

Science in policy

Principal–agent theory and the structure of science policy, revisited: ‘science in policy’ and the US *Report on Carcinogens*

David H Guston

This paper uses principal–agent theory to examine the structure of ‘science in policy.’ It draws from one in-depth case study of regulatory science in the USA, the production of the biennial Report on Carcinogens by the National Toxicology Program (NTP) of the National Institute of Environmental Health Sciences, particularly NTP’s review of saccharin as a potential human carcinogen in the late 1990s. The sources of data include extensive documentary review, observation of two public meetings of an advisory committee to NTP, and confidential interviews with seven of nine members of that advisory committee. The paper elaborates on the environment that precipitated Congress’s need for a reliable agent, in the creation of NTP as an intermediary to serve as that agent, in the articulation of an explicit set of terms for the performance of that contract, and in the shirking behavior that agents engaged in, despite such precautions.

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THE DELEGATION OF SIGNIFICANT authority from political to scientific actors is arguably the central problem in science policy, both analytically and practically (Guston, 1996). Varieties of the central problem of delegation play out through the logic of principal–agent theory, as described by an increasing amount of related work published in this collection and elsewhere (Braun, 1998; 1993; Caswill, 1998; Guston, 2000; 1999; 1996; Morris, 2000; van der Meulen, 1998). This work, however, largely concentrates on elaborating principal–agent theory in questions of the sponsorship of research, the role of research councils, and other aspects of what Brooks (1968) famously called “policy for science.”

Despite this understandable focus, principal–agent theory can also help illuminate the structure of science policy with respect to questions of ‘science in policy.’ Such questions include issues of peer review and other aspects of the use of expert advice for making policy decisions. By framing the central problem of science policy as one of delegation, scholars gain perspective on the deceptively simple question that politicians (or the public) may ask, “How do we trust scientists when they say and do things we have little substantive knowledge about?” Because such a question could be asked in either arena, principal–agent theory actually begins to provide the analytical union of ‘policy for science’ and ‘science in policy’ that Brooks himself sought (Guston, 1996).

This paper reconstitutes the ‘structure of science policy’ agenda for such issues of expert input into policy decisions. It draws from one in-depth case

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study of regulatory science in the United States — the production of the biennial *Report on Carcinogens* by the National Toxicology Program (NTP) of the National Institute of Environmental Health Sciences, particularly its review of saccharin as a potential human carcinogen in the late 1990s. The sources of data include extensive documentary review, observation of two public meetings of an advisory committee to NTP, and confidential interviews with seven of the nine members of that advisory committee.

The first section of the paper briefly introduces relevant points of principal–agent theory to articulate a preliminary structure of ‘science in policy.’ The subsequent sections elaborate how these issues play out in the design of NTP’s process for identifying carcinogens, that is, in the environment that precipitated Congress’s need for a reliable agent, in the creation of an intermediary to serve as that agent, in the articulation of an explicit set of terms for the performance of that contract, and in the avoidance of such rules that agents inevitably engage in, despite such precautions. It is my hope that demonstrating the principal–agent structure of ‘science in policy’ in this way will spur further theoretical and empirical development and contribute to questions of institutional design.

Structure of ‘science in policy’

As the introduction to this collection describes, the rudiments of principal–agent theory include the assumption of an asymmetry of information between a relatively ignorant principal who makes a delegation of authority to a relatively expert agent who receives that delegation. That the agent is more expert than the principal raises the prospect of two problems of delegation known as adverse selection (or hidden information) and moral hazard (or hidden behavior).

These problems are often understood by their temporal sequence. Adverse selection is the difficulty of choice the principal first faces in selecting the best agent to accomplish the chosen goals. The information that is hidden is precisely who is the best agent to delegate to or to fulfill the contract. Moral hazard is the difficulty the principal faces after the agent has been chosen and the contract let. The behavior that is hidden is how well the agent works to complete the delegation or to fulfill the contract.

The presence of a ‘bilateral monopoly’, that is, an exclusive relationship between a principal and agent for the production and consumption of whatever the agent is hired to produce, exacerbates this information asymmetry because there is no market, and therefore no reference price, no competitors, no substitutes, and so on, for the goods produced (Niskanen, 1971). This asymmetry exists regardless of the nature of the product. That the product in the case of ‘science in policy’ is esoteric knowledge may make the asymmetry even more profound.

The concept of the bilateral monopoly makes explicit that principal–agent theory describes a reciprocal relationship. Although principals and agents each have their own respective interests that create adverse selection and moral hazard, they also share an interest in creating and sustaining a mutually beneficial relationship over time.

Therefore, although it is customary in the literature to present principal–agent theory in a way that appears to favor principals in their efforts to control agents (particularly when such terms as ‘shirking’ are used to describe the behavior of agents when they fail to fulfill contracts) principal–agent theory may be applied from the perspective of the agent as well. This perspective is particularly important when framed according to how the agent may demonstrate to the principal that there is no shirking or hidden information or behavior injurious to the efficient completion of the contract.

The common-sense question above about trust may thus, with the insight of principal–agent theory, be decomposed into more balanced questions: “With which scientists should decision makers contract?”; “How do decision makers and scientists assure that the contract is being performed to expectations?”; and the reciprocal of the first question, “With which decision makers should scientists contract?”.

‘Science in policy’ questions are primarily structured as problems of adverse selection. Decision makers have questions for which there may be technical answers, and they must choose which experts to believe among the many offering expertise. Such questions also incorporate elements of moral hazard, for example, in the integrity of the scholarship on which the experts may draw in order to make their expert claims. However, defining and solving the moral hazard problems follow the prior discussion of adverse selection, because the principal and agent must first solve the problem of contracting before they solve post-contractual problems of performance.

From a delegation or hypothetical contract between decision makers and experts, the former receive benefits including: expert knowledge, insight, or early warning (for instance, Albert Einstein’s letter to President Franklin D Roosevelt about the possibility of the construction of atomic weapons, or scientists’ raising of global change issues onto the agenda); the potential solution to particular problems or questions (for instance, how to verify compliance with nuclear treaties through seismic surveillance, or whether

certain substances are carcinogenic); and legitimation for decisions that require technical sophistication (for instance, how to regulate environmental hazards, or how to fund publicly sponsored research).

The experts receive benefits including: direct payment as consultants or employees (for instance, being hired as a regulatory scientist or science advisor); indirect payment through appointments to positions that bestow authority, prestige, or access to specialized or privileged knowledge (for instance, being appointed as a member of a science advisory or peer review committee); and the psychic returns of seeing one's ideas implemented in a legitimated pursuit of the public good.

Assumptions made

As initially conceived, this perspective appears to assume that decision makers are sincere in their desire to hear scientific perspectives and that experts are sincere in offering perspectives they believe are correct. Such an assumption, however, is not necessary, because sincerity, or the lack of it, can be included in the framework of adverse selection. That is, some principals or some agents may decide to solve the problems of adverse selection by contracting only with others who are ideologically predisposed to agree. Indeed, this situation may be the prevailing norm of science advice.

We would then need to assume only that they want to transact with one another, and leave any speculation about the benefits from the transaction to observing the performance of the contract. Decision makers seeking only legitimation, for example, are likely to behave differently than those seeking early warning. Moreover, it is also plausible that many decision makers who appear insincere are merely overwhelmed by the problem of adverse selection. That is, they may behave as if they were not invested in sincere expert advice because the existing asymmetry of information has allowed insincere experts to convince them of their perspective. That disingenuous experts can deceive decision makers does not mean that decision makers do not desire sincere advice; further, it means that problems of agency are critical to public decision making.

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Embedded in this discussion is a further assumption that the opinions of scientists can, and actually do, differ. If scientific consensus were truly monolithic, then, although the bilateral monopoly would still exist between politics and science, there would be no need to select among agents. Once a question was determined to be a scientific one, one scientist's opinion would be just as good as the next. Although incorporating elements of adverse selection as well, the choice of 'scientific' or 'non-scientific' would displace the concerns attended to here.

However, because disagreement — even controversy — is a natural condition of the scientific community, at least three additional problems arise. First, even if closure might be anticipated, many political decisions cannot await eventualities, and decisions must be made in the absence of consensus or closure. Second, scientific consensus or closure is often a temporary phenomenon, ready to be overturned with the appearance of additional, compelling evidence. Third, scientific consensus or closure is not normally the product of entirely rational procedures, and neither is it the product of disinterested, market-like interactions. Such difficulties mean that political principals cannot rely on autonomously produced consensus or closure among scientific agents, but rather they must devise strategies of choice and delegate to chosen agents.¹

As in the case of health insurance, those potential agents most actively seeking to join the contract may have the greatest propensity to incur costs for the principals, that is, potential agents who will benefit most directly from the contract may provide self-serving information to the decision makers. One example is the problem of conflicts of interest among expert advisors. In most situations, potential advisors must have a direct financial conflict, for instance, they must work for a company whose product will be regulated by the contemplated action, in order to be disqualified from participating in a regulatory science analysis.

As shown in the saccharin case below, however, this proscription may not be sufficient to protect deliberations from conflicts or the appearance of conflicts. Another typical example of self-serving behavior is the recommendation that experts offer for more research on the topic at hand, even if more research does not reduce uncertainty, lead to greater consensus, or otherwise accord with the decision makers' aims by not actually being a necessary precondition for substantive political progress on the issue. Some believe this to be the case, for example, in the research agenda for climate change (for instance, Pielke and Sarewitz, 2002).

Strategies of the principal

We can derive a variety of strategies that a political principal would deploy in order to assure the soundness of the delegation of authority implicit in the exercise of scientific judgment for policy making.

By 'assure' I do not mean 'ascertain' or make certain, but rather I mean 'attempt to overcome doubt' about the delegation.

In the case of providing health insurance, the typical strategies to resolve problems of adverse selection involve excluding from the contract any potential agents who are, or have a propensity to be, ill, and providing incentives for those agents who do become party to the contract to remain healthy. (In this case, the potential insuree is relatively more expert than the insurer because the insuree has information about his or her own health that is relevant to the insurer's decision to carry and price the insurance.) The former solution typically requires the use of a monitor or intermediary, for instance, a physician who will examine potential agents for pre-existing or excluded conditions. This solution, however, raises that timeless reiterative problem: who will watch the watcher?

The latter solution requires writing a contract with appropriately detailed terms, for instance, discounts for completing fitness courses, although such solutions impose analytical costs in calculating the incentives and adjusting the terms of the contract properly. As a model, though, the case of health insurance provides two strategies: one of mediation, in which the principal and agent interact through an intermediary; and a second of procedure, in which the principal and agent interact only with explicit provisions the agent must abide.

The remainder of this paper applies this nascent framework to a case of 'science in policy' in the United States. It frames the discussion around the two general strategies — intermediaries and explicit procedures — as well as the overall scheme of attempting to break the bilateral monopoly by creating a well-regulated market for regulatory science.

I elaborate these strategies as implemented by the National Toxicology Program (NTP), a small agency in the US National Institute of Environmental Health Sciences (NIEHS), which is itself one of the more than two dozen National Institutes of Health. These strategies include NTP's intermediation between politicians and scientific agents, the writing of explicit contracts governing the behavior of those agents, and the promulgation of various rules that break down information asymmetries and make the behavior of the scientific agents more observable. These strategies, however, are not perfect, and the scientific agents do in fact find ways to 'shirk.'

Saccharin, part I: need for a reliable agent

A fruitful example of the confusion and conflict that problems of agency in science advice can cause is the case of saccharin in the United States in the mid-to late-1970s. Saccharin, a derivative of coal tar, has a long and controversial history as a non-nutritive sweetener and food additive (Priebe and Kauffman, 1980; Cummings, 1986; Marcus, 1997). After the

US Congress passed the Food Additive Amendments of 1958 to the Food, Drug and Cosmetic Act, the scientific and regulatory communities considered saccharin 'generally recognized as safe' (GRAS). Subsequent experimental evidence gathered in the 1960s, however, led the Food and Drug Administration (FDA) to revoke saccharin's recognition as safe in February 1972.

FDA also issued an interim guideline forbidding any new uses for saccharin while it awaited a report from the National Academy of Sciences (NAS). The interim guidelines were set to expire at the end of June 1973, but FDA extended them indefinitely, citing studies that found significant increases in the incidence of bladder cancer in the male offspring of test animals fed saccharin (US Senate, 1977, page 23).

In December 1974, NAS submitted its review of the various studies, suggesting that saccharin was a carcinogen, but pointing to serious problems in the studies because the effective agent could have been impurities rather than the saccharin itself. In Canada, a study was designed to resolve this ambiguity, but Senator Gaylord Nelson, chairman of the Select Committee on Small Business, thought FDA was dawdling, and he asked the General Accounting Office (GAO) to investigate FDA's handling of the regulation of food additives (Marcus, 1997).

In testimony before Nelson's committee in January 1977, GAO critiqued FDA's regulation of saccharin and "recommended that [FDA] promptly reassess ... the need for ... possibly discontinuing [saccharin's] use in food" (US Senate, 1977, page 27). Shortly thereafter, the other shoe dropped: the Canadian study found that saccharin, rather than the impurities, caused bladder cancer in rats. Invoking the Delaney clause — a provision in the 1958 Amendments that prohibited any carcinogens from being added to foods — FDA proposed in the *Federal Register* on 15 April 1977 to ban saccharin.

Despite this protective action by FDA, the public responded to the proposed ban with an outcry over losing the last substitute for sugar, as cyclamate had been banned in the 1960s. Congress responded, in part, by requesting a report from the Office of Technology Assessment (OTA, 1977). OTA surveyed the available scientific evidence on the carcinogenicity of saccharin, explored its potential health benefits for some consumers, and, in an unusual move for the policy analytic organization, commissioned short-term Ames tests of saccharin's potential mutagenicity. OTA (1977, pages 5–6) concluded that "[l]aboratory evidence demonstrates that saccharin is a carcinogen," albeit a weak one, and one for which epidemiological studies had not shown a carcinogenic effect in humans.

Nevertheless, saccharin seemed to meet the criteria proposed by the Occupational Safety and Health Administration to identify a "confirmed" carcinogen, and the tests that OTA commissioned also suggested that pure saccharin was indeed mutagenic. Responding to public pressure, but not wanting to

completely disregard FDA and the Delaney clause, Congress passed the Saccharin Study and Labeling Act (Public Law (PL) 95-203) that placed a moratorium on the saccharin ban, required labeling of all food products containing saccharin, and directed NAS to study the issue further.

Congress could not abide, however, such a dilatory and sloppy process whenever scientists suspected a potential carcinogen in the food supply. OTA, NAS, and FDA, as well as private-sector interests both for and against the continued use of saccharin, had a stake in assessing its carcinogenicity. Which agent should Congress choose? FDA, which applied a troublesome legal standard literally? NAS, which hemmed and hawed and asked for more research? OTA, which confirmed saccharin's mutagenicity but balked on the epidemiology? Other players with significant commercial and other interests to protect? Without consensus in the scientific community, and with the presence of patently self-interested advocates, Congress needed a reliable agent to identify carcinogens in future conflicts.

Creating NTP and the *Report on Carcinogens*

Not quite one year after it instructed FDA to defer regulatory action on saccharin, Congress passed the Biomedical Research Extension Act (PL 95-622), which, among other provisions, required the Secretary of the Department of Health, Education and Welfare (DHEW; now the Department of Health and Human Services, DHHS) to publish an annual report listing substances known or anticipated to be human carcinogens. Congress mandated that DHEW perform the task, but it delegated to DHEW the design of a process that would fulfill the mandate.

In 1979, DHEW created the National Toxicology Program (NTP) to implement this mandate through the publication of a *Report on Carcinogens*. NTP would also coordinate other toxicological research and testing activities, including programs at FDA, the Centers for Disease Control and Prevention (CDC), the National Cancer Institute (NCI), and NTP's parent NIEHS.

NTP established an elaborate advisory system in response to the congressional mandate to identify human carcinogens. Initially, two review groups, the NIEHS/NTP Review Committee (RG1) and the NTP Executive Committee's Interagency Working Group (RG2), contributed to the Report's decision making. In the first step of a detailed and iterative process, NTP receives a petition from any individual or group nominating a substance for consideration.² It then solicits public comment through notification in the *Federal Register*, trade journals, and its own publications.³ RG1 receives the original petition and all public comments and decides if the substance warrants further consideration. If not, the petition is returned to the petitioner, who is invited to resubmit it with further justification.

Otherwise, RG1 appoints a primary and secondary reviewer from within its ranks to shepherd the petition through the committee. The primary reviewer identifies relevant articles from only the peer-reviewed literature and, with the assistance of the secondary reviewer, selects those articles to be included in a draft report, which is prepared by staff with the assistance of a contractor.⁴ The reviewers then examine the petition, the citations, and the draft report for completeness and accuracy and, after making any necessary revisions, the primary reviewer presents it to RG1.

RG1 considers this material, as well as the public comments in response to the petition, and for substances with sufficient information it makes a recommendation for listing or delisting. RG1 can also conclude that, after the review, there is still insufficient information and return the petition to the petitioner. The members of RG1 vote on the recommendation, and RG1 forwards the petition to RG2.

RG2 receives the petition, the public comments, and the draft report. It assigns another reviewer, who leads RG2's iteration of roughly the same procedure. RG2 provides comments and recommendations for any changes to the draft report and votes its recommendation for listing or delisting the substance. In the initial design of the process, NTP's Executive Committee would then review the entire record for each substance, vote on each substance, and forward the record with its own comments and voting results to the director of NTP for decision. NTP then submits the report to the Secretary for review and approval and, finally, to Congress for publication.

Through this process, NTP institutionalized the determination of what substances are or might reasonably be anticipated to be human carcinogens. Through the review groups, NTP gathered many of the various experts from agencies that might otherwise have offered opinions directly themselves, and it solicited public input in a coherent and informed way. NTP became the analogue of the physician, the agent of Congress who is intermediary to other potential agents who were themselves attempting to assess the carcinogenicity of substances more directly.

NTP institutionalized the determination of what substances are human carcinogens: it became the agent of Congress who is intermediary to other potential agents who were themselves attempting to assess the carcinogenicity of substances more directly

This process embodied several strategies to combat the problems of agency. Limiting the agents to government employees minimized the threat of conflicts of interest, as did limiting the information used to the peer-reviewed literature. Although NTP sought public comment, no advocates and no information produced purely for advocacy could be dispositive in its decisions. The creation of two advisory committees, with two different constituencies, cracked the bilateral monopoly and increased the amount of information produced for the principal. Information from the confidential interviews supports this perspective, as informants distinguished between RG1 as an internal organ of NTP more concerned with toxicological evidence and RG2 as a broader, higher-level committee more concerned with the political and regulatory consequences of decisions.

Furthermore, the recommendations of the advisory committees are exactly that — recommendations. Political principals, including the NTP director, the department Secretary, and the Congress itself are responsible for the listing or delisting of a substance. This authority is more meaningful rather than simply formal because of the relatively obvious fact that RG1 and RG2 may sometimes disagree. The NTP director must then decide how to cope with a substance despite divergent expert assessments. Such was the case with the decision about saccharin, described further below.

Toward a more explicit contract

NTP followed this procedure until the early 1990s. In the 1993 NIH Revitalization Act (PL 103-46), Congress amended the law to provide for biennial reports because resources were wasted on annual reporting, and a biennial report would still provide “timely and useful scientific information to the regulatory agencies and the public while providing savings that would be better spent on testing additional agents” (US Senate 1992, page 41). NTP published the first biennial report, and the eighth overall, in 1998 (NTP, 1998). The *Eighth Report* also first implemented two crucial changes NTP made in 1995: the creation of a new, more public advisory committee; and the revision of the criteria used for listing carcinogens.

Through the first change, NTP expanded its review procedures by adding a third review committee — a standing subcommittee of the Board of Scientific Counselors (DHHS, 1996b). Like RG1 and RG2, this *Report on Carcinogens* Subcommittee appoints a reviewer from within its ranks to guide its discussion of whether the relevant information available about a nominated substance provides sufficient evidence to draw a conclusion about its carcinogenicity in humans. Unlike RG1 and RG2, however, the *Report on Carcinogens* Subcommittee deliberates in public.

Because it is composed of members who are not all employees of the federal government, the Subcommittee falls under the jurisdiction of the Federal Advisory Committee Act (FACA, PL 93-463). In addition to mandatory public meetings, FACA requires that such committees be “balanced” in their composition. NTP announces the public meeting of the Subcommittee in the *Federal Register* and other publications, soliciting public comment and inviting groups or individuals to submit written comments or to address the Subcommittee during its public meeting. Based on the prior record and any information from the public meeting, the Subcommittee makes further recommendations for changes to the draft document and a recommendation for listing or delisting the substance.

By creating this committee of external advisors, NTP invited a greater risk of conflicts of interest, although FACA ameliorates the worst kinds of conflict and self-dealing. NTP also extended the logic of multiple advisory panels to break the bilateral monopoly and release more information for the principal by encouraging competitors in the ‘market’ for information about carcinogens — in this case, a market that non-governmental experts participate in more completely. In interviews, members of the Subcommittee supported this interpretation, distinguishing the Subcommittee from RG1 and RG2 by its public (as opposed to bureaucratic) constituency and its greater expertise in epidemiology, public health, and human exposure.

In 1995, NTP also changed the criteria through which the various advisory committees arrive at their conclusions. As mentioned above, the committees deliberate on several possible outcomes for any nominated substance: that the given information is insufficient for deliberation; that a nominated substance should be listed as a known human carcinogen; that a nominated substance should be listed as reasonably anticipated to be a human carcinogen; or that a nominated substance should be delisted entirely.

The original criteria maintained that a substance should be listed as a known human carcinogen if and only if “[t]here is sufficient evidence of carcinogenicity from studies in humans that indicates a causal relationship between the agent and human cancer” (DHHS, 1995, page 30435). The original criteria maintained that a substance should be listed as reasonably anticipated to be a human carcinogen if and only if:

- “a. There is limited evidence of carcinogenicity from studies in humans, which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias or confounding, could not adequately be excluded, or
- b. There is sufficient evidence of carcinogenicity from studies in experimental animals that indicates that there is an increased

incidence of malignant tumors: (a) in multiple species or strains, or (b) in multiple experiments (preferably with different routes of administration or using different dose levels), or (c) to an unusual degree with regard to incidence, site or type of tumor or age at onset. Additional evidence may be provided by data concerning dose-response effects, as well as information on mutagenicity or chemical structure.” (DHHS, 1995, page 30435)

Note here that the criteria make precise science policy statements about how the agents are supposed to handle evidence, for instance, they must rely on “increased incidence of malignant tumors” and not, for example, consider benign tumors or lesions. It also specifies the inadequacy of a single animal-system model of carcinogenicity under normal circumstances. In order for there to be a reasonable anticipation of carcinogenicity in humans, there must be experimental evidence from more than one system, more than one species, or more than one route of exposure.

In April 1995, the Board of Scientific Counselors created an *ad hoc* working group, which held a public meeting to consider revising the listing criteria and procedures (DHHS, 1995). The working group did not recommend any changes to the criteria for determining a known human carcinogen. The stated criterion was modified in a modest way to instruct for a finding of known human carcinogenicity when “[t]here is sufficient evidence of carcinogenicity from studies in humans that indicates a causal relationship between *exposure to the agent, substance or mixture* and human cancer” (DHHS, 1996b; additions to the criterion from the 1995 changes in italics).

The working group did, however, recommend substantive changes to the criteria governing the finding that a substance is reasonably anticipated to be a human carcinogen. Beyond the pre-existing criteria listed above, the proposed criteria included consideration of route of exposure, mechanisms of action, and sensitive subpopulations. NTP adopted these suggestions, expanding them to include membership in a

“well defined, structurally-related class of substances whose members are listed in a previous Annual or Biennial Report on Carcinogens ... or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.”

NTP also added a descriptive paragraph:

“Conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes, but is not limited to, dose response, route of exposure, chemical structure, metabo-

lism, pharmacokinetics, sensitive sub populations, genetic effects, or other data relating to the mechanism of action or factors that may be unique to a given substance. For example, there may be substances for which there is evidence of carcinogenicity in laboratory animals but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore reasonably be anticipated not to cause cancer in humans.” (DHHS, 1996b, page 50499)

The political principal, Congress, did not impose these specific controls. Rather, the intermediary developed them under the principal’s watchful eye in order for the agents to demonstrate their successful performance of the delegation. Nobody would complain to Congress about NTP if its procedures were more open to FACA, whose requirements for openness as well as balance combat troubles of adverse selection.⁵ Scientists would not feel abused if NTP’s criteria were made more explicit and attuned to thinking within the broader scientific community. Indeed, NTP director Kenneth Olden, held that the new criteria and processes provided for “better science and better responsiveness” (DHHS, 1998b).

Saccharin, part II: shirking behavior

NTP first listed saccharin as reasonably anticipated to be a human carcinogen in its *Second Report*, published in 1981 (NTP, 1981), and saccharin appeared in all subsequent reports up to and including the *Eighth Report*. Responding to the call for nominations for the *Ninth Report*, the Atlanta-based Calorie Control Council (1997) nominated saccharin for delisting “on the basis of NTP’s new criteria incorporating the use of mechanistic data” in evaluating a potential carcinogen.⁶ By the end of September 1997, NTP had completed the draft background document on saccharin. In addition to reviewing the various toxicological and epidemiological studies of saccharin, the draft argued that:

“There is evidence of the carcinogenicity of saccharin in rats but less convincing evidence in mice. Mechanistic studies indicate that ... [t]he factors thought to contribute to tumor induction by sodium saccharin in rats would not be expected to occur in humans. The mouse data are inconsistent and require verification by additional studies. Results of several epidemiological studies indicate no clear association between saccharin consumption and urinary bladder cancer. Although it is impossible to absolutely conclude that it poses no threat to human health, sodium saccharin is not reasonably anticipated to be human carcinogen under conditions of general usage as an artificial sweetener.” (NTP, 1997, page RC3)

By arguing that the mouse studies were insufficient and the rat studies could be excluded by the newly admissible mechanistic data, the draft report argued that the criterion of multiple sites or species was not fulfilled. RG1 and RG2 voted 7–3 and 6–2, respectively, to delist saccharin (DHHS, 1998a), setting off speculation in the press about saccharin's ultimate abolition (for instance, Huber; 1997; Kaiser, 1997; McGinley, 1997).⁷

The *Report on Carcinogens* Subcommittee held its public meeting on 30–31 October 1997 to review the recommendations of RG1 and RG2 and to hear additional public comment offered by the Calorie Control Council in favor of delisting and by the Center for Science in the Public Interest opposed to delisting. At that meeting, the Subcommittee voted 4–3 to reject the draft report and continue listing saccharin. Table 1 shows the members of the Subcommittee and how they voted.

Press reports suggest that the members of the Subcommittee who voted to retain saccharin on the list displayed a certain precautionary outlook that was outside the scope of the criteria. Nicholas K (Kim) Hooper from the California Department of

Health Services said, "Delisting is going to weigh on my conscience if I'm wrong" (quoted in Stolberg, 1997, page A13). Franklin Mirer, the director of health and safety from the United Auto Workers, International (UAW), found the "equivocal" data from human epidemiological studies (which showed an increased cancer risk among some subpopulations) reason enough not to delist: "What I'm saying is the epidemiology is perhaps not strong enough to identify saccharin as a carcinogen, but it doesn't rule out that it's a risk" (quoted in McGinly, 1997). *The Wall Street Journal* reported that "[a]t least one member of the panel who voted to keep saccharin listed said he probably wouldn't have voted to add saccharin, if that had been the issue, but wasn't comfortable about delisting it" (McGinly, 1997).

In interviews, the members of the *Report on Carcinogens* Subcommittee diverged in their explanations of the outcome as much as they did in their voting itself. Some attributed the lack of consensus within the Subcommittee to individually different perspectives on risk-taking. Others attributed it to disciplinary differences. "I suspect that my particular bias," said a Subcommittee member from public

Table 1. Members of the Board of Scientific Counselors' Report on Carcinogens Subcommittee and how they voted on saccharin for the Ninth Report (consultants not listed)

Voting to delist	Voting to retain listing
A John Bailer, PhD Professor Department of Mathematics & Statistics Miami University Oxford, OH 45056	Eula Bingham, PhD Professor Dept of Environmental Health, ML 056 University of Cincinnati College of Medicine Cincinnati, OH 45267
Steven A Belinsky, PhD Scientist Inhalation Toxicology Research Institute Kirtland Air Force Base, Bldg. 9200 Albuquerque, NM 87115	George Friedman-Jimenez, MD Director, School of Public Health HHC/Bellevue Occup & Env Med Clinic Bellevue Hospital, Room CD349 462 First Avenue New York, NY 10016-9198
Clay Frederick, PhD Senior Research Fellow Mechanistic Toxicology Group Toxicology Rohm and Haas Company 727 Norristown Road Spring House, PA 19477	Nicholas K Hooper, PhD Head, Research & Methods Development Hazardous Materials Laboratory Department of Toxic Substances Control California Department of Health Services 2151 Berkeley Way, Annex 11 Berkeley, CA 94704
	Franklin E Mirer, PhD Director Health and Safety Department UAW International 8000 East Jefferson Avenue Detroit, MI 48214-2699
Not voting	
Arnold L Brown, MD University of Wisconsin Medical School 1300 University Avenue Room 1217 Madison, WI 53706 (Chair; only votes in case of tie)	Carol J Henry, PhD Director Health Environmental Science Department American Petroleum Institute 1220 L Street, NW Washington, DC 20005-4070 (Absent)

health, is “when in doubt, regulate.” Still others attributed differences to political agendas, as some “people were determined to delist for political or science policy reason” and some “are very industry oriented and are hesitant to call something a carcinogen, especially when it is on the cusp.”

Indeed, the Subcommittee members who voted to retain saccharin’s status as reasonably anticipated to be a human carcinogen developed a perspective about shirking that contradicts that portrayed in the media coverage. Whereas, the media portrayed the precautionary perspectives described above, several of those holding such perspectives suggested in interviews that those seeking to delist saccharin in essence “nullified the criteria.” Those favoring delisting neglected evidence in female rats that may have contradicted the mechanistic data. They conflated the hazard identification task of NTP, which is simply to determine carcinogenic potential, with a risk assessment for human consumption, which nobody believes is high for saccharin. They overemphasized the worth of human epidemiological data because many cancers that saccharin might cause would not yet have shown up in the study populations.

After the vote of the *Report on Carcinogens* Subcommittee, both the UAW’s Mirer and the chairman of the Subcommittee, Arnold Brown of the University of Wisconsin Medical School (who, as chairman, did not vote) “thought that it might be difficult” for Kenneth Olden, director of NTP, to contradict the panel and delist saccharin. Yet in December 1998, the full Executive Committee voted to delist saccharin.

From an anonymous source on the committee, *The New York Times* reported the committee’s vote was 6–3 (Grady, 1998), a margin that NTP later confirmed. According to members of the Subcommittee, the mixed vote “sends a message” about the underlying uncertainty in the data and the conflict of scientific judgment that the advisory committees could not have sent had they operated by consensus rather than reporting votes. The individual votes, and the record among the advisory committees, “should show the level of agreement that the data show,” and the record of disagreement “alerts people to the fact that [different opinions were] considered.”

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The full committee’s vote meant that saccharin had, like a tennis player, won its match for delisting 7–3, 6–2, 3–4, 6–3. Olden proposed to delist saccharin, and the *Ninth Report on Carcinogens*, finally issued in May 2000, contained 218 entries for substances known and reasonably anticipated to be human carcinogens (NTP, 2000). Saccharin was not among them.

Conclusion

The US National Toxicology Program was established under a delegation from Congress to assure the sound production of information about known and anticipated human carcinogens. As such, it is an expert agent for Congress, like the physician-intermediary between the health insurer and insurance seekers. NTP is a watcher of other agents — scientists themselves — who deliberate about what substances are or are not carcinogenic.

Initially, Congress rejected the provision of information about carcinogens from the “marketplace of ideas” consisting of a variety of federal agencies and advocacy groups, because that marketplace failed miserably with respect to saccharin. Instead, Congress chose to create a public agent to provide the product. Rather than establish a bilateral monopoly, however, by delegating the identification of carcinogens to a single expert advisory committee, NTP created a well-regulated scientific marketplace in which some degree of consensus and closure, as well as the liberation of a good deal of information, could be expected.

Congress did not mandate the details of NTP’s procedure but, following the same logic in the reciprocal principal–agent relationship, NTP designed its procedures in order to demonstrate to its political principal its faithful performance of the delegation. NTP established multiple advisory committees to represent interests both internal and external to the government. Laws such as the Federal Advisory Committee Act protected the integrity of the input from external advisors against such threats of adverse selection as conflicts of interest.

NTP promulgated highly specific criteria upon which the members of these advisory committees are instructed to formulate their judgments. NTP relied on a voting mechanism rather than consensus conclusions in order to embody the uncertainty in the underlying data and communicate this additional information to political principals.

Yet, in the end, just as the difficult case of saccharin challenged the absence of a clearly defined process, saccharin challenged the existence of one. Despite the formal reviews, the duly promulgated criteria, the open and public debate, and all the rest, the scientist-agents disagreed about the carcinogenic potential of saccharin. They even disagreed about how they disagreed, with some on each side portraying some on the other as having nullified the criteria,

or being too risk-conscious or too risk-taking, or too beholden to disciplinary or sectoral loyalties.

In the end, there may have been legitimate scientific disagreement, and there may have been shirking. We cannot know how difficult it would have been for Congress or any of the other actors in the absence of NTP as an intermediary, but the *Report on Carcinogens* process survived the controversy over saccharin, not to mention controversies with respect to other substances not recounted here. Also, Congress created that process because the pre-existing, *ad hoc* one could not survive the saccharin controversy, yet alone hundreds of iterations of it for each substance suspected of causing human cancer.

Principal-agent theory is not a complete theory of science advice — certainly not yet. It does at this point, though, prove a good map for issues of ‘science in policy,’ just as it has for issues of ‘policy for science.’ Principal-agent theory can help account for how a political principal delegates authority to a scientific agent, and the strategies that the scientific agent adopts to demonstrate its fulfilling the delegation in a competent way. Principal-agent theory can even account for how some scientist-agents continue to act on hidden information and shirk their responsibilities under those strategies.

Further research might focus on elaborating the strategies of intermediaries, procedural requirements, and the creation of regulated markets for information in other examples of delegation. Research might also examine other venues of ‘science in policy,’ including not just other executive agencies but also delegations to non-governmental organizations such as the National Academies and other professional societies that participate in decision making. Such research may provide not only more knowledge about the structure of science in policy, but more wisdom about questions of institutional design for science advice as well.

Notes

1. This argument is similar to that in Guston (2000) in which the political principal cannot rely on the autonomously produced integrity or productivity of the scientific agent and must therefore create new institutions to assure these requisites.
2. NTP may consider an ‘agent, substance, mixture, or exposure circumstance,’ but this paper will simply refer to ‘substance.’
3. This account is derived from NTP (1998), appendix C.
4. This process of writing and reviewing the report is similar to the preparation of the criteria document for the National Ambient Air Quality Standards under the Clean Air Act Amendments of 1977 (see Jasanoff, 1990, page 102).
5. This is one of the lessons from the literature on “fire-alarm oversight” by Congress over executive agencies (McCubbins and Schwartz, 1987 [1984]).
6. The Calorie Control Council is an association representing the low-calorie and reduced-fat food and beverage industry, see <http://www.caloriecontrol.org>. It supports the delisting of saccharin and the reapproval of cyclamate. In January 1997, FDA revoked a rule prescribing the display of warning signs at retail establishments about the sale of saccharin (DHHS, 1997); FDA initiated the action following a petition from the Calorie Control Council and under authority of a bill to amend the Federal Food, Drug, and Cosmetic Act to repeal

the saccharin notice requirement (PL 104-124) (DHHS, 1996a).

7. Huber (1997) writes, “If the panic establishment can confess error on saccharin, there may yet be a glimmer of hope for silicone, power lines, dioxin and tomorrow’s terror du jour, whatever it may be.” Although silicone breast implants have recently received a clean bill of health from a court-appointed panel of experts who reviewed data as part of the class action lawsuit, the same government committees that voted to delist saccharin voted unanimously, twice, to list dioxin.

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