REGULATORY CHECKBOOK

June 2, 2012

Responses of

Dr. Richard B. Belzer

to

Questions for the Record

on the Hearing

"How the Report on Carcinogens Uses Science to Meet its Statutory Obligations, and its Impact on Small Business Jobs"

Wednesday, April 25, 2012

QUESTIONS SUBMITTED BY DR. PAUL BROUN, CHAIRMAN, HOUSE SCIENCE, SPACE AND TECHNOLOGY, SUBCOMMITTEE ON INVESTIGATIONS & OVERSIGHT AND REP. RENEE ELLMERS, CHAIRWOMAN, HOUSE SMALL BUSINESS SUBCOMMITTEE ON HEALTHCARE AND TECHNOLOGY

1) How is the RoC's contribution to science or the public's understanding of substance hazards unique?

Based on my research, there appears to be nothing unique about the RoC's contributions to science. To prepare the RoC, the NTP performs no original research and conducts no original studies. While the NTP's substance profiles are peer reviewed, this is a captive procedure controlled by the authors. There is no peer review procedure in the world of scholarship that allows authors to control the selection of peer reviewers, dictate their charge, and choose whether to accept or reject their work.

Substantively, the RoC appears to be duplicative of other federal programs that perform hazard (but not risk) assessment, such as EPA's IRIS program and ATSDR's toxicological profile program. When the cancer assessment program of the International Agency for the Research on Cancer (IARC) is taken into account, the RoC is almost wholly redundant.

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To be sure, the EPA and ATSDR programs have similar defects. Each performs only "hazard" assessments (for carcinogens) and "safety" assessments (for non-carcinogens). A hazard assessment alone has little or no value for informing public and private decision making. A safety assessment is exactly what it sounds like: it tells the public what constant dose or exposure the agencies' scientists think is "safe." However, because "safe" cannot be defined scientifically, all safety assessments are policy decisions analogous to NTP listing decisions.

The other programs differ from the RoC, and are at least in principle potentially superior to it, because they produce more information. EPA and IARC, for example, have their own classification systems that provide for more than two categories. EPA and ATSDR also determine "unit cancer risk" estimates. These could be valuable if they objectively characterized average risk to an exposed population. Unfortunately, they do not.

First, unit risk estimates are almost always extrapolated from very high to very low doses using linear no-threshold (LNT) models. These models are preferred by agency scientists precisely because they tend to overstate estimated cancer risk. Second, unit risk estimates are obtained by using upper-bound predictions from these LNT models. The likelihood that they overstate cancer risk, even if all other modeling assumptions are correct, is 20 to 1. Third, they often are based on the assumption that humans are at least as susceptible to chemical carcinogenesis as the most sensitive rodent species tested in a laboratory. Because this is possible but highly unlikely, it is another source of upward bias in the estimation of unit cancer risks.

All three of these non-scientific assumptions is motivated by a highly precautionary, risk-averse view about what the government's risk management policies ought to be. And this is why hazard assessment—whether performed by EPA, ATSDR, or the NTP—is so highly controversial. What's going on is not risk assessment; it's policy making behind a façade of science.

The RoC is unique in one important respect. It is highly influenced, if not controlled by, something called the NTP Executive Committee, which consists of the Consumer Product Safety Commission, the Department of Defense, the Environmental Protection Agency, the Food and Drug Administration, the National Cancer Institute, the National Center for Environmental Health/Agency for

Toxic Substances and Disease Registry, the National Institute of Environmental Health Sciences, the National Institute for Occupational Safety and Health, and the Occupational Safety and Health Administration. Thus, it is not clear whether listing decisions are made by NTP Director Linda Birnbaum or by a politically complex interagency process. (Of the nine members, five are subordinate to the Secretary of Health and Human Services.)

Nothing about the procedures, discussions, actions or recommendations of the NTP Executive Committee is ever disclosed. This is highly peculiar if the RoC is a scientific compendium; after all, if it's "just science," then there is no policy making going on and nothing pre-decisional to legitimately keep from the public.

2) How does a weight-of-evidence assessment differ from what NTP does in the RoC?

The RoC program appears to use a strength-of-evidence framework, meaning that the only evidence that the NTP considers is evidence supporting listing. This has been alleged many times over the years, and it is verified by carefully reading the new procedures NTP intends to follow for the 13th edition.[1] The nomination process considers only "relevant data [that] support[s] the [NTP's] rationale" for listing, and the initial peer review considers only evidence that supports listing. The revised process identifies no role for negative or equivocal data.

Further, as I explained in my testimony, the NTP's listing criteria also provide no role for the consideration of negative or equivocal data.[2] The criteria speak only of the "evidence of carcinogenicity" (emphasis added) and they establish a non-scientific, wholly policy-driven process for deciding whether this evidence is "sufficient" or "limited."

In her testimony, Dr. Birnbaum asserted that NTP determinations are "based on scientific judgment with consideration of all relevant research data and input from advisory groups and the

[1] National Toxicology Program, 2012. *Process for Preparation of the Report on Carcinogens,* http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.

[2] National Toxicology Program, 2012. *Listing Criteria,* http://ntp.niehs.nih.gov/?objectid=47B37760-F1F6-975E-7C15022B9C93B5A6.

public." But she also stated that substance profiles contain only "the information which supports the determination…" This is identical to a strength-of-evidence framework with the simple proviso that only positive studies will be deemed "relevant," which is exactly what the NTP's nominations process and listing criteria do.

The NTP has never addressed, and Dr. Birnbaum did not discuss in her testimony, how the NTP conducts this review of "all relevant research data." It appears to be a black box. What does the NTP do with "input from advisory groups and the public" when it is not scientific? If listing decisions are scientific, then the only legitimate thing the NTP could do with nonscientific input is to ignore it. This poses a particular problem to the NTP because the advisory committee that performs peer review is directed by its charge to provide policy advice.[3]

It is useful to return to what we know and don't know about the NTP's actual procedures. First, we know that the NTP's listing criteria are inherently non-scientific. To reach a conclusion that a substance is a "known" carcinogen, all the NTP must do is deem the positive evidence from human studies "sufficient," which it has not defined. Thus, proof of "sufficiency" rests on undisclosed policy and political considerations.

Second, we don't know how the NTP evaluates research data. If the NTP takes account of negative and equivocal data in its reviews, it is not reflected in its public description of its process or in the text of its substance profiles. Because it has never published guidelines informing the public concerning how it exercises "scientific" judgment, it is appropriate to infer that the judgments it exercises are not scientific.

[3] For the 12th RoC, the NTP used BSC review to ratify its policy decisions, not to objectively evaluate the scientific record: "The BSC is charged to determine whether the scientific information cited in the draft substance profile for a candidate substance is technically correct, clearly stated and supports the NTP's policy decision regarding its listing in the RoC" (emphasis added). For the 13th RoC, the role of the BSC is ambiguous and front-loaded to a point in the process when little scientific information is available for review. The manner in which draft substance profiles will be peer reviewed is even more ambiguous, but it continues to focus on the ratification by scientists of NTP policy decisions. See footnote 1, section headed "Public Release of Draft RoC Monograph and Peer Review."

Rigorous weight-of-evidence frameworks, which take account of all data whether positive, negative, or equivocal, have been proposed many times over the years.[4] Federal agencies (including the NTP) resist adopting them. They resist because any credible weight-of-evidence framework would substantially curtail their capacity to make policy decisions behind a façade of science.[5]

There is another crucial point to be made about what the NTP actually does. In the January 2012 revised RoC process, the NTP defined the RoC as

> a Congressionally mandated, biennial document that identifies and discusses agents, substances, mixtures, or exposure circumstances (collectively referred to as "substances") that may pose a hazard to human health by virtue of their carcinogenicity.[6]

This is false, for Congress mandated no such thing. Moreover, nothing in the law authorizes the NTP to list substances "that may pose a hazard to human health by virtue of their carcinogenicity." The law requires the NTP to list substances that are "known" or "reasonably expected" to be human carcinogens. If the NTP were to actually list all substances that may be human carcinogens, the RoC could include thousands of substances, the number dependent only on how much Congress appropriates to the NTP (and its partner agencies) for preparation of the Report.

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[4] For an authoritative report recommending (again) the adoption of weight-of-evidence frameworks, see National Research Council, 2008. *Science and Decisions,* Washington, D.C.: National Academies Press, p. 81: "[Weight-of-evidence] is an example of how [agencies] may benefit from a structured characterization … of the exact role of a resource-intensive method in supporting the broader goals of public-health and environmental decision-making, which would include, among many other aspects, the use of good scientific practices and consideration of good communication practices. The method would require a more explicit valuation of important attributes of quality in decision support."

[5] The NTP acknowledges that it is engaging in policy making when it characterizes the RoC as a "public health document." See National Toxicology Program, 2011. Report on Carcinogens; 12th Edition, p. 3. In her testimony, NTP Director Dr. Linda Birnbaum used this phrase twice. This is code language for public-health precautionary legislative decision making, something the statute does not authorize the NTP to do.

[6] See footnote 1 (emphasis added).

I regret that I did not flag this in my testimony. At the time, I thought the text quoted above was poorly-written but stray governmental text, likely written by a committee, with no significant import. During the hearing, however, Dr. Birnbaum made very clear that what I had interpreted as merely slopping writing was actually very much intended. She opened my eyes to its true meaning and ramifications.

In her testimony, Dr. Birnbaum used this and similarly incorrect formulations of the NTP's statutory charge several times:

- "By identifying substances that may heighten the risk of cancer, the public is made aware of potentially life-threatening chemicals in our everyday lives."
- "The report lists a wide range of substances, including metals, pesticides, drugs, natural and synthetic chemicals, and biological agents that are considered cancer hazards for people in the United States."
- "A listing in the report indicates a potential hazard for cancer."
- "Reducing exposure to cancer-causing agents is important to public health and the Report on Carcinogens provides important information on substances that might pose a potential cancer risk,…"
- "I think it would be very important that we heard from some of the expert scientists who actually were involved in the conduct of these studies. I think that their expert, unconflicted advice would be very important to understanding the impacts that some of these compounds may have, have the potential to have on human health.
- "The RoC is not a regulatory document. It is a hazard assessment document. It looks at all the information, and I think that is important to state. It looks at all the information, both positive and negative, that is all evaluated and then the information which supports the determination of whether the compound has the potential to cause cancer … is compiled to make the public health document."
- "Our charge from the Congress is to evaluate the potential for compounds to be a known carcinogen or reasonably anticipated carcinogen."

Besides being false, each of these mischaracterization of the law abandons science as the arbiter of listing determinations. Outside of physics, there is no scientific definition for "potential." Similarly, to say that something "may" happen is to exclude only those events that are infeasible under any imaginable factual circumstance. Dr. Birnbaum has discarded science and replaced it with precautionary policy judgment, something that the law does not permit her to do.

A) What difference does that make when looking at data and studies?

A weight-of-evidence framework would result in many fewer substances being listed. This has to be true because the NTP currently lists any substance that it reviews as long as the positive evidence, considered by itself, is strong enough to be deemed "sufficient."

Under a weight-of-evidence framework, low-quality studies would be given low weight and high-quality studies would be given high weight—regardless of whether they support or contradict the hypothesis of human carcinogenicity. Most importantly, studies that definitively resolve crucial scientific uncertainties—whether in favor or against the hypothesis of carcinogenicity—would be given the greatest weight of all. Indeed, studies of this type would trump almost every other kind of scientific evidence.

Note that a weight-of-evidence framework rewards scientists for conducting high-quality hypothesis tests, and provides an even greater "bang for the buck" for performing studies that resolve crucial scientific uncertainties. Neither reward is possible under the NTP's strength-of-evidence framework. Low-quality studies that appear to support the hypothesis of carcinogenicity are fine. High-quality studies that contradict it are rejected. Studies that resolve crucial scientific uncertainties play no role in listing determinations—unless, that is, they resolve an uncertainty in favor of listing. Thus, the NTP's strength-of-evidence framework actually rewards scientists for conducting low-quality hypothesis tests and studies that merely generate new hypotheses that might be interpreted as suggestive of "potential" cancer risk. The NTP's approach is like a baseball game in which only the home team is allowed to bat and the umpires wear blindfolds.

The NTP's lack of transparency about how it "considers[] all relevant research data," in Dr. Birnbaum's formulation, undermines public confidence that these "considerations" are limited to science.

Occam's Razor argues for defaulting to the simplest explanation in the absence of information: the NTP's listing determinations are wholly controlled by policy considerations. What we do not know is whether these policy decisions are actually made by Dr. Birnbaum or by the NTP Executive Committee.

3) In your working paper on the Report on Carcinogens, you suggest legislative changes to improve the Report on Carcinogens. Do you think legislation is necessary to improve the RoC?

My research shows that the NTP Director has sufficient authority to make the RoC scientifically credible. Because the RoC has been a sustained source of scientific controversy for many years, however, it's clear that NTP Directors past have not been interested in doing so. It is reasonably to infer that they liked the ability to make legislative policy decisions while purporting to be mere scientists.

In her testimony, Dr. Birnbaum made clear that she has no intention of departing from the practices of her predecessors. She did not identify any feature of the RoC that she believed warranted reform. She expressed her support for the process changes announced in January—indeed, they could not have been finalized without it—despite the fact that they received near universal opprobrium from the public. Most troubling, she clearly stated her support for misinterpreting the law to allow the agency to list mere "potential" human carcinogens as if they were "known" or "reasonably anticipated" human carcinogens.

For these reasons, it is up to Congress to act if it wants the RoC to have value as a scientific compendium and to prevent it from continuing to have negative social value. Each of my reform suggestions presumes that Congress intended, and still desires, the RoC to be a valid and reliable scientific compendium. Each proposed reform would make the RoC more scientific, and thus increase its value as a tool for informed public and private decision making.

4) In your testimony, you note that the "NTP completely ignores exposure or dose in making its determinations." Why is it important for exposure or dose to be considered when providing information to the public about substances that have the potential to cause cancer?

The most important reason why the NTP should take exposure into account isn't scientific; it's statutory. The law establishes two thresholds that must be met before a substance may legally be listed. To date, all of the attention has focused on the first one—whether a substance is a "known" or "reasonably anticipated" human carcinogen. As I made amply clear in my monograph, my working paper, and my testimony, these determinations are not scientific. It is ironic that so much energy has been expended on science even though science is largely irrelevant to these determinations.

The second statutory requirement for listing a substance is "a significant number of persons residing in the United States are exposed" to it. In my testimony, I identified the three steps that must be taken to meet this statutory requirement:

- Define "a significant number of persons residing in the United States"
- Define a *de minimis* cancer risk level
- Estimate for each candidate substance the number of persons in the United States exposed above the de minimis cancer risk level

The first two tasks are strictly policy driven; science cannot define a "significant" number of anything, nor can it define a threshold cancer risk below which the public ought not be concerned. But science can objectively estimate the number of persons residing in the United States who are exposed above any specified dose or concentration.

The NTP has performed none of these tasks. Determining which, if any, of the 240 substances listed in RoC are accompanied by this information requires a significant research effort. I have skimmed the 12th RoC for this information and I have yet to find a single substance for which the NTP has taken this statutory text seriously.[7]

[7] An electronic search of the 12th RoC reveals not a single instance in which the statutory text on exposure is even mentioned.

From a public policy perspective, it is obviously important whether many, a few, or virtually no persons residing in the United States are exposed to a bona fide human carcinogen. By ignoring the statutory language, however, the NTP is saying it's not important at all. The only thing that matters is whether there are any conditions—actual, hypothetical, or even imaginary—in which a substance is a "known" or "reasonably anticipated" human carcinogen—or rather, as Dr. Birnbaum has reinterpreted the statutory charge says, whether ta substance "may" be a "potential" human carcinogen.[8]

5) In your testimony, you suggest that substance listings should be sunset to encourage revision. How would that requirement improve the Report on Carcinogens?

The NTP implements the RoC process in a way that is similar to the way people have voted in certain dictatorships: one person, one vote, one time. A substance that is listed is impossible to delisted unless the NTP wants to delist it. NTP considers only positive evidence supporting carcinogenicity; new science refuting this evidence is immaterial. Members of the public may petition for a delisting, but they have no right to compel a review. Even if they had this right, it would be an empty one.[9]

This means the NTP will advance to the listing process only those substances that it (or the NTP Executive Committee) decides to advance. The only substances that advance are substances headed to listing.

My proposal to sunset RoC listings would require the NTP to justify its decisions every several years based on the then-available science. This would not have much public benefit unless the NTP also was required to adopt one or more of the other proposed reforms,

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[8] In addition to the threshold requirement for listing that "a significant number of persons residing in the United States are exposed," the law also requires the NTP to include in each substance profile "information concerning the nature of such exposure and the estimated number of persons exposed to such substances." The NTP does not provide this information.

[9] The RoC Process referenced at footnote 1 notes that the NTP may decide to reject any delisting request, for any reason or no reason at all: "For those nominated substances not selected for evaluation, the NTP notifies the nominators."

such as a weight-of-evidence framework that is transparent, reproducible, and scientific.[10]

6) Your testimony suggests that the National Toxicology Program should be following a rote formula for deciding which chemicals to list. Is there any value to allowing NTP scientists to use their scientific knowledge to make judgments about the data?

The premise of this question is false. There are many alternative weight-of-evidence frameworks around, none of which contains "a rote formula."

In principle, NTP scientists probably ought to be able to "use their scientific knowledge to make judgments about the data." The problem is that they do not disclose how they do this. The public needs full transparency in order to gain the assurance that when NTP scientists exercise judgment, it is scientific judgment only that they are exercising, that they are doing so in ways that the scientific community at large considers reasonable, and that they are exercising scientific judgment in ways that treat similarly situated substances the same way. The NTP's refusal to disclose how its scientists "exercise judgment" convincingly communicates to the public that the judgments its scientists are exercising are policy judgments, not scientific ones, or that their scientific judgments would not be supported by the broader scientific community.

There is a significant limitation on the quality of scientific judgment that NTP scientists could ever exercise. NTP scientists would be the ones most knowledgeable about the science for a particular substance only in rare cases. I suspect, but cannot confirm with evidence, that NTP scientists become less willing to consider alternative scientific views when they are confronted by non-government scientists who have distinguished reputations gained from active research and prolific peer-reviewed publication. In a fair contest, few NTP scientists would be able to hold their own against these scientific stars. But the contest is not a fair one; NTP scientists get to be both contestant and judge, deciding which scientific evidence and arguments prevail. Listing decisions provide unique opportunities to cut the stars in the scientific profession down to size.

[10] A weight-of-evidence framework that is transparent but policy driven would not be much of an improvement.

Thus, the question is not whether NTP scientists should be allowed to exercise scientific judgment; it is whether they should be allowed to do so secretly, without accountability for the quality of their scientific judgments, and without even a requirement to publicly demonstrate that the judgments they exercise are genuinely scientific.

Historically, the NTP has used its Board of Scientific Counselors to provide the appearance of scientific endorsement of its policy-driven listing decisions. A much better use of the BSC would be to convert it into a body of independent, honest brokers, who arbitrate differences in scientific judgment between the NTP staff and nongovernmental scientists with equivalent or superior experience and expertise. If what NTP scientists are doing is exercising strictly scientific judgment, then they should welcome such a reform because it would validate them when they are correct and generally yield conclusions that are rarely, if ever, scientifically controversial. If the NTP were to reject such a reform, however, it would reinforce the widespread conviction that the discretion NTP wants to preserve is for its scientists (and officials) to make political and policy judgments under the guise of science.

7) You seem to be asking for a great deal of rigor and in-depth analysis for a decision making process that is meant to benefit the public. Are you suggesting that the system be made much more difficult for NTP to publish the RoC?

My reading of NTP publications indicates that it believes its current reviews involve ”a great deal of rigor and in-depth analysis for a decision making process that is meant to benefit the public.” In her testimony, for example, Dr. Birnbaum characterized them as “thorough” and based on “consideration of all relevant research data.” If this accurately characterizes what the NTP now does, the reforms I propose would not make NTP reviews any more burdensome.

If the NTP limited the RoC to science, and began to follow the law, it would be able to publish the RoC with much less controversy. The primary reason why the NTP has been unable to publish the RoC biennially is because its listings are policy decisions, not scientific determinations, and it can be challenging and time-consuming to make it appear as if science is dispositive.

Under a well-designed sunset provision, the NTP might have a much more demanding workload. But this would be true only if the

NTP was bureaucratically or politically determined never to delist substances irrespective of the scientific evidence.

The current RoC has no positive value to the public, and a case can be made that its public value is negative. For substances that are widely agreed by scientists to cause cancer in humans, an NTP listing is neither controversial nor contains any new information. In those cases, the social value of an NTP listing must be zero.

But for substances that, in Dr. Birnbaum's formulation, "may" have the "potential" to be human carcinogens, listings are inherently controversial on legal, scientific, and policy grounds. What's more, these listings mislead the public. When the NTP labels a "potential" human carcinogen as a "reasonably expected" carcinogen, it knowingly disseminates false information. To see why, consider two weather forecasts—one that says weather conditions make a tornado strike a "known" probability, and a second that says weather conditions create the "potential" for a tornado strike. It is critical to seek shelter in response to the first forecast but doing so makes no sense in response to the second.

For unexplained reasons, Dr. Birnbaum believes that it is an ethical practice to mischaracterize substances that "may" pose a "potential" cancer risk as "known" or reasonably anticipated" human carcinogens. Until this deceptive practice is ended, the RoC will continue to have negative social value to the people of the United States.

QUESTIONS SUBMITTED BY REP. PAUL TONKO, RANKING MEMBER, HOUSE SCIENCE, SPACE AND TECHNOLOGY, SUBCOMMITTEE ON ENERGY & ENVIRONMENT

1) You stated in your testimony that:

"In August of 2011, I was asked by the Competitive Enterprise Institute to conduct a short study trying to explain why the RoC had become so intensely controversial. Regulatory Checkbook received an honorarium of $5,000 for a completed published paper… Subsequently, Regulatory Checkbook supplied an additional $5,000 of unrestricted resources."

***This is not a very helpful disclosure of funding as neither Competitive Enterprise Institute nor your Regulatory Checkbook seem to have sources of funding aside from outside contributions or contracts*.**

A) Please identify the source of the CEI honorarium funds provided by CEI.

I do not know the source of the funds CEI paid to Regulatory Checkbook.

B) If you do not know the source of funds, did you ask CEI regarding the source and the kind of report envisioned?

I did not ask CEI about the source of its funding.

C) If you did not ask about the source of funds, please explain why you did not ask.

In my experience, every research sponsor, whether an individual, a corporation, a union, an advocacy group, a foundation, or a government agency, funds research in order to influence public policy. Thus, independent scholars always have the opportunity to skew their research in ways that appeal to their sponsors. Sometimes skewness is obvious, because even the pretense of objectivity is missing. Other times skewness can be quite subtle, such as when scholars draw inferences that cannot be supported by their research. Sometimes scholars work very hard to prevent being captured by their sponsors, by hewing to strict standards of integrity and objectivity.

But research cannot be skewed in favor of a sponsor if the identify of the sponsor is unknown. Preserving ignorance about the source of funds is the best way for independent scholars to ensure that the integrity and objectivity of their research is not compromised by sponsor interests. For that reason, anonymous sponsorship is the best possible evidence of the absence of sponsor bias.

2) Please identify the source of the $5,000 provided to you by your non-profit corporation, the Regulatory Checkbook.

As I testified, these funds came from unrestricted contributions, which are by definition intermingled. Donors have no control over how they are used. Before expending unrestricted funds, Regulatory Checkbook never seeks donor approval.