that a drug under review may be unusual and perhaps involves greater in-house information processing costs (I_N). A drug's "orphan" status may also indicate that an application entails relatively higher approval costs (P_A) or relatively lower rejection costs (P_R), as there may be fewer advocates pushing for approval.

The indicator variable capturing whether or not an application was filed before 2001, i.e., during the Clinton administration, may have information-processing (I_N) implications. As we mention in the literature review, the FDA's resources and, therefore, its ability to process applications in-house, may have increased during the years of our study. In addition, some may be inclined to think that consulting a committee did not provide as much political cover for the FDA after 2001 (i.e., that t decreased after 2001). Recall that the model indicates that

committees may be thought of as providing political cover in the sense that consulting a committee causes the FDA to place relatively more weight on making a technically correct decision. Recent events, such as the Plan-B controversy, have lead some to believe that the Bush administration placed less weight on making technically correct decisions than the Clinton administration (see Steinbrook 2004); and that it was perhaps more likely to pressure the FDA into contradicting committee advice, thereby decreasing the relative benefit to the FDA of consulting a committee. If the political cover that committee consultation provides went down after 2001, then the FDA should have been less likely to consult committees beginning in 2001.

The variable Consumer Voted Yes captures whether or not the consumer representative voted for drug approval. It serves as a proxy for the political costs of approval (P_A), as consumer representatives seek to protect the public against dangerous drugs (although the sign is reversed, as the variable indicates "yes" votes that imply lower approval costs). We also include some of the interest-group and media variables from Carpenter (2002). The Interest Group Count and the count of stories in the *Washington Post* may be seen as capturing the political costs of rejecting an application (P_R), as patient groups and disease advocates push for the approval of new drugs and media salience may make deciding against them relatively more costly.

Results

Below we present the results of the consultation, approval, and review-time models.

Consultation Model

The results of the consultation probit model appear in Table 3. Recall that the theoretical model emphasizes that higher information-processing costs (captured by NME, Priority Review, Orphan Drug, Accelerated Approval, and perhaps Filed Before 2001 for drug applications; and captured by Expedited Review and perhaps Filed Before 2001 for devices) should lead to more

referrals (H1). The results bear this out, as all variables except Orphan Drug and Accelerated Approval have statistically significant effects and are positively related to the probability of committee consultation. Indeed, drug applications concerned with new molecular entities—perhaps the best indicator to the FDA that an in-house evaluation would be relatively costly—are more likely to be referred to committee. These results also are consistent with the notion that committee consultation reduces political uncertainty (H2). Applications for unusual drugs or devices likely make it difficult for the FDA to anticipate the costs that political groups may impose—something that a risk averse agency would find costly—and consulting a committee may reduce this cost.

[Insert Table 3 about here.]

Overall, the analysis does not enable us to say too much about the political cover that consulting an advisory committee provides for the FDA (H3). The positive and significant coefficient for Filed Before 2001 is consistent with the notion that committee consultation provided less political cover for the FDA after 2001; but an increase in the FDA's capacity to process applications could be driving the results. In addition, recall that applications for drugs that receive a Priority Review designation and devices that receive an Expedited Review designation likely involve large political costs if rejected. That these variables are associated with higher probabilities of committee consultation also is consistent with the notion that the FDA consults committees in part to protect itself from political costs. But, again, the data do not allow us to tease out this effect with much confidence.

Finally, we also estimated a consultation model with the *Washington Post* variable and the Interest Group Count variable for a random sample of our observations, accounting for about 10 percent of approved drugs; but we found no statistically significant relationships. [Moffitt

(2002) obtains a similar result using Carpenter's data, so we are relatively confident that these results are valid.] Nevertheless, the inclusion of these variables, as well as the other variables that likely capture some political factors (e.g., Filed Before 2001, Expedited Review, Priority Review, etc.) provides us with added confidence that the NME indicator captures the relatively higher cost for the FDA of evaluating an application in-house—in other words, that the FDA's policy uncertainty at least in part drives its decision to consult advisory committees.

Approval Model

The results of the Heckman probit drug approval models appear in Table 4. Model 1 employs a parsimonious specification and is limited to votes on primary indications. Model 2 includes a host of controls and is limited to votes on primary indications. Finally, Model 3 includes the same controls as Model 2 but includes votes on multiple indications.[14] A benefit of including votes on multiple indications per application is that we get more variation on the Proportion Yes variable. Notice that the Rho coefficients are not statistically significant in any of the equations, suggesting that selection bias is not important. Of course, this is subject to the caveat that the selection model is only based on approvals.

Recall that the theoretical approval model predicted a higher probability of drug approval with higher values of $p = \Pr(b/r > 1)$ (H4), lower probability of approval with higher values of P_A (H5), and higher probability of approval with higher values of P_R (H6). Respectively, the

[14] Drug applications referred to committee may be subjected to multiple votes corresponding to multiple possible uses—i.e., multiple "indications." Except for Model 3 in Tables 4 and 6, models are estimated for only one "primary" indication per application so that we do not put too much weight on certain drug applications. When the primary indication was unclear, we chose the indication that was most salient or that biased the analysis against obtaining the results our theory suggests. For example, when we had the choice of two unapproved indications to designate as primary indications, we chose the one with the highest proportion of committee members voting "yes."

proportion of committee members voting for approval (Proportion Yes), whether or not the consumer representative voted for approval (Consumer Voted Yes), and the presence of disease advocates (Interest Group Count) capture the parameters of the theoretical model. Model 1 reveals that only the proportion of committee members voting for approval has an effect that is statistically significant. The magnitude of the committee vote's effect is substantial: moving from 50 percent voting yes to unanimity increases the approval probability by 28 percentage points, from 0.64 to 0.92; and this effect is strong across the three models.

The Consumer Voted Yes variable is not statistically significant and has unstable effects across the three models. This may be due in part to our ability to discern confidently the vote of the consumer representative in only 47 of 101 unique drug applications, suggesting a possible error-in-variable problem. Another reason may be that preference conversion is likely to occur during committee deliberation—as committee members from the scientific community incorporate consumer concerns and consumer representatives are provided with more information on the actual dangers of the drug at hand. Studies have documented that scientific and medical experts consider political concerns when offering advice (Jasanoff 1990; Smith 1992), suggesting that political as well as technical information is transmitted via the overall committee vote. This finding is also consistent with the notion that consulting a committee helps attenuate political costs.

[Insert Table 4 about here.]

Model 2 and Model 3 are meant primarily to test the robustness of the findings in the first model. In them we include a host of variables, including an interaction between the committee vote and the Filed Before 2001 dummy. This interaction term captures whether or not the FDA is less likely to follow committee advice under the Bush administration—i.e., whether or not the

FDA is less likely to follow "scientific" advice, as some media accounts suggest. A positive coefficient for this interaction would indicate that the FDA under the Bush Administration places less weight on committee votes than the FDA under the previous administration. The coefficient for the interaction of Proportion Yes and Filed Before 2001 was statistically zero, so it appears that the FDA has not changed the weight it places on committee votes over the two administrations. Also note that in Model 2, variables that are likely to capture higher rejection costs (Priority Review and Accelerated Approval) and lower rejection costs (Orphan) are associated with higher and lower approval probabilities, respectively. In other words, the results are consistent with the notion that organized interests influence FDA approval decisions.

Review Time Models

The results of the models estimating application-to-approval time appear in Table 5. These models include a variable (Committee) indicating whether or not the FDA consulted an advisory committee, as well as all of the covariates from the consultation model. Note that the model for drug applications is a Cox proportional hazards model and that the hazard ratio is reported. Variables with coefficients greater than 1 are associated with reduced review times and those with coefficients less than 1 are associated with increased review times. The devices model, however, employs a lognormal hazard and the coefficients may be interpreted in a standard fashion.

Recall that our hypothesis is that committee consultation does not increase review time (H7). The results of the drugs model are consistent with this hypothesis, whereas the results of the devices model contradict it. Committee consultation does not have a statistically significant effect on the time it takes to approve a drug application, but it is related to longer approval times in the devices model (which includes only one control variable). Expectedly, the Priority Review

classification is associated with reduced review times, as the program is meant to reduce review times; interestingly, the Expedited Review classification does not reduce review times for devices.

[Insert Table 5 and 6 about here.]

The results of the models estimating meeting-to-approval time appear in Table 6. The model estimating approval time for devices includes approvals only, whereas the model estimating review time for drugs includes approvals and non-approvals. Again, we report the hazard ratios for the drug models, whereas we report standard coefficients for the device model. The first drug model includes a parsimonious specification and is limited to primary indications, the second drug model includes a host of controls and is also limited to primary indications, and the third model includes multiple indications.

In view of Carpenter's theory, our model suggests that review time will decrease as the FDA becomes more certain about whether or not a product's benefits outweigh its risks—in other words, as p approaches 1 (H8)—holding Carpenter's covariates for interest-group presence and media salience constant for the drug models. The results indicate that approaching committee consensus on average contributes to a substantial reduction in post-meeting approval times, even when controlling for the programs intended to reduce post-application review time: Priority Review and Expedited Review.

Overall, the results suggest that committee consultation may actually reduce overall drug approval time when committees are able to provide the FDA with a sufficient amount of certainty that approval is the correct decision. For example, on average, it takes the FDA 526 days to approve a new molecular entity after the agency has filed a drug application, and it takes an average of 525 days to approve such a drug if it is referred to committee. However, the overall

time it takes to approve an NME drug when all committee members vote for approval is only 456 days. This total includes the time it takes to schedule and organize a meeting. This finding is consistent with Moffitt (2002), who employs Carpenter's (2002) data to estimate the effects of committee consultation on overall approval times. On the other hand, the overall approval-time model for devices, which includes fewer controls, suggests that committee consultation is less likely to provide sufficient policy certainty to result in lower overall approval times.

Discussion

The results support Carpenter's (2002) claim that longer approval times should be attributed to the FDA's attempt to reduce its policy uncertainty. It appears that the FDA employs advisory committees as a tool to collect and process information about drugs; that the nature of the policy-relevant information these committees yield affects review times as Carpenter suggests; and that his theory also largely applies to devices and to drugs that are not new molecular entities. These findings are robust to the inclusion of variables that account for modified review procedures, limits on review times, and the FDA's political concerns. As in Moffitt (2002), however, the results indicate that the variables measuring media salience and interest group presence are not as important as Carpenter (2002) claims.

The results also are consistent with the control theory of McCubbins, Noll, and Weingast (1987, 1989) and Balla and Wright (2001), as well as other theories of bureaucratic accountability that require that agencies utilize committee advice. It was clear prior to this analysis that legislative coalitions influence the membership of FDA advisory committees (Schulman et al. 2002), but the impact of the information these members provide was unknown. Prominent accounts in the media, such as those about the Plan-B controversy, even led some to believe that the FDA regularly ignored the "scientific" advice of committees in order to make

politically-charged decisions. Our results indicate that such instances are atypical. The information that committees yield typically has a substantial impact on the FDA's decision to approve a drug or device, an impact that has not changed over the last two administrations; and the level of certainty committees relay is a significant predictor of the time it takes the FDA to make a decision after committee consultation.

That said, the significance of the "Filed Before 2001" variable suggests that the FDA became less likely to consult advisory committees beginning in 2001. Perhaps the agency's application-processing capacity increased from 1997 to 2006; or, as some suggest, perhaps there was a politicization of the drug and device review process that has affected the willingness of the FDA to consult committees that are "stacked" with scientific interests and expose decisions to greater public scrutiny. In other words, perhaps the political cover that committee consultation provided declined. We do not want to focus too much on the political implications of the 2000 presidential election because we lack the data to isolate this effect. Whatever the reason for the FDA's choice to consult fewer committees beginning roughly in 2001, our results suggest that the potential for committees to serve as a control mechanism has declined.

We also cannot generalize too much about the effective accountability function of federal advisory committees. The scientific advisory committees that the FDA employs are hardly representative of all federal advisory committees—which come in many different forms, perform very different functions, and ostensibly serve very different interests (see, e.g., Jasanoff 1990). Indeed, the FDA itself consults committees to perform tasks that differ significantly from drug and device approval. And the extent of legislative coalitions' impact on committee membership may be questioned. For example, there are popular and academic accounts of the Bush administration stacking advisory committees (e.g., Steinbrook 2004). In addition, although one

study of FDA committee members with conflicts of interest reveals that these members' biased votes were never pivotal (Lurie et al. 2006) our theoretical and statistical models suggest that any given member may be influential in a probabilistic sense. The point is that a minimal amount of bias in committee membership may have an effect on FDA behavior and we cannot say how much those in the executive branch, including the FDA, are able to influence decision-making through the selection of committee membership.

Our analysis suggests, however, that the FDA must collect and process technical and political information to make decisions; that this information processing is costly in terms of time and resources; that the FDA appears to consult advisory committees when in-house information processing is relatively costly and the political stakes of its decisions are high; and that the information that committees relay has an impact on the content and timing of its decisions. These results are also consistent with anecdotal evidence that advisory committees increase the visibility of FDA decision-making and make it costly for the FDA to make decisions that contradict committee advice. In other words, our results, taken in conjunction with existing scholarship and anecdotal media accounts, reveal that FDA drug and device approval committees likely serve a control function.

Finally, the analysis tells us something about the impact on review times of committee consultation. Our theoretical model does not offer precise predictions about how committee consultation should affect overall review times, and we may lack the statistical controls necessary to isolate its effect. In addition, although existing scholarship suggests that review times for approved drug applications do not differ systematically from those of non-approved drugs, the analysis for the most part utilizes data on approved product applications. Nevertheless, the results suggest that, on average, committee consultation does not extend overall review times

of drug applications, and that under some circumstances consultation may reduce overall review times if the committee sufficiently reduces the FDA's policy uncertainty. On the other hand, on average, consulting a committee seems to increase the overall time it takes to approve a medical device.

Conclusion

Advisory committees are commonly used to support federal rulemaking. Political scientists have largely focused on why they are created and their potential role in delegation, assuming that committees make a difference in some way. Because FDA committees record votes that provide a quantitative measure of consensus, and therefore certainty, we were able to show that greater certainty actually affects agency decisions. In other words, that at least in this specific case, tactics such as stacking-the-deck could make a difference.

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Table 1
Variables for New Drug Application Approvals from 1997-2006

Variable	Description	Parameters	N	Mean	SD	Min	Max
Delay – Application	Delay in days from the time the FDA received the drug application, to the time the application was approved.	–	892	553.87	503.41	46	4112
Delay – Meeting	Delay in days from the time the FDA held the committee meeting to consider the NDA, to the time the application was approved.	–	127	278.10	416.82	9	3038
Proportion Yes	Proportion of committee members who voted for NDA approval.	$p = \Pr(b/r > 1)$	178	0.63	0.36	0	1
New Molecular Entity	Whether or not the drug at hand is a new molecular entity (NME). The CDER identifies a drug as and NME if it contains "an active substance that has never before been approved for marketing in any form in the United States."	I , u	1058	0.30	0.46	0	1
Priority Review	The 1997 Modernization Act also requires "fast track" procedures "that facilitate the development and expedite the review" of a new drug "if it is intended for the treatment of a serious or life-threatening condition and it demonstrates the potential to address unmet medical needs for such a condition." The CDER may grant NDA's a "priority review" designation that sets a 6-month review timeline, as opposed to the 10-month timeline for "standard" applications. It appears that patient groups are most significant in prompting this designation (Carpenter 2004b).	I , P	1058	0.23	0.42	0	1
Orphan	Whether or not the NDA is for an orphan drug. The 1983 Orphan Drug Act and its amendments provide for assistance in the development of drugs that treat "rare diseases and conditions."	I , P	1058	0.10	0.30	0	1
Accelerated Approval	Whether or not an NDA is being reviewed using criteria established under the "accelerated approval" program that the FDA implemented in 1993. The designation changes the medical evidence requirements for the approval of drugs that may address life-threatening diseases.	I , P	1058	0.07	0.25	0	1
Filed Before 2001	Whether or not an application was filed during the Clinton administration.	I , t	1058	0.40	0.49	0	1
Consumer Voted Yes	Whether or not the consumer representative (if present and voting) voted for approval.	P	195	0.29	0.45	0	1
Interest Groups	Count of national interest groups that focus on the disease the drug is meant to treat. Tallied for committee-referred drugs only.	P	195	19.28	40.47	0	206
Media Salience	Measure of salience for the disease listed as the primary indication of the NDA. Tallied for committee-referred drugs and a sample of non-referred drugs.	P	280	116.73	218.11	0	1656

Table 2
Variable for Pre-Market Device Application Approvals from 1997-2006[15]

Variable	Description	Parameters	Obs	Mean	SD	Min	Max
Committee Referral	Whether or not the PMA was referred to committee. Excludes PMA's with duplicate listings. 127 original PMA's (34%) are referred to committee in our dataset.	–	371	0.34	0.48	0	1
Delay - Application	Delay in days from the time the FDA received the device (PMA) application, to the time the application was approved.	–	374	444.90	335.95	7	2410
Delay - Meeting	Delay in days from the time the FDA held the committee meeting to consider the PMA, to the time the application was approved.	–	129	242.28	273.40	3	1476
Proportion Yes	Proportion of committee members who voted for NDA approval.	$p = \Pr(b/r > 1)$	149	0.80	0.30	0	1
Filed Before 2001	Whether or not an application was filed during the Clinton administration.	I , t	398	0.54	0.50	0	1
Expedited Review	The FDA Modernization Act of 1997 demands the expedited review of applications for devices that "provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human diseases or conditions." The CDRH has implemented an "expedited review" procedure for devices it finds meets the criteria set forth in the law. A device that the CDRH deems to meet such criteria is placed at the beginning of the relevant review queue and the Center allots more resources to the review of that PMA.	I , P	375	0.17	0.38	0	1

[15] Data include all original PMA approvals from 1997-2005; 2006 approvals are for committee-referred PMAs only.

Table 3: Probability of Consultation
(Probit models w/ robust std. errors; unique approvals only)

	Drugs		Devices	
NME	0.53	***		
	(0.13)			
Priority Review	0.87	***		
	(0.15)			
Expedited Review			1.37	***
			(0.19)	
Orphan Drug	0.07			
	(0.19)			
Accelerated Approval	0.33			
	(0.22)			
Filed Before 2001	0.50	***	0.32	*
	(0.12)		(0.14)	
Constant	-2.02	***	-0.85	***
	(0.11)		(0.12)	
N	964		371	
Wald Chi-Square	111.38	***	53.01	***
Pseudo R-squared	0.19		0.13	

Two-sided z-tests or Chi-square tests: ***p<0.001; **p<0.01; *p<0.05

Table 4: Probability of Drug Approval
(Heckman probit models w/ robust std. errors)

	(1)		(2)		(3)	
APPROVAL EQUATION	(N=129)		(N=129)		(N=178)	
Proportion Yes	2.19	***	2.60	***	2.04	***
	(0.47)		(0.76)		(0.49)	
(Prop Yes)*(Filed Before2001)			-0.36		-0.05	
			(0.97)		(0.62)	
Filed Before 2001			0.78		0.43	
			(0.69)		(0.44)	
Consumer Voted Yes	-0.22		-0.18		0.03	
	(0.30)		(0.32)		(0.26)	
NME			-0.75		0.24	
			(0.61)		(0.24)	
Priority Review			1.61	***	0.77	
			(0.41)		(0.25)	
Orphan Drug			-1.12	*	-0.52	
			(0.45)		(0.28)	
Accelerated Approval			1.07	*	0.31	
			(0.47)		(0.30)	
Interest Group Count	0.00		0.00		0.01	
	(0.00)		(0.01)		(0.01)	
Washington Post			0.00		0.00	
			(0.00)		(0.00)	
Constant	-0.11		-1.11		-1.74	***
	(0.59)		(1.35)		(0.39)	
SELECTION EQUATION	(N=987)		(N=987)		(N=1036)	
NME	0.74	***	0.79	***	0.71	***
	(0.14)		(0.12)		(0.11)	
Priority Review	0.56	***	0.48	***	0.63	***
	(0.17)		(0.14)		(0.13)	
Orphan Drug	0.25		0.31		0.16	
	(0.19)		(0.18)		(0.17)	
Accelerated Approval	0.30		0.29		0.46	*
	(0.20)		(0.21)		(0.19)	
Filed Before 2001	0.30	**	0.28	*	0.46	***
	(0.11)		(0.11)		(0.10)	
Constant	-1.78	***	-1.77	***	-1.69	***
	(0.09)		(0.09)		(0.09)	
MODEL						
Rho	-0.42		0.16		0.32	*
	(0.29)		(0.54)		(0.14)	
Wald Chi-Square	27.25	***	43.65	***	66.46	***

Two-sided z-tests or Chi-square tests: ***p<0.001; **p<0.01; *p<0.05

Table 5: Hazard Models for Application-to-Approval Review Time

(NOTE: z-scores reported below hazard ratios for Cox model)

	Drugs (Cox)	Devices (Lognormal)
Committee	0.85	0.16 *
	[-1.11]	(0.08)
NME	1.10	
	[1.05]	
Priority Review	2.24 ***	
	[6.06]	
Expedited Review		0.05
		(0.10)
Orphan Drug	0.92	
	[-0.52]	
Accelerated Approval	1.31	
	[0.99]	
Constant		5.80 ***
		(0.04)
N	865	N=371
Wald Chi-Square	52.15 ***	LR=5.89*

Two-sided z-tests or Chi-square tests: ***p<0.001; **p<0.01; *p<0.05

Table 6: Hazard Models for Meeting-to-Approval Review Time
(NOTE: z-scores reported below the hazard ratios for the Cox models)

	Drugs (1) (Cox)	Drugs (2)^ (Cox)	Drugs (3)^ (Cox)	Devices (Lognormal)
Proportion Yes	7.41 ***	4.99 *	6.24 ***	-1.41 *
	[5.73]	*[2.38]*	*[3.42]*	(0.67)
(Prop Yes)*(Filed Before2001)		1.80	1.51	-0.15
		[0.73]	*[0.61]*	(0.80)
Filed Before 2001				-0.16
				(0.69)
Consumer Voted Yes		1.07	1.12	
		[0.22]	*[0.48]*	
NME		0.95	1.28	
		[-0.22]	*[1.15]*	
Priority Review		2.49 ***	1.86 *	
		[3.51]	*[2.36]*	
Expedited Review				0.19
				(0.19)
Orphan Drug		0.59	0.76	
		[-1.62]	*[-0.94]*	
Accelerated Approval		1.19	0.95	
		[0.54]	*[-0.18]*	
Interest Group Count	1.01	1.01	1.01	
	[0.82]	*[0.62]*	*[1.09]*	
Washington Post	1.00	1.00	1.00	
	[-1.55]	*[-1.06]*	*[-1.40]*	
Constant				6.28 ***
				(0.59)
N (approvals)	129 (89)	129 (89)	178 (115)	N(App)=128(128)
Wald Chi-Square	39.88 ***	66.23 ***	69.43 ***	LR = 22.10***

Two-sided z-tests or Chi-square tests: ***p<0.001; **p<0.01; *p<0.05

^The variable "Filed Before 2001" is not included in the second and third models because the Cox models allow the initial hazards to vary by year.