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PUBLIC AND ORAL VOTING IN FDA s' ADVISORY COMMITTEES

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In the 1960s, western states began passing laws and creating organizations to control more efficiently medicine quality. Public agencies were formed whose tasks were to approve or refuse to approve medicines for marketing, oversee medicines' possible effects, and, if it was deemed necessary, restrict their use or withdraw them from the market entirely.

In fulfilling these functions, agencies have to make "reasoned use of available scientific data" in reaching decisions and transmitting what they consider useful information to prescribers and patients. These decisions and actions must all be founded on reasons; that is, they must be supported by arguments and made in the service of public health.The United States Food and Drug Administration, created in the early twentieth century, was the first such agency to require and organize pre-marketing medicine approval—in 1962.

This text analyzes the decision-making procedures—specifically, the voting procedures—used by FDA "Advisory Committees," consultative committees of outside experts assembled by the FDA to assist it in performing its medicine evaluation task.

The FDA began using advisory committees systematically in 1972. This development, observable in all United States federal agencies of the time, is explained by at least three factors: the increasing complexity of the technologies implicated in products under FDA control; the passing of new legislation; the rise of consumer activism, which exposed agency decisions to consumer surveillance and criticism. Advisory committees were created to perform three functions: 1) to provide the FDA with assistance from outside specialists; 2) to enable viewpoints to be expressed and taken into account that would otherwise not be represented within the agency; e.g., those of consumer organizations; 3) to protect the FDA by strengthening the credibility of its evaluations and the acceptability of its decisions through the use of a public consulting arrangement (Sherman 2004). As we shall see further on, the respective importance of the three functions has varied over time. In fact, the FDA only uses advisory committees for what are considered delicate evaluations —delicate in that the available scientific data renders decision-making particularly difficult and/or the drug or disease involved is controversial.

The consultative nature of the committees should not lead to underestimating their importance. They are of course not the final decision-makers since their recommendations are not binding. But the general orientations they bring to the fore are decisive for both the FDA, which follows AC recommendations in 70% of cases, and the drug companies, as well as for the public watchdog organizations. Furthermore, though only consultative, ACs are called upon to produce recommendations in ways akin to collective decision-making: experts have to give individual

answers to FDA questions by way of voting, and their aggregated votes are understood to reflect the overall committee orientation and its opinion. In sum, advisory committee collective recommendations do not have the normative status of decisions but are reached using classic collective decision methods (Urfalino 2011).

The FDA is made up of six centers. The one that concerns us here is the Center for Drug Evaluation and Research (CDER), which uses anywhere from 16 to 18 committees (the number varies slightly as new committees are formed and existing ones redefined). Almost all committees are specialized by broad disorder category, in turn related to a set of organs or the relevant physiological function. There is an Arthritis Drugs Advisory Committee, for example, and a Cardiovascular and Renal Drugs Advisory Committee. At different times there have been one or two horizontal committees; e.g., the Drug Safety and Risk Management Advisory Committee, created in 2002.

Each committee is composed of members—the standard number is 11—appointed for four years with the status of special government employees (SGEs). Members are selected for their competence. Each committee includes a consumer representative and a drug industry representative; the latter is not an SGE and cannot vote. Each committee has a chairperson. Additional experts may be invited to join the committee for a given meeting as necessary. The number of voting members varies on average from 6 to 18 depending on absences and number of guest specialists of the pathology or medicine being examined. It may go as high as 30.

FDA advisory committee meetings usually last an entire day. At the beginning of the meeting, the FDA services and the drug company that owns the medicine under examination present the relevant data and their own analyses. At this point, any guest members present their interpretation of the question under discussion. Meetings are open to the public, and observers may intervene in the discussions after duly registering themselves. Committee members may in turn put questions to public orators. Members then collectively deliberate on each of the two to six questions set out by the FDA beforehand. Committee members only may participate in these deliberations, but they remain public. On some FDA questions, the deliberation leads to voting. At these points, the chairperson requests each member to vote either Yes or No or say Abstain.

There is great concern to keep the entire process transparent, as attested by the presence of an audience and the fact that the FDA makes the entire content of AC meetings available on its

website. Meetings are carefully recorded in their entirety, and one month afterward, a 300- to 500-page full transcript of the meeting may be consulted on the FDA website.[1]

1. The 2007 reform of FDA Advisory Committee decision-making procedures

It has been said that the history of the FDA is the history of all official reports that have been written on it. And indeed, caught between the drug industry and consumer representatives, torn between the concern to maintain conditions for fostering innovative therapies and the duty not to allow risky or less than fully effective medicines onto the market, the FDA has been the focus or cause of many public controversies since its creation. It is kept under critical surveillance by the media and a number of different patient advocate organizations. The U.S. Congress, whose task is to oversee all federal agencies, is quick to launch official inquiries into FDA weaknesses. The 2000s have been marked by controversies around several medicines; the FDA has been accused of showing insufficient concern for American patient safety, having an overly conciliatory attitude toward the drug industry, and not developing adequate means for controlling industry-designed drugs. The largest controversy and the one receiving the most media attention followed 2004 Merck's withdrawal of its anti-inflammatory drug Vioxx®. The FDA and other western agencies were accused of failing to evaluate the real risks of taking the drug and harshly criticized for not withdrawing it from the market before the drug company itself did.

1.1. Controversies around conflict of interest in advisory committees

Advisory committees themselves have not been immune to controversy. Given that one of their stated functions or purposes is to open up the FDA decision-making process to outside experts and the public, they themselves have become, predictably, the focus of increased attention. Moreover, despite the fact that the FDA's final decisions, which it reaches by consulting analyses by its own inside experts, are likely to comply with advisory committee recommendations, FDA critics accuse the agency of not following AC recommendations often enough.[2] For its part, the

[1] For a detailed presentation of AC proceedings see Sherman 2004. Transcripts are full verbatim. All documents cited or shown during the day-long meeting are likewise made available for consultation on the FDA AC meeting website. Researchers therefore have exceptionally complete source material for studying AC deliberations and decisions.

[2] In an open letter published in 2006 in the *Lancet*, three members of Public Citizen's Health Research Group deplored the fact that the FDA had followed AC recommendations in only 51 out of 71 cases from 2001 to 2004, and that AC meetings had been held for a mere 24% of the 147 new molecules under FDA study from 2000 to 2006 (Tapley and al. 2006).

agency has made these committees into crucial instruments of FDA credibility and decision acceptability.

In this high-visibility position, advisory committees have been sharply criticized—the criticism is of course aimed at the FDA itself—in connection with the issue that comes up most frequently in the drug and medical research sector as a whole: conflict of interest. Federal regulations and internal FDA recommendations are aimed at reducing occurrences of conflict of interest and controlling their effects. Would-be committee experts have to disclose any income they earn from work for pharmaceutical companies, and if that income exceeds a certain amount they may be not be allowed to sit on the committee. But given that the FDA is of the opinion (together with a significant proportion of the professional worlds involved) that the most highly competent experts are also those most likely to collaborate at least sporadically with the drug industry, it has also developed a waivers procedure for such potential members (McComas 2005). This means that some proportion of AC members participating at any given meeting is likely to have financial ties with the company whose medicine is being evaluated or with a competing firm.[3] This state of affairs is often criticized, the fear being that the experts' individual recommendations and the committee's collective recommendation will be biased in favor of some or all of the drug companies involved (Lurie and al. 2006).

Criticism reached a peak in February 2005 following the work of a committee set up to determine whether or not two of Pfizer's anti-inflammation medicines, Celebrex® and Bextra®, should remain on the market and whether Merck's anti-inflammation drug Vioxx® could be approved again for marketing. The vote—a close one, slightly in favor of the highly controversial Bextra® and Vioxx®—surprised the informed public and raised suspicions, leading *The New York Times* to commission a study on committee members' financial ties. It turned out that ten members (of 32) had financial ties with one or more drug companies, most with Pfizer (Harris and Berenson 2005; CSPI 2005). As the critics saw it, this was a sign that advisory committees themselves, like FDA top management before them, had come under the influence of the drug industry.

[3] Competing firms are companies that own medicines in the same therapeutic category as the one being evaluated by the given committee.

1.2. The new voting arrangement: still open but simultaneous and visual rather than oral

It was in this overall social and media context, specifically during the drafting of a new federal law on FDA scope and funding, that the FDA reformed its advisory committee voting procedures. That reform is of central importance to this discussion.[4]

The reform has been in effect since July 30, 2007. It stipulates that voting is to be simultaneous rather than sequential. Committee members used to vote in sequence orally: after naming himself or herself; each member voted, then passed the microphone on to another. Now, after discussion of each FDA question and any requests for clarification of the question itself, the chairperson is required to ask all members wishing to vote "yes" to the question to raise their hands at the same time; this procedure is then repeated for "no" and "abstain" responses. Once votes have been counted, the microphone is passed around again so that each voter can repeat his or her vote orally for the record. The microphone then goes around one last time to allow members wishing to do so to explain their vote.

The official reason given for this reform was concern that the first voters would influence later ones (italics ours):

> There has been much discussion inside and outside FDA regarding sequential versus simultaneous voting. Some have expressed concern that sequential voting, in which members cast public votes in turn, has the potential to compromise the integrity of the result.
>
> For example, scholars and social scientists have studied the risk of "momentum" in sequential voting, exploring whether some sequential voters may be influenced, perhaps even subconsciously, by the votes that precede theirs, *especially if those votes are nearly identical or signal a clear trend.* This potential risk may be aggravated in the advisory committee setting, where votes are often conducted in full view of a passionate public and participatory audience.
>
> In the case of sequential voting, there is also a potential risk that comments made by a committee member or a designated federal officer (DFO) during the vote could inappropriately affect the deliberations of those who have not yet voted.[5]

Specifically, as indicated by the clause in italics, the concern was to prevent conformism. This concern was consistent with the substance of most criticism of the FDA and its ACs: they were not being attentive enough to the dangers associated with medicines up for approval, and they had an over-accommodating attitude toward the drug industry. The suspicion was regularly expressed that conformism on the part of advisory committee members worked in favor of the

[4] The reform was introduced in the form of a "guidance" publicly disseminated in 2007 as a draft open to discussion; it was definitively adopted in 2008. However, the procedure recommended in the guidance actually went into effect for advisory committee meetings on July 30, 2007. Meanwhile a reform went into effect making it harder to obtain a conflict-of-interest waiver (the ceiling for conflict-of-interest income was lowered) and numerically limiting the proportion of waivers the FDA could grant. Guidances do not have the status of laws and must comply with the Federal Act on Advisory Committees, which applies to advisory committees in all federal agencies.

[5] FDA 2008a: 4-5.

drug companies. That suspicion had been sharpened by the extremely high percentage of unanimous votes and heavy majorities.[6] Passing this reform worked to protect the conditions that would enable the potential critical minority on ACs to be heard.

A second drawback of the earlier method is also mentioned in the FDA document:

> Another potential risk is that comments could alter the meaning (or interpretation) of the question at issue in such a way as to cast doubt on whether all members voted on the identical question. (*ibid.*: 5)

This observation points up an aspect of the reform not directly addressed in the agency's presentation of it. The status purpose of the reform was to replace sequential voting with simultaneous voting—and this has elicited generally favorable comments. But that change was accompanied by another, which seemed nothing more than its lateral technical consequence: oral voting was replaced by hand-raising.[7] And the effect of this was to dissociate two acts : the silent vote itself and the necessarily oral one in which each member explains his or her vote.[8] This chronological separation precludes voters from giving their votes even a slightly different meaning from the meaning attached to the "yes" and "no" the FDA has asked for in response to its questions.

There are three remarkable features to the 2007 reform:

-- it emphasizes the switch from sequential to simultaneous voting, whereas

-- there was a second change, thought of as merely a technical correlative of the first: a switch from oral voting to hand-raising (now voting by machine);

-- the reform did not affect the feature that seems to everyone both inside and outside the FDA the only acceptable way to proceed: voting is open and public.

As we see it, the most remarkable feature of all is the one on which there is perfect consensus: open voting. This will be the focus of part 2. The second most remarkable move was to put an end to oral voting—that form of voting is the focus of part 3. Once we understand the specific effects of oral voting, we will be in a position to examine the import of the shift from sequential to simultaneous voting.

[6] Of the set of 38 votes we assembled (see 3.1.), 17 were unanimous—i.e., 45%. Of the 21 remaining votes, the average majority was 65% and in 9 cases the majority was over 75%.
[7] In 2009 hand-raising was replaced by machine-voting; the rest of the procedure has remained unchanged.
[8] It should be recalled that between these two acts there is another one, also understood to be purely technical: raised hands or electronic votes are translated into "yeses" or "nos" spoken into a microphone for recording purposes.

2. Why open, public voting?

As seen, the issue of financial ties between members of advisory committees and drug companies is central to debate over how these committees work. It is therefore reasonable to ask why secret voting has never been contemplated as a means of combating the possible negative impact of such ties on the validity of expert opinions to the FDA.

What is remarkable here is that the practice of public voting seems the obvious way to proceed to all concerned, both players within the FDA and outside it, including, in the latter category those who criticize how the agency functions and accuse it of not working hard enough to combat conflicts of interest. Everyone involved—the FDA itself, advisory committee members, the vigilant public, regular FDA critics, and the press—seems to think public voting is the only right way to proceed. This is attested by the fact that no one suggests comparing the advantages and disadvantages of secret and open voting. FDA documents for reforming voting procedures, made public in 2007 and 2008, mention secret voting in passing only once, simply to assert that it would be unsuitable for advisory committees (see 2.4. for the extremely brief justification of this assertion).

Moreover, the voting procedure reform of 2007 replacing sequential oral voting with simultaneous hand-raising clearly did not affect voting publicity. The main reason given for the shift to simultaneous voting once again indicates that secret voting has never been seriously contemplated; it is in fact sequential voting that facilitates influence, as the choices of first electors can influence those of later ones. Secret voting would effectively counter any such influence, but it is precisely because secret voting seems so obviously undesirable to all concerned that simultaneous voting appeared the only solution.

Given that there are no objections to open voting and that it seems so clearly the right way to proceed that there is little or no need to justify its use, we need to attempt to discover why this procedure is systematically favored. We see four possible reasons, related respectively to a) the nature of the ties and influences that must be countered, b) probability of unanimous voting, c) the benefits to be had from public surveillance of committee functioning, and d) the nature of the opinions that these advisory committees are called upon to produce.

2.1. The strength of the idea of collusion between experts and the drug industry

Given longstanding concern about the issue of possible financial ties between advisory committee members and pharmaceutical companies, it is at first glance surprising that secret voting has never been seriously considered as a means of neutralizing the impact of such ties (there is no source evidence to suggest it has).

Generally speaking, how the publicity or secrecy of voting is valued is necessarily related to the nature of ties between experts and businesses. The type of voting a decision-making body prefers is directly related to the type of influence it wishes to see impacting on voters' choices or, on the contrary, wishes to prevent from impacting on those choices. The argument used to support public voting has not changed since Antiquity: having voters vote openly, publicly, is a means of guaranteeing the quality of the decision thus produced. A voter forced to vote in full view of the wisest or noblest, peers or public opinion, is understood to be voting under a salutary kind of pressure; he or she will be less inclined to favor candidates or proposals arising from motives judged unacceptable. The opposite reason has of course been historically adduced in favor of secret voting: secret voting guarantees voters freedom to choose despite and against possible pressures on them judged harmful or illegitimate. In other words, secret balloting short-circuits any relations of dependence that may obtain between the voter and another person or group. It does so on two conditions:

1) the material conditions in which the voter votes allow for keeping his choice from among several candidates or proposals visually secret;
2) secrecy is not merely possible but required. If voting secrecy is at the discretion of the voter, those who may threaten him if he doesn't vote their way or promise him something if he does could require him to manifest his choice. As Schelling noted (1980: 19), to be entirely free to choose, a voter has to be required to keep his choice unknown.

In a chapter of *Political Tactics* entitled "Of Open and Secret Voting," Jeremy Bentham took a nuanced position, giving priority to openness while explaining that in several types of situations secret voting is preferable:

> *In general, it is very desirable that the voting should be open rather than secret.* Publicity is the only means of subjecting the voters to the tribunal of public opinion, and of holding them to their duty by the restraint of honour. … This rule must be subject at all times to widely extended exceptions (Bentham [1791] 1999: 144-145).

Open voting as Bentham saw it is not suitable when, instead of subjecting the voter to the beneficial effect of public opinion, it puts him at the mercy of particular interests. In such cases, secret voting is the type that allows for neutralizing what are considered the harmful effects of dependence. Nonetheless, Bentham explains, even in such cases it cannot be assumed that secret voting will effectively dispel the danger. How effectively secret voting works depends on the nature of the link tying the voter to particular interests. Bentham identifies two types of interests, making the point that voting secrecy impacts on them unequally:

> *Votes ought to be given secretly in all cases in which there is more to fear from the influence of particular wills, than to hope from the influence of public opinion.*
>
> What are the cases? To answer this question, it is necessary to distinguish two species of interest: the one factitious, the other natural.
>
> Interest is purely factitious when the voter has nothing to gain or to lose in consequence of his vote, except when his vote is known.
>
> Interest is natural when the voter may lose or gain in consequence of his vote, even should it remain unknown.
>
> For example, the interest which results from the contract whereby I engage to sell my vote to stranger, is a factitious interest.
>
> Secret voting destroys the influence of factitious interest: it has no effect upon the influence of natural interest (*ibid*.: 145-146).

In his translation of Bentham's text, which was also an adaptation for French readers, Etienne Dumont added the following example of natural interest, i.e., interest immune to the desirable effect of voting secrecy: "the interest that leads me to vote in a way that would obtain a lucrative situation for my father or son is a natural, pre-established interest" (Bentham/Dumont [1791] 1822: 190).

If we formulate Bentham's distinction slightly differently, shifting the emphasis from cause of voter's interest to whether or not the interests implicated in the decision are shared by decision-makers, we can widen its scope:

-- Dependence exists when the voter has an incentive to vote in accordance with the will of a third party who has interests at stake in the vote and is in a position to proffer either positive or negative incentives—promises or threats—for voting in his (the third party's) interest, which the voter would not spontaneously do if there were no pressure on him. Dependence is short-circuited by secret voting.

-- Collusion exists when voter and third party are linked by some tie or engaged in the same activity and therefore have identical interests in the success of a particular decision option. Secret voting will have no impact on collusion.

The difference between these two types of ties raises two questions:

1) Does it hold for relations between the pharmaceutical industry and medicine experts?

The immediate answer seems to be yes. For example, a clinical physician wishing to publish scientific articles on medicines and having a financial interest in clinical trials—either for himself or the hospital unit he works in—can readily be seen as dependent on certain drug companies. If he is called upon to vote openly, he may think that whether or not the company/ies he works for or would like to work for will invite him to participate in clinical trials will depend on whether or not he votes in favor of marketing their molecules. Secret voting would enable him to vote for or against molecule marketing approval on the basis of professional conviction alone, without fearing that the companies that developed that molecule will refuse to collaborate with him in the future.

On the other hand, a clinical physician with stock shares in a pharmaceutical company has the same interest in the value of those shares as the firm in question. When he participates in an advisory committee meeting called to approve or withdraw a molecule belonging to that company, he knows that a collective committee opinion—and especially an FDA final decision—that is consistent with the interests of the firm in question will have significant impact on the value of his stock. Having stock in the company puts the expert in a potential collusion situation. Here, secret voting would have no effect. Conversely, open voting would at least enable a wary public to note a possibly illegitimate slant among share-owning experts.

2) Do the FDA and its critics make this distinction?

This distinction never appears in comments, criticisms or defenses by actors implicated in, affected by or concerned to keep tabs on the work of the advisory committees. Even more strikingly, it is also absent from waiver procedures allowing an expert to participate in an advisory committee despite avowed financial ties to the company at issue in the given meeting or to a direct competitor of that company. Income from all the different possible sources—stock shares, contracts for clinical trials, consulting activities—income that actually creates different types of ties between experts and companies, is simply added up indifferently. Difference in the type of

influence that these different income sources are likely to have on expert voting is not taken into account; it does not seem to have been identified or thought about at all. This is clear from the 2008 *Guidance* text on conflict of interest criteria and waiver conditions, which attaches decisive importance to *amount* of income involved in the conflict of interest. Consider the last criterion of "Step 8" of the algorithm for determining whether a potential member is eligible to sit on the committee:

> Is the combined value of the employee's personal disqualifying financial interests and those of his spouse and minor children $50,000 or less? (FDA 2008b: 18).

Waivers for experts whose "disqualifying financial interests" are above $50 000 must be considered exceptional. But what concerns us here is that the amount of "disqualifying financial interest" is the sum of all income from a pharmaceutical company or companies affected by the decision, regardless of whether that income is in the form of stocks or a contract.[9] Clearly ties are assessed in terms of intensity (total annual monetary amount) rather than type of relation obtaining between expert and drug company.

FDA critics, the press, *Public Citizen* and clinicians, all of whom regularly contest the value of advisory committee expert assessment, have never called into question this way of assessing physician-experts' financial ties with drug companies. Critical studies aimed at detecting committee members' undeclared financial ties, or ties not taken into account by the FDA, use the same categories as the FDA itself and simply add up income regardless of its source (i.e., stocks, or sporadic or prolonged collaboration) (CSPI 2005).

What is the significance of this non-differentiation? The FDA is always likely to minimize the impact of financial ties, while its critics are of the opinion that those ties work in favor of the pharmaceutical

[9] This is attested by the method given for calculating the sum: "Under Step 8, staff should calculate the total value of the disqualifying financial interests that are his personal interests, those of his spouse and those of his minor children. Disqualifying financial interests include only financial interests that are currently held. Some examples of an employee's personal financial interests would be stocks or investments that he owns, his primary employment relationship, his consulting work, patents/royalties/trademarks owned by him, his work as an expert witness, and his teaching/speaking/writing work. If the employee's spouse and/or minor children have personal disqualifying interest, these should be included in the total value. In calculating the value of an employee's disqualifying financial interests attributed to a financial interest that extends into the future, such as a contract or employment, staff should include current financial interests over a one-year period of time. For example, if the employee has a $100,000 personal consulting contract that covers a five-year period of work, he would be deemed to have a financial interest in the consulting contract of $20,000 per year. If the employee's relationship is ongoing but there is no specified dollar amount for future work, staff should calculate the amount of the financial interest over the previous 12 months. If the combined value of these disqualifying financial interests is greater than $50,000, the member would not ordinarily be considered for a waiver and would not participate in the advisory committee meeting. If the answer is "yes," staff should proceed to Step 9" (FDA 2008b: 18).

industry and against patients (Lurie and al. 2006; FDA 2006). However, above and beyond that divergence, the two "opponents" share the same understanding of the possible impact of financial ties: if they have an impact it is under the form of a collusion. Whatever the nature of the financial tie between an expert and a company, the understanding is that that tie is likely to make the expert behave as if he shared the company's interests, not as if he were involved in a relation of dependence that the advisory committee voting system might try to protect him from.

The belief that the possible effect of financial ties is necessarily collusion rather than dependence seems to us a sound one. First, the hypothesis that cooperating with pharmaceutical companies will incline experts to approve medicines for marketing is plausible. The entire set of actors—the FDA and its critics—underestimate the bias created non-voluntarily by conflict-of-interest impact and overestimate the voluntary dimension of such conflicts (Chugh and al. 2005 ; Moore and al. 2005b). However, they are surely right not to distinguish dependence from collusion given the nature of exchanges between clinicians and drug companies. Let us reason for a moment in terms of dependence. Let's imagine an expert who works with company A by taking part in clinical trials of company A's medicine X. Suppose the expert prefers not to go against company A's wishes because it is developing a set of medicines to combat the pathology he specializes in (in this case we can readily understand his desire to keep working with the company). If this is the case, then the company is benefiting from this particular clinician's dependence on it. And it is in this situation that secret voting could be considered preferable, because it would allow this clinician to break free of his constraining dependence on the company, whereas open voting leaves him open to possible company retaliation. However, if the clinician has let himself in for such dependence, it seems reasonable to assume that the relationship with the firm is itself strong and rich enough that 1) it produces bias; 2) it has gone beyond mere economic exchange and actually corresponds to what Blau called "social exchange" (Blau 1964). This type of exchange, which assumes the existence of a multitude of reciprocal services and constant reiteration of mutual trust, is indeed more one of collusion than dependence.[10] And we can hypothesize that the mechanism operative here is of the "all-or-nothing" variety: either a clinician has sufficient financial, professional and moral resources not to feel dependent or he doesn't, in which

[10] On this point we can only speculate as we have no systematic data. Above and beyond the afore-cited studies on voting by advisory committee members who obtained waivers and statistical analyses showing that scientific articles written as part of drug-company funded studies are on average more favorable to the company's medicines, we know of only a few isolated cases, revealed during public controversies or court trials. Example: A reputed clinician writing in 2007 in the *New England Journal of Medicine* published a critical meta-analysis of Avandia®, a Glaxo-Smith-Kline (GSK) anti-diabetes medicine; the article sparked public debate on the medicine's value and Avandia® sales ultimately fell. It was later learned that one of the referees chosen by the *NEJM* to review the article had sent it to GSK before publication—the referee had participated in some clinical trials for the company—thereby enabling GSK to attempt to pressure the critical clinician and prepare its reaction to his article more quickly than it otherwise might have. The referee was found to have infringed the confidentiality rule to GSK's benefit since the company did not know he had an article that went against its commercial interests. The referee's act was therefore clearly one of collusion (cf. United States Senate 2010).

case his feeling of dependence and the conditions of the dependence relationship are extremely likely to produce collusion.

The important point here, however, is not whether this understanding of relations between experts and industries is well-founded or not. In order for it to work in favor of open voting—as clearly it does—it would simply have to be shared by all players: the FDA, FDA watchdogs, FDA critics. And indeed, it is the opinion of all these players that the work that experts do with pharmaceutical companies creates the possibility of collusion. Quite cogently, then, this understanding of the tie between clinicians, academic scientists and the pharmaceutical industry leads players to prefer open voting to secret voting.

2.2. The probability of unanimous voting

We have mentioned the two conditions that must be met if voting is to break the dependence tie between a voter and a third party with an interest in the decision: 1) material organization allowing the voter to keep her choice secret, and 2) the requirement that voters not make their choices known or visible. We need to add a third condition: it has not to be possible to assess the results of the voting in a way that precludes guessing how voters voted. This means that unanimity must reasonably seem improbable.

The fact is that unanimity voting is fairly common on advisory committees. All research into the question has reached the same conclusion. From 1998 to 2005, Diana Zuckerman (2006) studied meetings of six FDA advisory committees on medicines, randomly chosen from a total of 16 committees. She only studied votes bearing directly on marketing approval or withdrawal. This gave her 50 voting situations. Of that total, 27 were unanimous—i.e., 54%.

We studied voting by the same six advisory committees from January 2005 to July 2007, this time focusing on all medicine evaluation votes. Our selection criteria were therefore broader than Zuckerman's. While she chose to study only the final-decision vote—Should the molecule be approved for marketing/withdrawn from the market?—We took into account not just these votes but those preceding them, involving assessment of the benefits, risks, etc. associated with the proposed molecule. This gave us a total of 38 voting situations, of which 17—45%—were unanimous.

Clearly, then, secret voting would not protect voter anonymity even half the time; this information is crucial in understanding why secret voting has been rejected (if ever it were

seriously envisaged). The reasoning is not completely valid, however, since we are applying what was observed of open voting to secret voting. It is reasonable to hypothesize that if we could somehow observe the behavior of these same committees during secret voting, the results would be different, since open voting is likely to facilitate conformism and artificially swell consensus. However, the very low number of starkly divided results and high number of strong majorities (see Appendix I.3. Table 2) lead us to think that what explains most cases of unanimity is not pressure to conform but indeed expert opinion convergence. This means that even if voting were secret, it is likely that the number of unanimity votes would significantly reduce the anticipated benefits of secrecy. Each voter would know that the odds were about 1 to 2 that her choice would in fact be revealed by the advent of a unanimous vote.

2.3. The publicizing vocation of advisory committees

Bentham's nuanced thinking on the comparative advantages of secret and open balloting brings to light more effectively than unilateral pleas for one or the other could do the conditions in which each type is appropriate. Namely, it shows how virtuous open voting is actually conditioned by the nature of the influence—i.e., whether it serves particular interests or the general interest:

> The cases in which publicity would be dangerous, are those in which it exposes the voters to the influence of *seductive* motives more powerful than *tutelary* motives. In judging whether a motive ought to be referred to the class of *seductive* or *tutelary* motives, it is necessary to examine whether, in the case in question, it tends to produce more good or more evil – whether it tends to favour the greatest or the small number (Bentham [1791] 1999: 145).

Publicity is thus considered desirable when the segment of the public attentive to the general interest is larger—and weighs more in the minds of voters—than the segment representing particular interests. Given the assumption that the harmful effect of possible ties between committee members and the particular interests of pharmaceutical companies cannot be countered by secret voting, open voting at least exposes experts to the view—the tutelage, to use a form of Bentham's word—of public overseers, e.g., consumer organizations such as *Public Citizen*. This means that consumer organizations and FDA and drug company critics better represent the general interest than the drug companies themselves and that surveillance of those companies, facilitated by the publicity of debate and advisory committee voting, will induce the FDA to be more respectful of the general interest. This supposition corresponds well, as we see it, to the dominant ideas in this context and is congruent with the purposes that advisory committees were designed to serve.

Since 1972 when they were created, advisory committees have had three stated purposes: to provide the FDA with assistance from highly competent specialists outside the agency; to integrate viewpoints that are not spontaneously represented into the decision-making process; to protect the FDA from criticism by ensuring that its decisions are framed by a public consulting arrangement. The first purpose assumed great importance from the 1970s to the mid 1980s, when scientific procedures for measuring medicine performance were being developed and learned by an increasing number of specialists, including within the agency itself. However, in the 1990s, characterized by reiterated controversies around medicines and FDA decisions, the third purpose came to the fore. Critics and the press are reputed to exert pressure on the FDA and AC members to respect the interests of American citizens—pressure that works against the business cynicism of the drug companies and what critics consider insufficient FDA vigilance. Advisory committees' vocation for "keeping things public" has thus become increasingly important.

This understanding of where interests lie is congruent with the analytic checklist proposed by Warren to describe trust in institutions: citizens need to know the tasks that institutions were designed to perform, i.e., to have a "normative idea" of them; they need to know that institution members risk sanctions if they do not perform those tasks as set out; lastly, institutional transparency must be such that outside critics can criticize how institutions are functioning and thereby trigger sanctions. In Warren's schema, critics function as citizen representatives (Warren 1999: 349; Quéré 2005).[11] Predictably, critics of the FDA agree with this analysis. More remarkably**,** it is reasonable to conclude on the basis of FDA public declarations to the effect that advisory committees are essential in fostering public trust in the quality of its decisions that the FDA too shares this analysis.

The publicity vocation of advisory committees, bolstered as it has been with the passage of time, represents a strong plea in favor of the public character of their debates and voting. A "mixed" arrangement might be contemplated: public debate and secret voting. However, the possibility of obtaining secret voting results not in line with the drift of the preceding public debate would induce suspicion of duplicity and cancel out the virtues attributed to public debate. The advisory committee "vocation" thus suggests that both debating and voting should indeed be public. And the reigning idea of the nature of the experts' opinion is perfectly consistent with this.

[11] It should nonetheless be noted that this configuration is likely to be made more complex (if not rendered vulnerable) when groups representing a segment of consumers find that their interests converge with the drug companies'. This occurred for a time in the early 1990s in the U.S., when AIDS patient advocacy associations began demanding—for readily understandable reasons—precisely the same thing the drug industry had been calling for years: accelerated marketing approval procedures for new molecules. Since then, patient associations in Europe as well have often made common cause with the drug companies on particular issues. This of course complicates the dominant view of how particular and general interest are distributed.

2.4. The nature of expert opinions

The preference for public voting can also be linked to the dominant notion of the nature of the opinion an expert's vote is supposed to express. Texts on and practices of FDA advisory committees alike make it clear that experts' opinions are thought of as a whole that includes both the expert's vote itself and the reasons he or she gives to support it. Rather, this whole may be described as the "movement" that determines opinions, the understanding being that this "movement" should be made public.

Reasons and votes

The brief, dismissive mention of secret ballots in the FDA text on preferred voting procedures reads as follows (italics ours):

> Transparency and public participation are critical features of advisory committee process. The use of secret ballots, long a hallmark of the American electoral experience, generally is not appropriate in the advisory committee context *because the expert opinion of each member should be clearly understood and identified with that expert.* (FDA 2008a: 4)

Once again, this is the only mention of secret balloting we have been able to find in FDA documents, including both studies and critical comments elicited by advisory committee functioning. The passage also very briefly defends the public character of expert voting. That justification is made up of two parts:

-- every expert's opinion has to be readily understandable;

-- it must be possible to identify each opinion with a particular expert.

The fact that the two ideas are run together by way of an "and" within a single dependent clause suggests how closely they "go together" in collective representations; indeed, they seem inseparable. Secret voting is unacceptable because one advisory committee purpose is to collect the opinion of each expert, an opinion understood as a set that includes both the reasoning that went into it—i.e., the reasons that made the decision-maker favor a positive or negative answer to the FDA question—and that answer itself. On the one hand, the FDA insists on obtaining a vote which is a clear answer to its questions: "Votes can be an effective means of communicating with FDA because they provide feedback on discrete questions" (*ibid.*: 4). In practice the agency is careful to ensure that voting is on extremely precise questions, and answers must correspond to one of only three options: yes, no, abstain. On the other hand, it wishes to collect the reasons that led the expert to vote one way or another. It therefore is concerned to collect "opinions" in accordance with two distinct but related meanings of that term: 1) opinion as a conclusion

reached through reflection and presentable as an argument on the question under study; 2) opinion in the sense of a single answer out of a predetermined list of acceptable answers (Yes, No, Abstain), also understood to be related to the expert's thinking. In sum, the expert's meaning-2 opinion is understood to be the conclusion of a meaning-1 opinion. More exactly, in response to the question asked, the expert either has or reaches a meaning-1 opinion that then leads him to decide in favor of one of the three possible meaning-2 opinion options. We are therefore dealing with a notion of opinion that distinguishes between but does not separate meaning 1) and meaning 2). The fact that the two are considered inseparable precludes any "public reasoning"/secret balloting combination.

The spectacle of determining opinions

The desire to collect an opinion understood as a whole that encompasses not just answers to FDA questions but also the reasons that led each expert to vote yes or no is manifest in advisory committee procedures: experts are requested to explain their choices. On this point, the aim of the 2007 reform was simply to separate clearly the two distinct phases of voting: simultaneous hand-raising and explaining one's vote. Oral voting had opened experts up to the temptation of linking individual comments, their vote, and their explanation of that vote together in the same moment of speaking. In some instances they were actually invited to do so. Some session presidents encouraged them to do all these things at once; others proposed going around the table a second time to collect explanations and comments.

With this in mind, it is useful to try to circumscribe the exact nature of experts' explanations for their votes. FDA voting session transcripts show that requesting experts to explain their vote amounts not so much to a real requirement as an ideal that exerts a powerful grip on actors' thinking. First, it should be noted that in a significant proportion of voting situations, "yeses" and "nos" are uttered without any reasons being given. Second, when the voting does go together with comments, those comments are more likely to be recommendations linked to the answer rather than justifications of the answer. Lastly, whenever experts do provide real explanations for their votes, those explanations are very likely to be very short. Experts are likely to mention a single point or consideration each, as if that explained why they voted no rather than yes or vice-versa. But they do not explain—nor are they asked to do so—why the point they mention deserves to be considered more important or decisive than any other.

These explanations, then, cannot be claimed to constitute the whole of the reasoning culminating in the given vote. There is indeed the idea that such reasoning has been done, but the reasoning

itself is not presented; at the very least it is not required of experts. This observation also holds for the FDA itself and for medicine evaluation agencies in general: they do justify their decisions, but justification texts seldom go over one or two pages.[12]

It is illuminating to contrast what advisory committees publicize of their deliberations with what is publicized by constitutional courts such as the US Supreme Court, where open voting and a written statement of judges' reasons are both compulsory. In constitutional courts, the reasons that led judges to make this or that decision are written up at length; these statements document all stages in the decision-reaching process and how they were connected. Advisory committee decisions also have to be justified and the justifications may be contested. Still, the reasoning that was operative in reaching the decision is not recounted step by step for the purpose of justifying that decision.

This difference between medicine evaluation committees and constitutional courts renders the requirement that advisory committee debate and voting be public more intelligible. In the FDA context—i.e., close surveillance of its activities and frequent contesting of its decisions—public exposure of all committee meetings seems meant to compensate for the fact that it is impossible for members to formulate individual or collective opinions as arguments framed by reference texts and decision interpretation history in such a way that the line of reasoning leading to a given decision can be perfectly, exhaustively recounted in a text. At the very least, there is no habit of proceeding this way. The reason that all advisory meeting comments, exchanges and information have to be transcribed is that, in contrast to what jurists must know how to do, these committees do not have any established means at their disposal for formulating their expert reasoning.

Moreover, in pursuing the comparison between the two types of deliberating bodies, it is important to note that the notion of publicity does not mean the same thing for them. In the U.S. Supreme Court, publicity is ensured by the written word. Judges' debates and possible negotiations are not exposed to external viewers. Conversely, though each FDA advisory committee produces a document ranging from 300 to 500 pages and available for consultation on the agency's website, that document is actually a full transcript of recorded meetings.[13] There is no writing procedure during or after meetings. The small audience that attends AC meetings and the larger public that reads AC meeting transcripts or watches video recordings of them are directly observing a specific moment or watching a recording of it: the moment when experts

[12] The low proportion and brevity of real explanations for votes do not contradict FDA insistence that it is interested both in votes and experts' reasons for them. The FDA takes into account not only explanations for votes but also reasons mentioned in discussions that precede voting—reasons that voters themselves regularly cite.
[13] Video recordings of some FDA meetings may now be purchased by the public.

meet to produce a recommendation. What is offered to the outside world is a recorded and to some degree dramatized sequence—the "movement" through which opinions were determined. Publicity here amounts to spectacle more than anything else. What has to be made transparent—visible or audible—to the public since it cannot be restored in the form of written argument is the "movement" through which expert opinions were formed, the conditions and process by which they were determined. This movement begins with the as-yet-undetermined will of the expert,[14] proceeds through her reception of information and participation in the debate, and concludes with the move in which she "decides" by answering "yes" or "no" to FDA questions.

*

* *

Why vote publicly when the main problem to resolve is drug company influence on experts? The following arguments were identified for and against secret voting and public voting:

Table a: The arguments for and against secret and public voting

	Secret voting	Public voting
Collusion	harmful	preferable
Occurrence of unanimous voting	irrelevant	–
ACs " publicity" vocation	unsuited	preferable
Opinion/reasoning	unsuited	*necessary*

1) The possible effect of ties between firms and experts is thought of as a relationship of collusion rather than dependence. Collusion is protected by secrecy; conversely, it can be identified and exposed by public voting, making it possible to identify the connection between a tie and a vote.
2) The significant probability that voting will be unanimous sharply diminishes the protection provided by secret balloting.

[14] The FDA wants experts' opinions to be undetermined at the beginning of the process. If an expert had already formed an opinion, this would be understood to reflect possible intellectual bias (Rettig and al. 1992; O'Riordan 2009; Usdin 2009).

3) Advisory committees' vocation for making and keeping FDA decision-making processes public and transparent is incompatible with secret voting.
4) Experts' votes should be closely related to their reasons for them, and those reasons should be made public.

These arguments have just been reconstituted on the basis of what characterizes the situation of FDA advisory committees, and taking into account ideals and norms that are widely shared within the FDA and outside it. Once again, only the fourth argument is explicitly cited, and only in one agency document. It is therefore reasonable to inquire into the relevance of the other three arguments, arguments of which there is no trace in any public FDA documents. We have asked, How do these arguments reinforce the decision-making rules that are used? The following conjecture provides an answer: when a decision-making rule is established, it benefits from inertia; unless there are perceptible disadvantages associated with its use, unless actors who would have some interest in changing that rule contest it, then the rule is not changed, even though the people who use it cannot spontaneously cite the reasons for which it was established.[15] But if people should begin to doubt the rule's value, protagonists affected by use of the rule will look for reasons to justify either keeping or scrapping it. This holds for public debating and voting in advisory committees. The arguments enumerated here seem to us the logical result of the overall context in which those committees function; i.e., the way conflict-of-interest impact is conceived; the strong likelihood of unanimous voting; the set task of these committees; how the nature of experts' opinions is conceived. This set of arguments would seem to amount to a kind of reflective equilibrium in favor of public voting, should the value of that way of proceeding ever come to be doubted.

[15] It is important to note, however, that the only argument mentioned in an FDA document is also the strongest—see the table a.

3. **The trouble with oral voting**

As explained, the July 2007 reform of FDA advisory committee procedure was presented first and foremost as a switch from sequential to simultaneous voting. But this change implied another that seems to us just as important: oral voting was replaced by hand-raising and more recently by electronic voting. What are the specific properties of the original method, oral voting?

First, most voting procedures—hand-raising, standing/sitting, preprinted ballots, different colored balls—ensure that the voter provides a single, unequivocal response to a motion that can be modeled as follows: "To Question A, do you answer 'Yes' or 'No'?" The precision of the outcome produced by such methods is due to two complementary features: a) voters must choose from among options that were defined before they cast their votes; b) votes for each option are perfectly homogeneous so adding them together is unproblematic. The first point concerns the clarity of each individual decision; the second what Bentham called "the principle of the identity of the motion."[16] These two features are what allow for correctly aggregating individual votes. Oral voting, on the other hand, raises problems for vote aggregation in that individual voters have some latitude when expressing their responses (even when the question immediately precedes the response). And the variation that this is likely to generate renders individual votes less clear and may render the voting result inexact.

3.1. Analyzing non-discrete answers

To identify manifestations of the latitude implied in voting orally, to measure the effects of such latitude and detect its potential impact on the balloting result and therefore the validity of that result, we determined and systematically studied a balloting corpus comprising all FDA medicine-related advisory committee meetings that included voting on FDA questions and were held in the years 2005, 2006 and from January 1 to July 29, 2007; that is, the nearly two and a half years of committee meetings leading up to the reform, which officially went into effect July 30, 2007. Our balloting corpus is made up of 13 committee meetings, during which a total of 38 questions were put to a vote and a total of 737 individual votes were cast (see Appendix I.1 for greater detail).

To analyze vote+additional utterance sequences systematically, we read all the relevant FDA AC meeting transcripts as well as other meeting-related documents (rosters, minutes, etc.). We

[16] Bentham ([1791] 1999: 91) first uses the phrase "the identity of the terms of the motion and those of the resolution"; a few pages further he speaks of the "principle of the identity of the motion" (*ibid.*: 95). Moreover, what led Condorcet to prefer the use of a written ballot was not so much secrecy itself as the discipline imposed by secret balloting: "It is therefore to ensure opinion precision and exact counting, and to accommodate human weakness without compromising truth, that this method should be preferred" (Condorcet [1788] 1986: 345).

studied the detailed proceedings of 38 voting sessions; i.e., meeting minutes listing FDA questions and indicating "yes," "no" and "abstain" scores and full transcripts of the concluding phase of the meetings, consisting in discussions immediately prior to voting, vote-casting, and individual members' explanations of their votes. For each meeting this phase corresponds to 30 to 50 transcript pages.[17]

We then sorted vote-related utterances into 5 categories by possible status in connection with the vote. An additional utterance can

1) explain the speaker's vote: the committee member substantiates his or her "yes," "no" or "abstain" answer with one or two reasons for it;
2) manifest the speaker's difficulty clearly choosing one of the three authorized answers; this difficulty could be manifested in one of three distinct ways:
    a) utterance suggests the speaker is indecisive;
    b) utterance suggests that the "yes" (or "no") answer could be matter of degree when in fact it cannot; we have called such utterances "small yes";
    c) utterance is meant to explain speaker's vote in response to the question but in fact does not clearly manifest the nature of that response;
3) suggest that speaker's "yes" or "no" is actually a response to a slightly different question than the one posed by the FDA; we have termed such answers "yes but";
4) concern the nature of the FDA's question or the problem under discussion; such responses have the potential effect of reopening debate;
5) amount to a comment or proposal**;** more generally, non-identifiable as a type 1, 2, 3 or 4 utterance.

There are no specific words in AC members' utterances that allow for making these distinctions. For example, it may not make sense to file a given voter's "yes but" vote in the "yes but" category, since that category is reserved for utterances that call into question the "identity of the motion" corresponding to the FDA question.[18] The example of the AC meeting held in February

[17] The aim of systematically analyzing all meetings held within a strictly delimited, pre-reform period is to give an idea of the quantitative weight of the phenomena identified. In the definitive version of this text, the plan is to present percentages. To have more examples, we will include some committee meetings held prior to the period as well as meetings of different committees studied in previous research (Urfalino 2011).

[18] We named the categories "yes but" and "small yes" because these types of utterances fairly regularly include, respectively, the expressions "yes but" and "no but" or "minimally yes" and "a mild yes." But the occurrence of those expressions is neither necessary or sufficient for filing an answer in one of these categories.

2005 on three COX2-type anti-inflammation medicines will clarify our way of proceeding. A question on one of these molecules read: "Does the overall risk-benefit profile for rofecoxib support marketing in the U.S.?" To this question, 17 committee members answered "yes," but six of these yes-voters said more than yes. And two of the members voting "no" mentioned other considerations at the moment they cast their vote—remarks that cannot be understood as explanations of their vote. Consider the verbatim answers of the six yes-voters and the two no-voters:

> VIOXX® 2005, Q3b[19] :
> -- "Yes, but."
> -- "Yes, with reservations."
> -- "Yes, but at lower dose, 50 milligrams."
> -- "Yes, but only for children."
> -- "Yes, with restrictions."
> -- "Yes, with restrictions."
> -- "I would say overwhelmingly no, although if individual patients can petition the company under some mechanism, I would support that."
> -- "No, but with a possible compassionate-use program."
> (Arthritis Drugs AC and Drug Safety and Risk Management AC, joint meeting of February 16-18, 2005, transcript, vol.3, p. 334-336)

The first two "yes" answers reflect the expert's difficulty deciding; we put them in category "small yes." The next four answers also follow the "yes, but" model and were indeed filed in the "yes, but" category, category 3. Responding affirmatively to the question of whether a medicine should be put on the market while specifying a different dose from the one in the question or adding that the motion should be restricted to children amounts to answering a different question than the one put by the FDA, which in this case bore on approving the molecule for a specific dose and for all adult patients. The meaning of the two "yes, with restrictions" answers is harder to grasp since neither speaker specified what his or her restrictions were. But these answers also seem responses to a slightly different question than the FDA's.

The two "no" answers are not "no, buts" or "small yeses" or supporting explanations. Both those members preferred not to allow the medicine on the market. But they also thought that if for some reason patients could not be treated with other available drugs, they should be able to take Vioxx® as part of a compassionate-use program, regardless of the fact that the medicine had not been approved for sale. In answering this way, they were putting forward a complementary

[19] We follow the convention of designating these examples by the name of the medicine under study—either the international name of the molecule (here rofecoxib) or, for better known medicines, the brand name (here Vioxx®)—followed by meeting year and FDA question number.

measure that would not affect their decision not to approve sale of the drug. We filed these utterances in category 5, proposals and comments.

Category 1 and 5 answers correspond to what the voter was expected to produce: a non-composite answer + an explanation for it, or a non-composite answer + complementary comments or proposals. The three other types of answers are not what was expected. They illustrate three distinct problems with oral voting, problems that the 2007 reform has undoubtedly helped to resolve. Those problems are:

-- the "identity of the motion" problem;

-- the indeterminacy problem;

-- the problem of distinguishing between debating and voting.

3.2. The "identity of the motion" problem

The type of answer that we have called "yes, but" has drawbacks that can affect balloting results and the meaning of collective opinions or recommendations. Bentham noted these drawbacks when examining the method adopted by the "Haute Guyenne" provincial assembly in 1779 in compliance with a royal edict. That method consisted in reducing to two the number of opinion options open to assembly members on a given question, then choosing the one that garnered the most votes. Bentham observed that this way of clarifying the many opinions expressed in the assembly had the effect of confusing the notions of debating and voting, and that the plurality ultimately won by one or the other authorized opinion was likely to be made up of heterogeneous wills that could not logically be added together. The only way to comply with the "principle of identity of the terms of the motion and those of the resolution" (Bentham [1791] 1999: 91) was to discuss no more than one motion at a time and put that motion to a vote immediately after discussion.

FDA ACs comply with Bentham's wish for a single "yes" or "no" vote on each motion. But the fact that members vote orally means that remarks can be made at the moment of voting that seem to reopen debate on that motion. The potential effect of this is to imperil "the identity of the motion and the resolution."

The four "yes, but" votes at the 2005 Vioxx® meeting, Q3b—i.e.:

. « Yes, but at lower dose, 50 milligrams. »

. « Yes, but only for children. »
. « Yes, with restrictions. »
. « Yes, with restrictions. »

—leads us to define "yes, but" answers as follows: a "yes, but" (or "no, but") answer in response to a "Yes or no to A?" question is in fact an affirmative or negative answer to a different question: "Yes or no to A'?" where A' is a similar but distinct motion from A. This means "yes, but" answers cannot legitimately be added to "yes" votes and "no, but" answers cannot legitimately be added to "no" votes.

AC members are seldom attentive to the nature of their responses because those responses seem to them like comments or recommendations of the sort the FDA wishes to obtain and the chair regularly solicits.[20] However, a "yes, but" answer is much more than a comment or recommendation. It amounts to changing the motion that conditions the voter's approval. In some cases—e.g., approving a drug but at a lower dose or for children only—the change may be readily detected by an outside observer. In others it is difficult to say whether what gets added on to a "yes" or "no" answer amounts to a change in the motion or simply a recommendation. In some cases speakers specify that the substance of their additional utterance conditions their vote—a move that attests to the problematic nature of such utterances. Consider the following two occurrences:

> FORMOTEROL 2005, Q2a:
> Called upon to vote for or against adding a warning on the label of a drug called formoterol, one member switched his vote, explaining :
> "Mr Chairman, I want to change my no vote to yes, given that my colleagues also have expressed the caveat that caused me to vote no."[21]
>
> ARIFLO 2003, Q3:
> Questioned two years earlier on whether it was possible to dismiss a given side-effect as a safety concern of Ariflo, the 12 members of the same committee answered in the affirmative, yet one specified:
> "The way I read the question I think everyone's answer should be no with the caveats, but to go along with what I have heard here so far I would say yes, with the stipulation that there be the kind of follow-up that Dr. Surawicz and Dr. Cross both mentioned."[22]

[20] Speaking immediately before a vote on the dose recommended by the owner company, the chair of the April 24, 2007 Antiviral Drugs Advisory Committee meeting on approving a molecule for treating AIDS said, "I think we should go around now and vote yes/no as we have been asked on this. If you have additional caveats, feel free to put them in" (transcript, p. 313).
[21] Pulmonary-Allergy Drugs Advisory Committee, meeting of July 13, 2005, transcript, p. 333. The voting outcome was 12 yes, 0 no, 1 abstain.
[22] Pulmonary-Allergy Drugs Advisory Committee, meeting of September 5, 2003, transcript, p. 235.

This voter, who clearly did not feel he could say "yes" and leave it at that and who sought to link his approval to a condition affecting the meaning of the motion under examination, may be understood to have hesitated between "yes, but" and "no, unless."

It also sometimes happens that up against voters' questions or in reaction to a "yes, but" answer, the chairman or an FDA official will intervene to request the voter to be sure to respond to the exact motion being examined. Such interventions are aimed at maintaining the semantic identity of all "yes" and "no" answers. Consider the following two flagrant examples:

> ARIFLO 2003, Q1:
> Asking if Ariflo was an effective enough treatment for a given lung disease to justify giving it marketing approval. Just before putting the question to a vote, the chairman asked an FDA official to clarify the meaning of the question. At that point a member named Dr Apter requested consideration of another alternative: "I would like to be able to say yes but with postmarketing recommendations." The FDA official ruled out this option, saying: "I mean, that can be something which you can put out as a discussion and as a comment that we take, but the voting is really as it is. Am I clear on that?"[23] Clearly the FDA official was moving to preclude a "yes, but" answer.
>
> SPIRIVA 2002, Q1:
> One year earlier, the same committee was called upon to answer the same question for a different drug. The first voter answered "yes, but," eliciting a correction from the chairman. Their exchange proceeded as follows:
>
> "DR. PATRICK: Yes, on the basis of the Phase IV recommendation.
> CHAIRMAN DYKEWICZ: Well, we have to have an answer though. It can't be qualified. It has to be yes or no. If you believe that the data that currently exists is sufficient to approve the drug or whether you would defer approval, in which case you would say no. You would say no?
> DR. PATRICK: No. Yes. Yes.
> CHAIRMAN DYKEWICZ: You would say yes?
> DR. PATRICK: Yes."[24]

Interventions by the chair can aggravate rather than correct affirmative answer heterogeneity, as in the following example (entire voting procedure quoted, our italics):

> CELEBREX 2006, Q2:
> "DR. BATHON (Chair): … So, the question is do the available data demonstrate that Celebrex is safe in the treatment of juvenile rheumatoid arthritis? We will start on this side of the room with Dr. Sandbord. Say your name and yes or no.

[23] Pulmonary-Allergy Drugs Advisory Committee, meeting of September 5, 2003, transcript, p. 214. Dr. Apter ultimately said, "My answer is yes, but there have to be postmarketing studies"; his vote was counted as a "yes." The score was 3 "yes," 7 "no."
[24] Pulmonary-Allergy Drugs Advisory Committee, meeting of September 6, 2002, transcript, p. 315-316. The final score was 8 "yes," 3 "no."

DR. SANDBORG: Christy Sandborg, no.
DR. GORMAN: Richard Gorman, no.
DR. DAUM: Robert Daum, yes for the duration of the study that was observed.*
DR. PROSCHAN: Mike Proschan, no, but I think it doesn't demonstrate that it is unsafe either.
MS. DOKKEN: Deborah Dokken, no.
MR. LEVIN: Arthur Levin, no.
DR. WEISE: No less safe than other current uninvestigated agents. Am I allowed to abstain?
DR. BATHON (Chair): Yes.
DR. WEISE: Abstain
DR. MORRIS: Was it yes, short term; no, long term? Is that our vote ?
DR. BATHON (Chair): I think yes or no is what we want.
DR. MORRIS: Just yes or no?
DR. BATHON (Chair): Yes.
DR. MORRIS: No.
DR. HOLMBOE: Yes, only in the time that was studied compared to another agent. That is it.*
DR. BATHON (Chair): Joan Bathon, no.
DR. CHESNEY: Joan Chesney, no.
DR. LEHMAN: Tom Lehman, I think in the context of the rest of what we do the answer is yes.
DR. O'NEIL: Kathleen O'Neil, a very deliberate and considered yes in comparison to other drugs and the standard we use in other drug approvals.
DR. DAVIS: John Davis, yes in the short term compared to other non-steroidals.*
DR. BOULWARE: Dennis Boulware, given the instruction earlier, as compared to the current medications used I would have to say yes.
DR. BATHON (Chair): Dr Turk, can we get your vote?
DR. TURK[answering by phone]: Yes. Can you hear me?
DR. BATHON (Chair): Yes, we can hear you.
DR. TURK: Yes in the context of the short duration.*
DR. BATHON (Chair): So, we have eight "no," seven "yes" and one abstention. …"[25]

The official count was 7 "yes," 8 "no" and 1 "abstain." But 4 of the 7 votes counted "yes" were in fact "yes, but" (indicated by an asterisk): the "but" made the voter's approval conditional on a short-term prescription period—identical to the clinical trial period for which the safety of the drug had been demonstrated. And the passage in italics represents another remarkable occurrence. Instead of saying "yes, but for the short term" like the four other "yes, but" voters, Dr. Morris asked if it would be possible to vote separately on the short-term and long-term questions. The chair ruled this out after letting one "yes, but" vote go by and before allowing three others. In reaction to these developments, Dr Morris voted "no." In strict logical terms, all the "yes, but" answers had the same meaning as Dr Morris's "no" vote. To be consistent, the chair should have applied the same restriction to all the other "yes, but" answers as she imposed on Dr Morris—in which case those three "yes, but" answers would have been counted as "no" and the score would have been 3 "yes," 12 "no" and 1 abstain. Alternatively, Dr Morris's "no" should have been considered a "yes, but," in which case all 5 "yes, but" responses should have

[25] Arthritis Drugs Advisory Committee, meeting of November 29, 2006, transcript, p. 304-306.

been invalidated for not answering the FDA question. The score would then have been 3 "yes," 7 "no," 1 "abstain," and 5 "invalid ballots". For either of these counting methods, the official "no" vote would have been much stronger.

Three lessons may be drawn from the afore-cited examples:

1) What we have identified as "yes, but" votes do indeed affect the identity of the motion.
2) Committee members and chairs are unlikely to perceive this; whether they do or not depends on the individual. The point is therefore subject to contingency and varies by individual and from one committee to another. Some members do perceive the identity of the motion problem, as attested by their questions; some chairs and FDA officials also perceive the problem and try, more or less skillfully, to resolve it. But in most cases, "yes, but" answers are confused with comments and recommendations,: the underlying assumption being that they are to be added to another set of votes when doing so actually changes the meaning of those votes.
3) In strict logical terms, "yes, but" votes should not be added to "yes" votes. In fact, they are more likely to resemble "no, unless" votes, and when they do, it makes sense to add them to "no" votes. In other cases, it would make more sense to think of them as invalid responses or abstentions in that they do not answer the question at hand. The motion A' that they express an opinion on is clearly different from the motion A that they have been called upon to approve or reject. In committee practice, however, "yes, but" answers are often counted as "yes" votes.

Considering the entire set of votes studied, the question arises as to the effect of "yes, but" votes on FDA AC collective opinions and on the exactitude of those outcomes. There are two answers to this question: A) Quantitatively, "yes, but" votes only affected the final outcome of 1 of the 38 votes we studied, and they had no impact on FDA decisions; B) The point should not be dismissed, however, because the virtual absence of impact is due to vote distribution structure.

A) "Yes, but" votes do not usually tip the voting result, for one of two opposed reasons: either they are isolated instances within an otherwise unanimous or strong majority vote, or else almost all "yes" votes are in fact "yes, but" votes, in which case voting on the question "Yes or no for motion A?" ultimately produces the collective outcome "Yes for motion A'."

Only two votes in our corpus of 38 should be revised to reflect the impact of "yes, but" votes. Interestingly, these were the two votes that attracted the most media attention—for other reasons. Both figured in the February 2005 joint committee meeting on Cox-2 drugs. It should be recalled that a few months after Merck withdrew Vioxx® from the market, the informed public was scandalized by two slight-majority AC voting outcomes, one in favor of keeping Pfizer's Bextra® on the market (17 "yes," 13 "no," 2 "abstain"), the other approving returning Vioxx® to the market (17 "yes," 15 "no"). If the "yes, but" votes had been counted and distinguished from the "yes" votes, the majority in favor of Bextra® would have been smaller still and the tide would have turned against Vioxx®:

- Bextra®: **14 "yes,"** 13 "no," 3 "yes, but" ("yes, but" in this case meant approval on condition that dose and prescription period be limited) et 2 "abstain."

- Vioxx®: 13 "yes," **15 "no,"** 4 "yes, but" (approval on the afore-mentioned conditions).[26]

As mentioned (see 1.1.), these two votes galvanized FDA critics and moved *The New York Times* to inquire into financial ties between joint committee members and the drug companies affected by this recommendation. However, and despite the critics' vigilance, all attention was on the showdown between "yes" and "no" voters. That attention was of course sharpened by the suspicion of a financial motive or bias in favor of approval, and this in turn worked to obscure what we consider a remarkable feature of those votes; namely, "yes" vote heterogeneity and the illogic of adding together heterogeneous responses.[27] The selective media attention also obscured the fact that the experts might have had reasons—and not just financial motives—for voting as they did.

B) It could be claimed that these observations on "yes, but" voting are finally empirically irrelevant. It is true that "yes, but" votes had very little impact on the set of votes studied.[28] However, it would be a mistake not to examine this phenomenon more closely. The fact that "yes, but" votes do not have greater impact on ballot results is explained by strong convergence of individual expert opinions. Of the 38 votes studied, 17 were unanimous. For 9 votes the majority was over 75%; 5 of those 9 produced a majority over 90%. There would surely be more

[26] What's more, 2 of the 13 "yes" votes for Vioxx® were "small yes" votes (see 3.3. for the definition of this category).
[27] Only one committee member, Dr. Shafer, who had voted "yes" for Bextra® and "no" for Vioxx®, suggested a less stark interpretation of events, and in doing so emphasized the fact that qualifying the meaning of "yes" and "no" votes worked to attenuate the opposition between them: "After the meeting [Dr. Shafer] asked how his vote [on Vioxx®] was counted: 'no, with exceptions' or 'yes, with restrictions'? 'Those positions are not very far apart. I think my colleagues on the committee all struggled, as I did, between "no, with exceptions" and "yes, with restrictions" in casting their votes'" (Malone 2005).
[28] This is especially true given that the FDA, criticized across the board after Merck withdrew Vioxx®, did not follow the committee's small-majority recommendations. A few weeks after the committee meeting it requested Pfizer to withdraw Bextra®, and it did not encourage Merck to put Vioxx® back on the market.

frequent cases of "yes, but" votes tipping the outcome if there were more small majorities; in that case, packets of 3 or 4 "yes, but" votes could actually shift the majority. In only 5 of the 38 votes was the majority-minority vote difference equal to or below 3, and in only 3 ballots was there a 4-vote difference (see Appendix I.1. Table 1).

Oral voting, then, can deleteriously affect the meaning of a vote, but the strength and frequency of expert opinion convergence significantly reduces this risk.

3.3. The problem of indeterminacy and of some votes influencing others

As we saw in Section 2.4., experts are supposed to reach their own judgments in AC committee meetings. This means forming an opinion; specifically, it means that each expert is supposed to reflect on the question at hand in order to decide in favor of one of the options: "yes," "no" or "abstain." Once again, these committees are called upon to produce non-binding recommendations or advice rather than decisions—and as we know, advice need not take the form of a « yes » or « no » answer. However, over time, advisory committee recommendations have been increasingly required to resemble binding decisions. This is clear from a 1992 report by the Institute of Medicine (IOM):

> The IOM committee discussed at length a proposal by one member that advisory committee votes on questions before them be scaled (for example from one to nine), rather than binary (yes, no). This proposal is based on three premises. First, safety, effectiveness, and other factors considered in advisory committee recommendations are continuous variables. Second, given that there are no definitive empirical bases for deciding issues before an advisory committee, the FDA should seek to determine both the range and strength of the experts' opinions. Third, a good deal could be learned by frequent scaled votes about the multiple facets of component questions that come before a committee, including the distribution of views among members on particular issues, as well as any persistent voting patterns or apparent biases. ... The IOM committee was intrigued by the proposal but found it too novel and formalistic to recommend for general adoption by the FDA. The committee favored

> binary votes that forced individual members to resolve uncertainty in an up-or-down manner and provide unambiguous advice to the agency. (Rettig and al. 1992: 189-190).

The rejected proposal would have enabled committees and their members to produce advice that would reflect the complexity of the work of evaluating drug molecules, a complexity attested to by the facts that drug performance is measured by scale and that evaluating drug molecules is a multi-dimensional operation. If this proposal had been adopted, ACs would have been asked to provide the FDA with finely graduated, differentiated assessments, and the FDA alone would have done the work of reaching the final decision.

In fact, the FDA chose a different approach and procedure: in addition to providing complex advice or arguments in favor of one way of proceeding over another, ACs and AC members are expected to proceed as if they themselves had to decide whether or not to approve the given medicine for sale (or withdraw it from the market). This is why experts are called upon to give clear-cut, discrete answers indicating which course of action should be undertaken: approve or not (withdraw or not).[29]

Oral voting enabled AC members to graduate their answers by responding to FDA questions with such expressions as "a small yes," "a barely yes," "yes, minimally," "a mild yes." Members even occasionally mentioned entire sets of considerations while presumably voting yes or no. In cases where such composite utterances made it difficult to identify a clear "yes" or "no" answer, the chair requested a more precise answer and sometimes even stated the answer he or she had reached by interpreting the member's utterance (see Appendix II for examples).

These clear manifestations of experts' difficulty making up their minds raised for us the question of the influence that some votes may exert on others. The social sciences, specifically social psychology, have continually noted a connection between indeterminacy and influence. Individuals called upon to make a judgment or choice who do not themselves have a firm conviction on the question to be decided or action to be taken are particularly open to influence from others.

[29] Committee members seldom use their right to abstain. Our 38-ballot pre-reform corpus included two ballots with one abstention and one with two, for a total of four abstentions out of 737 individual votes. It is interesting to note that after the reform, the abstention rate rose by a factor of 8, from 0.5% to 4%—a major increase, though the rate has remained low.

Good and bad influence

Here we need to explain what we mean by influence. FDA material and observers' comments offer no definition of influence; the 2008 *Guidance* simply mentions that influence can operate consciously or unconsciously. However, the implicit FDA definition does seem consonant with the more precise one used in the social sciences. It is useful to distinguish between power and influence. In a power relationship, actor A can affect the choices of actor B by making promises or threats, including implicit ones, i.e., by acting on B's future situation; B will then anticipate the costs and benefits of his choice (Crozier, Friedberg 1980; Friedberg 1997). In situations of influence (rather than power), A directly affects B's preferences without changing his present or future situation (Chazel 1992). However, this definition does not specify the range of ways in which influence can exert itself. In fact, influence can be rational—as it is when due to the impact of an argument—or it can constitute an unconscious mechanism: suggestion or imitation. Influence, then, can be rational or not, conscious or not.

This definition enables us to discern good and bad influence at work within ACs. Rational influence, related to argumentation and argumentation-based exchanges among members, is considered good. The switch to simultaneous voting, meanwhile, was aimed at precluding what is considered the non-rational, potentially unconscious influence of one vote on another. Why do actors value the impact produced by reasons and reasoning, even seeking to produce that impact, while disapproving influence of votes on other votes? There seem to be two implicit concerns here:

1) to distinguish between reasons and judgment. In arriving at a judgment, the subject fits reasons together to form an overall argument, the purpose being to reach a conclusion; it is then that conclusion that is expressed by his or her vote;

2) to confer different collective statuses on reasons and judgment: it is desirable for actors to share their reasons with each other and thereby influence each other, but the other side of this understanding is that each actor has to reach his or her "own" judgment, in his or her own way.

Reasons, then, are to be shared whereas the judgment reached by weighing or fitting together reasons is to remain autonomous and unshared. It is important to be able to add up judgments without having them influence each other. In *Lettres écrites de la montagne*, Rousseau, working to defend himself against the Republic of Geneva's machinations against him, offers an excellent illustration of the distinction between the two terms. To show respect for his interlocutor-reader

and preserve a chance of convincing him without influencing him, he explicitly asks that reader to listen to his reasons without accepting his judgment:

> What, then, would I do, Monsieur, to merit your trust and justify, to the best of my ability, your esteem? This: rightly distrusting myself, I shall tell you not so much my opinion as my reasons, which you shall then weigh and compare, and you shall choose. But go further still: be ever wary—not of my intentions: God knows they are pure—but of my judgment. (Rousseau [1764] 1964: 688, [translation AJ])

Rousseau thus invites his interlocutor to make his own judgment, while hoping to convince him of the value of his reasons. Bad influence, then, is influence that bears on the final determination of the subject's opinion. It can be exercised consciously, as when an expert is tempted to follow the opinion of another committee member whom he thinks of as more competent than himself, or by a phenomenon of which the subject is not herself conscious. In all such cases, influence diminishes the number of fully formed judgments and undermines the truth value of opinion convergence. The understanding is that committee's recommendations should be reached by adding up individual points of view, abilities, and, ultimately, the reasoning of the different members.[30]

With all of this in mind, what do the transcripts of AC meetings tell us about the influence of votes on other votes prior to the 2007 reform? First, it is important to note that there are instances of influence that cannot be observed. For example, a member who is preparing to vote "no" may end up voting "yes" after hearing the "yes" answers of other experts. No one can detect that member's first intention; the only way to know of it is for he himself to say that he changed his mind.

[30] We have cited the distinction between reasons and judgment because it seems an accurate representation of FDA vocabulary and the way AC expert committees function. However, 1) other distinctions could have been used, such as understanding and will, a pair long used in philosophy of the mind and chosen by the tandem Bentham-Dumont. Bentham explained that secret voting would not put an end to the beneficial influence of "enlightened persons": « but happily the secret mode of election does not diminish the influence of mind on mind » (Bentham [1791]1999:146). Dumont added: "[voting secrecy] only bears on the influence of will over will" (Bentham/Dumont [1791]1822: 191); and 2) the problem is essential but also extremely complicated: neither of these distinctions is entirely satisfactory: a) distinguishing judgment from reasons does preserve the rational dimension involved in reaching an opinion, but the assumption that actors assemble and connect their reasons, thereby developing a complete argument that will lead them to voting one way rather than another seems debatable; b) distinguishing between understanding and will establishes a sharper boundary between the public aspect of reaching an opinion and the private one, but only by sacrificing the rationality of the voter's final decision, which ends up seeming an irrational leap or, at best, an a-rational power to decide, indexed on a metaphor of attention or watching (Ricoeur 1966, 2007: pt I, ch. 4).

Other instances of influence are observable, either in the transcripts or the voting results themselves. The ones we have found may be partially—but only partially—imputed to sequential voting, for the following reasons:

-- in sequential voting the weight of the task of making what is akin to a collective decision is not equally distributed among the individual committee members;

-- the hypothesis that sequential voting induces majority-following voting behavior is plausible;

-- in FDA AC meeting transcripts we find a few cases of vote switching during the voting but the switches are likely to have been due to the fact that voting was oral rather than to the fact that it was sequential.

Sequential voting and the unequally distributed weight of individual decision-making

Sequential voting allows for situations where committee members who vote last can calculate whether or not their vote will change the final score; e.g., if the voting prior to their turn indicates a strong majority that cannot be affected by the remaining votes—theirs. The transcripts show only one occurrence of a committee member explicitly noting this fact:

> KINERET 2001, Q4:
>
> last voter's utterance:
>
> DR. WOFSY: David Wofsy. I have the good fortune, I think, in sitting in this place at the table, unlike the other people who have voted, to know that it is 5 to 2 at this point, and my vote won't swing the balance. [laughter]
>
> In the next three pages of transcript, the expert explains why it is hard for him to make up his mind and why he has ultimately decided to vote "yes." The final score was 6 "yes," 2 "no," 1 "abstain."[31]

This expert's remark is just one example of the inequality induced by sequential voting. Given that voting is sequential and public, all committee members can see how the score is evolving. This in turn means either that the last voters' votes have decisive weight because they are in a position to swing the majority or that their weight is insignificant because there is already a firm majority and their votes cannot affect it.

[31] Arthritis Drugs Advisory Committee, meeting of August 16, 2001, transcript, p. 197.

Sequential voting and conformism

Has the shift from sequential to simultaneous voting been concomitant with a fall in unanimous voting and heavy majorities—what we could call a conformism index?

To answer this question we examined a second set of ballots, made up of votes taken by the same six committees from the day the reform went into effect (July 30, 2007) to the end of 2009 (see Appendix I, sections 2 and 3 for descriptions and a comparison of the two ballot sets). The following table compares the two sets of ballots in terms of unanimous voting, majorities equal to or greater than 75%, and voting convergence rates, defined as the ratio of unanimous scores + heavy majorities to total number of ballots.

Table b: Unanimity and heavy majority ballots, voting convergence

	Pre-reform	Post-reform
Number of unanimous votes	17 (45%)	30 (36%)
Number of majorities ≥ 75%	9 (24%)	29 (35%)
Voting convergence rate ≥ 75%	*26 (69%)*	*59 (71%)*
Total number of ballots	38 (100%)	83 (100%)

These results demonstrate the plausibility of the hypothesis that simultaneous voting reduces conformism—against a backdrop of strong expert opinion convergence. We observe a considerable drop in proportion of unanimity votes (45% to 36%) after simultaneous voting was instituted. We also observe a considerable increase in proportion of majorities equal to or stronger than 75% (from 24% to 35%). The voting convergence rate, meanwhile, has remained stable (69% to 71%).

The above hypothesis is based on the understanding that two phenomena may be combined: a) experts' opinions tend to converge, and it would be mistaken to understand that convergence as conformism; on the contrary, we can reasonably assume that in most and indeed nearly all cases the information on which experts base their evaluations allows for opinion convergence; b) some committee members, observing the convergence, are inclined to follow the majority because they have not made up their minds or because they actually support the minority position but do not

dare affirm this. Comparing the two sets of ballots confers a degree of plausibility on this hypothesis. However, it would be important to verify it for more ballots by increasing number of years and number of ACs studied.

Vote-switching

Another way of identifying the influence phenomena that may be operative during committee voting is to study vote-switching. In the years prior to the reform, committee members occasionally requested to switch their vote, and they could do so up until the end of the voting. For questions voted on before the reform (studied by means of meeting transcripts) we found five meetings in which at least one member changed his or her vote, for a total of 15 switched votes—very few. Either the voter 1) changed his or her position during the voting or 2) changed his or her position when the question was put to a revote. Though few in number, the switches are worth examining.

The previously discussed 2005 vote on Bextra® offers a case of 2)—an aspect of this controversial meeting that, once again, was noted by neither the FDA nor its critics. That vote, on whether or not to keep the drug on the market, exhibits one property of oral voting: the risk of disorder. Two members did not give clear answers during the initial balloting, but this only became clear to the actors when examining the vote after members had voted on Vioxx®. The Bextra® question was then put to a revote, and 10 voters switched their vote, reducing the number of abstentions and increasing the "no" vote. In the end, the majority in favor of keeping the medicine on the market was smaller than for the first vote. Here it can reasonably be concluded that what reduced the number of abstentions during the second vote was the fact that just after the first vote a committee member protested against the high number of "abstains" (details in Appendix III).

In the other four meetings there were one or two vote changes only, and they occurred during the voting itself. The following table presents the effect of these changes on final scores:

Table c : Vote switching in the course of balloting

Meeting	Type of change	Score before the change	Final score (with the change)
Formoterol, 2005,Q2a (transcript p. 329-333)	1 No to Yes	11 Yes, 1 No	12 Yes, 0 No
Ketek, 2006,Q2c (transcript p. 420-422)	1 Yes to No	4 Yes, 6 No	3 Yes, 7 No
Kineret, 2001, Q4 (transcript p. 189-194)	1 Yes to No	7 Yes, 1 No, 1 Abstain	6 Yes, 2 No, 1 Abstain
Serostim, 2003, Q4 (transcript p. 164-173)	2 Yes to No	4 Yes, 5 No	2 Yes, 7 No

The changes were minor and did not swing the majority. But the main lesson to be learned from them can only be gleaned from the transcripts. The first two changes were clearly linked to utterances that earlier voters had added to their votes. The other two took place only after the voting had been interrupted by renewed discussion. This means that observable vote changes were due not to the factor put forward to justify abolishing sequential voting—i.e., the impact of early votes on later ones—but rather to the fact that oral voting is likely to restart discussion or reintroduce components of the deliberation during the voting itself. Oral voting allows committee members to link their votes to utterances that violate the distinction between debating and voting, a distinction that the procedure itself is meant to underline and protect.

3.4. Debating or voting?

Throughout this section we have been pointing out the effects of the leeway characteristic of oral voting, underlining how it can affect the identity of the motion, weaken the requirement to make up one's mind and give a clear-cut answer, and facilitate influence. We could also have pointed out less noticeable flaws and disorders, such as simply miscounting « yes » and « no « votes.[32]

But we should not try to grasp the effect of oral voting exclusively in terms of its flaws, for two reasons: a) some of the facts that the 2008 Guidance on voting procedures identified as dysfunctional and requiring correction were thought of before the reform as normal and even desirable; b) the very notion of oral voting is problematic.

(a) Prior to the reform, debates and voting were conducted differently depending on committee and committee chair. Many actors were already concerned about ensuring a strict separation between debating and voting, and in this they anticipated the reform. But regardless of the

[32] In our ballot set (all votes held from 2005 up to the reform), we identified three occurrences of vote miscounting, all corrected by FDA officials either during the meeting or later in the meeting minutes. None affected the majority.

precautions taken, the concept and practice of voting that prevailed at the time worked to blur any pre-established boundaries between the two. Before the reform, two partially contradictory ideas coexisted: the idea that answers to FDA questions had to be both discrete, though accompanied with an explanation for the vote, goes hand in hand with the idea that even as the chair went round the table collecting each member's vote, experts might still be reaching their definitive answer, and they could even change answers.

In this situation it was considered almost normal for a committee member to pass when asked to vote, since listening to his or her colleagues was understood to help him or her decide.

> ARIFLO 2003, Q1:
>
> - *Chairman*: Dr. Cross?
> - *Dr. Cross*: My answer is maybe but I have to decide which way to go. Can I pass for now and listen to other comments as we go around the table?
> - *Chairman*: I am going to have to ask somebody how we do procedurally. Yes, we can let you pass, but not everybody can pass.[laughter][33]

Given that the reasons one cites to explain one's vote are likely to convince other members who have already voted, some chairs considered vote-switching normal and even desirable. Here we have run up against precisely the sort of debating/voting mix that Bentham condemned:

> KETEK 2006, Q1:
> Just before the vote, the chair declares:
> "After we have heard everyone's rationale, there is going to be an opportunity to change your vote. I would suggest that changing one's vote is not necessarily a sign of weakness."[34]

Clearly this chair was expressing quite the opposite of a fear that early voters could influence later ones, since as he saw it, when members voted and gave reasons for their vote, the whole procedure was still one of exchanging arguments. Before the 2007 reform, FDA ACs functioned in exactly the same way as the French provincial assemblies that Bentham described: those bodies had no concepts, words or practices that differentiated "between original motion, motion in amendment, argument and vote" (Bentham [1791] 1999: 97).

b) The very notion of oral voting is problematic, and the practice itself weakens the boundaries between debating and voting. Unless speakers practice firm discipline when giving their answers—and this would surely be awkward for all concerned as it would affect each personally:

[33] Pulmonary-Allergy Drugs AC, meeting of September 5, 2003, transcript, p. 216. Moreover, we saw that during the first vote on keeping Bextra® on the market, one committee member said "I pass" instead of voting.
[34] Anti-Infective Drugs AC and Drug Safety and Risk Management AC, joint meeting of December 14-15, 2006, transcript of the Dec. 15 meeting, p. 350.

members would be called to order individually, the chair, of course, having to reiterate that intervention—oral voting gets contaminated with something that is not voting and is very likely to lead to utterances that will in turn lead participants a) to call for reopening debate (because the identity of the motion has been affected or because having the opportunity to comment enables speakers to give "graduated" answers) or b) to reiterate aspects of the deliberation (i.e., give reasons for their choices that are in turn likely to affect the following opinions and even make previous voters change their votes) or c) make remarks that will have the effect of reopening debate.

The advantage of hand-raising (the method implemented by the 2007 reform in place of oral voting) and electronic voting (which took the place of hand-raising) is that they materially enact the separation between debating, voting, and explaining one's vote without it being necessary to call anyone to order. These methods thereby ensure that the identity of the motion remains intact while maintaining the requirement that experts make up their minds and firmly separating the sequence in which mutual influence is allowed—i.e., debate, deliberation—from the voting itself, in which it is important to preclude mutual influence.

The contrast between oral voting and the other procedures also teaches us something about the nature of voting. The characteristics of voting that are violated by the oral variety are :

-- segmentation: voting should not be accompanied with comments likely to change the meaning of the vote;
-- isolation of the act: voting is a single expressive act, to be detached from the "story" (reasons, motives, hesitations, influences) that led the voter to choose one of the possible alternatives;
-- finality of the act: once the voter has voted, the vote cannot be changed;
-- semantic invariability: the meaning of the vote is fixed in advance rather than being determined by the individual voter.

This contrast suggests that oral voting is a kind of debating-voting hybrid. It would be aberrant to require debate to exhibit the characteristics that voting requires. "Oral voting" amounts to a particular way of expressing one's will, but it does not comply, as voting does, with the demands involved in collective decision-making. Bentham was clearly exasperated by the confusion reigning in pre-Revolutionary French provincial assemblies, and he repeatedly contrasted them to the British Parliament, which he represented as a great advance and indeed a great discovery: over time, Bentham maintained, men had discovered the conceptual and practical distinctions necessary to parliamentary practice (Bentham [1791]1999: 97-98). But he may have overlooked another feature of the difference between the two types of assemblies: because in France the King had the last word on all assembly proposals, those assemblies were not actually concerned to comply with collective decision-making requirements. As Bentham observed, their deliberations usually produced a series of opinions. This in turn kept provincial assembly

members—noblemen, clergymen, members of the *tiers-état*—from forgetting their sense of rank. The King's authority and last word meant that participants could each preserve their freedom of expression during deliberation and voting. This in turn explains the absence of clear differentiation between, and indeed the overt combining of, debating and voting—designated in the *Ancien Régime* by the verb "*opiner.*"[35].

In this assembly practice, also used in the Paris Parliament (Rogister 1995), each member, or "*opinant*," gave his opinion (chronological order was determined by social rank). Then members whose opinions proved not to be widely shared were asked to choose between the two opinions that had received the highest numbers of "approbations." The opinion ultimately chosen was the one to which the greatest number of assembly members rallied. In this sequence, where opinion-expressing gradually developed into opinion selection, "giving one's opinion" could indeed amount to a mix of formulating an opinion (in both Bentham's and Condorcet's sense of drafting a motion) and deciding to support a pre-stated opinion (i.e., voting for a given motion).

But in contexts where results are not reached by this "decanting" process, giving an opinion and voting are distinct from each other. When it comes to uttering an opinion, collective decision requirements did not apply, and "*opinants*" had "sovereign" control in expressing their opinions. When it comes to voting, the fact that a collective decision was being made immediately affected participants' latitude for expressing themselves. Returning to the twenty-first century and the FDA, we see an analogy between Bentham's opposition between French provincial assemblies and the English Parliament and the opposition between pre- versus post-reform AC voting. When voting orally, AC experts were free to express themselves; they lost this in the shift to hand-raising. Before the reform, they could qualify the meaning of their "yes" or "no" votes and/or manifest difficulty choosing. But that freedom was costly, since they had no control over how their wishes would be integrated into the collective result. Experts voting "yes, but" or "small yes" were of course able to express their qualifications, but their votes might well be counted "yes." With the hand-raising procedure, they do not have any more control over the conditions in which their votes are aggregated than they did with oral voting, but formatting opinions in this way enables each voter to concentrate on voting in a way that will ensure that his or her vote will work to achieve a result as close as possible to the one he or she really supports. The voter who, prior to the reform, was tempted to contest how the motion was phrased and the meaning of positive and negative responses is now forced to accept the semantic invariability of his or her vote; such voters now have to determine whether they want to go with the "yeses" or

[35] In the French *Littré* dictionary (1872), *"opiner"* is "1° to say one's opinion in a deliberation; 2° to be of the opinion that"…

"noes" and they can no longer delude themselves that somehow their opinions will not be formatted or standardized. It may well be that none of the externally imposed alternatives an AC voter has to choose from really satisfy her wishes. This means that it is up to her to choose which of the alternatives will reinforce the collective opinion that comes closest to (or is least remote from) the one she supports—or to abstain and thereby choose not to impact on the vote.[36] Moreover, with hand-raising or electronic voting, positive or negative votes cannot be indeterminate or unclear. These methods channel voter indecision into the "abstain" option.

The hypothesis that what brought about the observed changes was the change in voting procedure seems substantiated by the sharp increase in abstention rates observed after oral voting was discarded.

Table d: Abstention numbers and rates in pre- and post-reform ballot sets

Pre-reform	Post-reform	
4 (0.5%)	51 (4.1 %)	"Abstain" number (rate)
737 (100%)	1236 (100%)	Total of individual votes

We can hypothesize that some committee members who would have uttered "yes, but" votes before the reform either voted "no" or abstained after the reform went into effect. Likewise "small yeses" have perhaps been replaced by "abstains."

Once again, FDA advisory committees are consultative, as were provincial assemblies. But their opinions and recommendations have to take the form of collective decisions. In reaching those decisions, then, members are subjected to the tension between the complexity of an expert opinion and the simplicity of the voting format that makes vote aggregation possible. Oral voting was a sort of compromise that moderated that tension. Perceiving the drawbacks of oral voting led to discarding it.

Conclusion

It should suffice to conclude by underlining two points:

[36] This kind of voting cannot be qualified as strategic or sophisticated in Farquharson's sense (1969); i.e., a voter who actually prefers option B votes for option A because voting for B would produce a collective result—option C, for example—further from B than A. On the contrary, such decision-making is done at a lower level than anticipation of the effects of vote aggregation. However, it does concern the strategic dimension of voting. Given that the constraints of collective decision-making are present from the moment an opinion is expressed, that opinion must from the outset take into account the collective, interactive dimension of voting. What introduces the strategic dimension is the constraint placed on self-expression.

1) type of publicity and the understanding of what is implied in making a judgment. The shared understanding of the nature of expert reasoning has a considerable impact on what type of publicity is considered desirable. Here we have emphasized the contrast between publicity through writing and publicity as transparency. The understanding of what is implied in evaluating medicines and what kind of decision-making this involves oscillates between a) the scientific ideal of demonstration operative in clinical drug trials and b) an understanding of decision-making as a event in which individual decision-makers confronted with a full set of considerations make up their minds through a somewhat mysterious act of will. In b) the decision-making process has the status of a "black box" which, because it cannot be opened or made legible, has to be watched carefully to ensure that no undesirable "input" (interests, dependency, intellectual biases, unconscious influence) gets inside and that all good "input" (information, reasons, discussion) does get inside. In the end, the vigilance meant to ensure that AC meetings proceed smoothly and correctly, the concern for transparency—here, what seems to be valued is the "show" of individual minds being made up—seems closely related to the fact that the notion of decision-making that prevails in these committees is indeed b): a somewhat mysterious determining of the will. In fact, understanding the act of will as a kind of a black box exacerbates the concern to make its functioning transparent. This in turn indicates one possible means of making controversies around decision-making on medicines more intelligible (if not of reducing the degree to which decisions on medicines are contested or the strength of the suspicion that committee members are colluding with the pharmaceutical industry); namely, that the work of formulating opinions on drug molecules could model itself at least partially on the work of formulating judgments in the legal sphere.

2) Underneath the reform as defined by its designers, another reform may be operative. The 2007 FDA reform can be described in two complementary ways, both of which are accurate: 1) it was a move from sequential to simultaneous voting; 2) it was a move from oral voting to hand-raising. The 2008 *Guidance* emphasizes the first description; our analysis shows that the second description is more relevant, in that it absorbs part of the first. If our analysis is valid, then what is the status of this interpretative discrepancy? We can make the following two conjectures (noting that they are not mutually exclusive):

a) In reforming its decision-making rules, the FDA invoked first and foremost a concern to combat the danger that some votes would influence other votes. We have seen that by discarding oral voting, the reform actually went further than precluding this danger. But this overtly declared motive—i.e., precluding the operation of influence—also corresponded most directly to some criticism of the way the ACs functioned. That criticism bore above all on the waiver system

enabling experts with financial ties to drug companies to sit on the committees. FDA critics were also concerned to maintain the independence of expert judgment, and they were attentive to all aspects of committee operation that might reduce that independence. What they were not attentive to was the disorder produced by the oral voting procedure. We can therefore hypothesize that by reforming its voting procedures, the FDA managed to attain two general aims that often prove difficult to reconcile: resolving a real problem and escaping blame (Hood and Rothstein 2001).

b) The complexity of collective decision-making makes it difficult—for observers and even more so for implicated actors—to have perfect control of how collectively reached decisions are understood and to know how decision-making rules should be reformed. The reform that the FDA implemented may be having more far-reaching effects than the agency was hoping for. If so, this is a matter neither of blindness nor full awareness of what the reform would change but rather a kind of myopia in which emphasis was laid on the less relevant of two descriptions of the reform.

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Appendices

Appendix I: The two sets of ballots studied

We chose the same 6 randomly selected advisory committees studied by Zuckerman (2006): Antiviral Drugs AC; Arthritis Drugs AC; Dermatologic and Ophthalmic Drugs AC; Gastrointestinal Drugs AC; Pulmonary-Allergy Drugs AC; Reproductive Health Drugs AC.

Urfalino had already done a study of the meetings of these committees (Urfalino 2011).

I.1. Pre-reform ballot set (2005-July 29, 2007)

- 6 committees
- time span: 2005 – July 29, 2007
- 13 meetings; 38 ballots
- 1-10 ballots per meeting
- 7-32 voters per meeting
- 737 individual votes, including 4 abstentions

Results:

-- 17 of the 38 ballots—45%—were unanimous.

-- 9 of the 38 ballots—24%—resulted in majority votes equal to or greater than 75% of votes cast.

-- 26 of the 38 ballots—68%—resulted in voting convergence equal to or greater than 75%.

Table 1 : Majority-minority differences

Majority-minority differences	**Number of ballots**
≤ 4	7
> 4	14
Unanimity	17
Total	38

I.2. Post-reform ballot set (July 30, 2007 through 2009)

- 6 committees
- time span: July 30, 2007 through 2009
- 23 meetings; 83 ballots
- 1-11 ballots per meeting
- 4-27 voters per meeting
- 1236 individual votes, including 51 abstentions

Results:

-- 30 of the 83 ballots—36%—were unanimous.

-- 29 of the 83 ballots—35%—resulted in majority votes equal to or greater than 75% of votes cast.

-- 50 of the 83 ballots—71%—resulted in voting convergence equal to or greater than 75%.

I.3. Comparison of the 2 sets of ballots

Table 2: Unanimity and score convergence

	Pre-reform	Post-reform
Unanimity votes	17 (45%)	30 (36%)
≥ 75% majority votes	9 (24%)	29 (35%)
< 75% majority votes	12 (31%)	24 (29%)
Total	38 (100%)	83 (100%)

Table 3 : Abstentions and abstention rates for the two sets of ballots:

Pre-reform	Post-reform	
4 (0.5%)	51 (4.1 %)	Number of "abstains" and abstention rate
737	1236	Number of individual votes

Appendix II: Manifestations of voter indecision

VITRASE 2003, Q7:

During a vote on whether the benefits of the ophthalmological drug Vitrase outweighed its risks, the "yeses" had a slight majority: 7 "yes" to 5 "no." But two of the "yes" votes were graduated (our italics):

- "I think *yes, not the most positive yes, but yes."*

- "*Yes, minimally."*

While a third expert uttered his vote only upon insistence from the chair after a long moment of waffling that went from "small yes" to "no" before settling on "yes":

"I think I might give *a mild yes"*

[followed by] "I could say *very mildly yes"*

[followed by] "I will say no."

[Intervention of the chair, Dr. Fong] Fong: "So, to summarize, I think you would say yes you could imagine a situation if it can be shown to be effective."

Expert: "Right."

In response to the resulting confusion about the vote count (was it 6 to 6 or 7 to 5?), the chair turned to the expert and requested him to state his vote again. Expert: "So I guess you could put me as a yes."[37]

PHOTOFRIN 2003, Q4:

The committee was asked to decide whether a 5-year period was sufficient for evaluating the reduction of cancer risk the medicine was said to provide. The score was 9 "yes" to 1 "no," but 5 of the 9 "yes" votes were "small yes," as shown in the following quotation from the transcript (our italics; voters' names deleted from first example):

"I'd say yes."

"It's *barely adequate*."

[37] The question read: "Do the benefits of using Vitrase outweigh the risks in the treatment of vitreous hemorrhage?" Dermatologic and Ophthalmic Drugs Advisory Committee, meeting of March 17, 2003, transcript, p. 237.

Chairman: "So *a small Y."*

(Laughter).

"No."

"Yes."

"*A barely yes.*"

(Laughter).

"Yes, and I would add the comment after the 5-year data, I would be comfortable having it in the indication."

"Yes."

"If maximum is taken out and just provide 5 years."

"Yes, minimum."

Chairman: "And mine is a yes also."[38]

KETEK 2006, Q2c:

- Chairman: "Dr. Proschan."

- Dr. Proschan: "I am clueless on this. I have no …"
- Chairman: "Abstain. Dr. Morris?"
- Dr Morris: (…)
- Dr Townsend: "I wouldn't feel the need to limit it to second-line or third-line. I don't know if it is the place to bring this up. I think it may be worthwhile to put in some wording about using telithromycine after another macrolide and the possibility for increased hepatotoxicity in that situation. So anyway."
- FDA meeting secretary: "Is that a no, Dr Townsend?"
- Dr Townsend: "A no"[39]

Lastly, the chair's comments on the substance of the committee's collective recommendation or opinion may themselves introduce graduation and degree:

[38] Gastrointestinal Drugs Advisory Committee, meeting of June 26, 2003, transcript, p. 187.
[39] Anti-Infective Drugs AC and Drug Safety and Risk Management AC, joint meeting of December 14-15, 2006, transcript of the Dec. 15 meeting, p. 421-422.

SALMETEROL 2005, Q1b:

After an unanimous vote—13 "yes", 0 "no"—that included 2 "yes, but" and many comments—the chair said: "I think that we have a unanimous vote here but, clearly, the warning is there that none of us feels 100 percent yes."[40]

Appendix III: The two Bextra® ballots

The February 2005 meeting of the Drug Safety and Risk Management AC and the Arthritis Drugs AC joint committee focused on three COX-2 anti-inflammation drugs that had been controversial for several months. It first examined Pfizer's Celebrex®, then Pfizer's Bextra®, then Merck's Vioxx®. For each molecule two questions were asked, the first about the risk of cardiovascular accidents associated with the drug; the second whether the risk-benefit ratio made it legitimate to keep the medicine on the market (or in the case of Vioxx®, to reapprove marketing). At the start of the vote on keeping Bextra® on the market, the third voter said he was "unclear," but it is in turn unclear if he was abstaining or intended to give an answer later. The fourth voter said "I pass"—another answer that is hard to interpret: was he abstaining or intending to vote later? The first five votes were as follows:

1- "Yes."

2- "Yes."

3- "I am concerned that we are adding a new risk to something that already has a black-box warning. So I am unclear here."

4- "I pass."

5- "Yes."

The voting procedure continued and at the end, the chair and the FDA representative forgot to get clarification on the status of the responses by the two experts in question, probably because they had observed, without commenting on the fact, that a clear majority was shaping up. They may have thought that the two answers amounted to abstentions. The meeting continued and Vioxx® came up for examination. It was only after voting on Vioxx® that the chair called for a second vote on Bextra®, and then only after being called to order by the FDA officials present. We cannot know if the FDA representatives put the question to a second vote because of the two unclear votes or whether those votes had been counted as abstentions and they deemed unacceptable a vote score in which nearly one-fourth of voters—10 out of 32—had abstained.

[40] Pulmonary-Allergy Drugs Advisory Committee, meeting of July 13, 2005, transcript, p. 320. The meeting concerned the implications of recently available data related to the safety of long-acting beta-agonist bronchodilators (salmeterol and formoterol). The FDA question read: "Based on the currently available information, do you agree that salmeterol should continue to be marketed in the United States?"

As it happened, the second result differed from the first:

	YES	NO	ABSTAIN	"I pass", "unclear"
1st vote	15	7	8	2
2nd vote	17	13	2	-

Individual vote switches were as follows:

1st vote 2nd vote	YES	NO	ABSTAIN	"I pass" "unclear"	2nd vote score
YES	14	1	2	-	17
NO	1	6	4	2	13
ABSTAIN	-	-	2	-	2
1st vote score	15	7	8	2	32

The most important changes caused by the 8 (or 10) switched votes were the fall in number of abstentions, from 8 (or 10) to 2, and the switching of 4 abstains to "no." The first vote was thus more strongly in favor of keeping Bextra® on the market than the second: the gap between majority "yes" and minority "no" narrowed from 8 to 4 votes. It is difficult here to know the exact cause of these votes changes. However, the most probable hypothesis is the impact of an objection made just after the first vote by the member named Dr. Nissen, a "yes" voter, against the number of abstentions. He argued that since all committee members had the same data at their disposal, it was impossible for the collective decision to result from amputating such a high proportion of abstentions, and he requested that for all later ballots each voter have clearly made up his or her mind: formed a clear opinion.

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