

COURTNEY M. PRICE
VICE PRESIDENT
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February 18, 2005

Associate Director for Communications
Office of the Director
National Institutes of Health
Building 1, Room 344
9000 Rockville Pike
Bethesda, MD 20892

Via e-mail: InfoQuality@od.nih.gov

Re: Naphthalene -- Information Quality Act Request for Reconsideration

Dear Sir or Madam:

This is an Information Quality Act (IQA)¹ Request for Reconsideration of the January 18, 2005, response from Dr. Christopher J. Portier of the National Toxicology Program (NTP) to the April 1, 2004 request by the Naphthalene Panel (Panel) of the American Chemistry Council (ACC) for the correction of information disseminated by the NTP (Request for Correction) concerning the Background Document for Naphthalene (Background Document) and the review of scientific data relevant to NTP's consideration of naphthalene for possible listing in the 11th *Report on Carcinogens (RoC)*.² A copy of the Panel's Request for Correction is appended as Attachment 1 and a copy of Dr. Portier's letter as Attachment 2.

¹ Section 515(a) of the Treasury and General Government Appropriations Act for Fiscal Year 2001, P.L. 106-554; 44 U.S.C. § 3516 (note).

² See Letter from Christopher J. Portier, Ph.D., Associate Director, NTP, to Courtney M. Price, Vice President, CHEMSTAR, ACC (Jan. 18, 2005) (NTP Response); Letter from Courtney M. Price, Vice President, CHEMSTAR, ACC, to National Institutes of Health, Associate Director for Communication (Apr. 1, 2004) (Request for Correction).

By letter dated January 25, 2005, the Panel notified your office of its intent to file this appeal within the prescribed period. Subsequently, on January 31, 2005, the NTP issued the 11th *RoC*, in which naphthalene is listed as "reasonably anticipated to be a human carcinogen." Issuance of the 11th *RoC* underscores the significance of the Panel's earlier Request for Correction and the urgency of the present appeal but does not otherwise

The Panel believes strongly that Dr. Portier's response on behalf of the NTP, in denying the Panel's Request for Correction, ignores both the letter and spirit of the IQA and the implementing guidelines issued by the Office of Management and Budget (OMB Guidelines),³ the National Institutes of Health (NIH), and the U.S. Department of Health and Human Services (HHS),⁴ (collectively, the Guidelines). The NTP Response also ignores the serious and specific concerns discussed by the Panel in its April 1, 2004 letter and at earlier stages in the review process for naphthalene. This appeal does not reproduce in full the analyses set out in the Panel's April 2004 Request for Correction, and we respectfully refer you to Attachment 1 for additional detail as to each of the items raised here.⁵

As a result of the enactment of the IQA, and as is evident from OMB's subsequent steps to formulate carefully and comprehensively its implementing guidance for federal agencies, improving the substance and process of information collection, review, and dissemination to the public has become a major priority of the executive branch. "Quality," the central term, encompasses (1) "objectivity," whether the information is "presented in an accurate, clear, complete, and unbiased manner, and as a matter of substance, is accurate, reliable, and unbiased"; (2) "utility," its usefulness to the intended users, including the public; and (3) "integrity," which refers to its security.⁶ As noted below and discussed in the Panel's Request for Correction, each of the specific items identified for correction involves either or both of the "objectivity" and "utility" factors addressed in the Guidelines. Given that "influential scientific information" is involved -- as NTP concedes in its response -- the applicable quality requirements are commensurately stricter.⁷

Background Document

The Panel requested that the NTP correct significant errors and omissions in the Background Document for naphthalene, and the NTP declined to do so, despite the focal role of the Background Document as the so-called "document of record" for the three scientific peer reviews for *RoC* decision-making and its undisputed status as "influential scientific information" disseminated by the NTP. As such, its failure to meet applicable standards for objectivity and

change the analysis. If this appeal is granted, which we strongly believe is the proper disposition, the listing of naphthalene in the 11th *RoC* should be revisited also.

³ 67 Fed. Reg. 8452 (Feb. 22, 2002).

⁴ See <http://www.hhs.gov/infoquality/part1.html>.

⁵ Please note that Attachments A-H to the Request for Correction include previous correspondence from the Panel and other relevant documents.

⁶ 67 Fed. Reg. at 8453.

⁷ *Id.* at 8455, 8460.

utility necessarily mar the whole of the ensuing process -- including, in this case, the description of naphthalene in the 11th *RoC* as “reasonably anticipated to be a human carcinogen.”

The NTP Response declines to address the specific items for correction described on pages 11-15 of the Request for Correction, characterizing these as requests for “the NTP to formulate and assert its opinion regarding the interpretation of study findings presented in the Background Document for Naphthalene” and stating that “it would be inappropriate to do so,” because “the NTP will only respond to issues you raise that question the accuracy of factual information” as a matter of policy.⁸ It takes the position that, “[i]n background documents, the NTP declines to draw conclusions about the data described or include interpretative information and evaluation like you have requested, because, in the NTP’s view, to do so could introduce bias.”⁹ In stating that the reviewing scientists are left to make their own judgments, based on such background documents and the public comments addressing them, the NTP ignores the key point: the Panel has not asked NTP to provide its own conclusions or interpretations as to the data.

Instead, the Panel has requested NTP to include additional data or detail and to more clearly set out its reasoning in the Background Document, especially where the document relies on outdated or otherwise questionable information. To reject the Panel’s request as asking for “interpretation” or “evaluation,” and thus contrary to NTP policy, is to ignore the reality that the failure to include such additional information is itself a judgment that skews the picture presented to reviewers and compromises its accuracy. As the OMB Guidelines observe, “Sometimes, in disseminating certain types of information to the public, other information must also be disseminated in order to ensure an accurate, clear, complete, and unbiased presentation.”¹⁰ Unless the Background Document is corrected, not only its objectivity but, necessarily, its utility will continue to be compromised.

The heightened standard of quality for the use of influential science in agency decision-making, which Congress adopted in 1996 for health decisions under the Safe Drinking Water Act (SDWA),¹¹ further supports the Request for Correction of the Background Document. As the OMB Guidelines note -- in adopting the SDWA standard for health, safety, and environmental information disseminated by federal agencies -- “to the degree that an Agency action is based on science,” the agency must act in accordance with the following directive: The agency must use “(i) the best available, peer-reviewed science and supporting studies conducted

⁸ NTP Response at 5.

⁹ *Id.*

¹⁰ OMB Guidelines, 67 Fed. Reg. at 8459 (Section V.3.a).

¹¹ 42 U.S.C. § 300g-1(b)(3)(A).

in accordance with sound and objective scientific practices; and (ii) data collected by accepted methods or best available methods (if the reliability of the method and the nature of the decision justifies the use of the data).¹² By failing to revise the Background Document to conclude -- or at least address -- the studies and issues identified in the Panel's Request for Correction, NTP has simply failed to use the best available science. NTP cannot avoid this obligation by describing as a "policy choice" its refusal ever to amend Background Documents. The policy choices the IQA cannot reach are choices an agency makes based on the best available science when the science does not compel one choice or the other. But the IQA does not authorize an agency to make a "policy choice" not to use the best available science in the first place.

RG1 and RG2 Summary Reports and RG2 Meeting

The NTP Response also rejected the Panel's Request for Correction of the Review Group (RG) 1 and RG2 summary reports, influential scientific information on which the reviewing public relies, as the NTP Director also relied upon in the listing decision for naphthalene. Although the RG1 summary report reasonably would be expected to present clearly the basis for the group's analysis of such critical issues as the relevance of the cited rodent studies to human beings, no such analysis is discernible from the document. The NTP Response does not adequately justify letting the summary report remain uncorrected, as it cites what the reviewing committee "felt" was sufficient rodent study evidence to support human carcinogenicity. There was no meaningful explanation of how this far from automatic conclusion concerning the rodent data actually was reached or justified.¹³ Nor is the RG2 summary report any more transparent, despite the fact that it was subject to more rigorous pre-dissemination review requirements that took effect October 1, 2002, under the OMB Guidelines¹⁴ and despite the group's reliance on the flawed -- but uncorrected -- Background Document. The RG2 meeting itself was subject to these same standards and failed to meet them for the same reasons. Allowing the RG1 summary report to stand in its current form would undercut the objectives of objectivity and clarity, and the Panel maintains that it must be corrected; the RG2 summary report and the proceeding on which it was based both should be rescinded, and a new proceeding convened, based on a corrected Background Document.

The NTP Response includes an overview of NTP's process for reviewing *RoC* nominations. As described in the Response, the review process is orderly, with timely availability of both Background Documents and comments submitted by the public to the three reviewing bodies. The Panel's Request for Correction contains details of the disorderly manner in which the naphthalene review was conducted (see especially Attachment H to Attachment 1).

¹² See OMB Guidelines, 67 Fed. Reg. 8457 and 8460 (Section V.3.b.ii.C).

¹³ NTP Response at 7.

¹⁴ See OMB Guidelines, 67 Fed. Reg. 8459 (Section III.4).

As discussed in depth at public meetings held in October 1999 and January 2004, NTP's review process can be described as anything but orderly in practice, and seems designed to give the appearance of engaging the public while ensuring that little substantive stakeholder involvement actually occurs.¹⁵ For this reason, the American Chemistry Council has urged NTP to consider replacing the current *RoC* review process with a process modeled along the lines of that used by NTP's own Center for the Evaluation of Risks to Human Reproduction.¹⁶

NTP Subcommittee Proceedings

As discussed in detail in the Request for Correction and in previous correspondence, the Panel also sought correction of the irregular and highly prejudicial actions on November 19, 2002, by the Chair of the *RoC* Subcommittee (Subcommittee) with respect to (1) his distribution of information without prior review by the Subcommittee or the public; and (2) his introduction of bias and a lack of objectivity into the proceedings by such actions. As further discussed in the Request for Correction, not only do the Subcommittee proceedings constitute "influential scientific information" within the meaning of the Guidelines, their actual influence hardly can be overstated. The Subcommittee meeting is the third and final scientific review group convened before the recommendations for decision go to the NTP Executive Committee and the NTP Director. It is not only the last scientific review group in the progression but the only one with an external peer review proceeding that is open to the public and permits the consideration of prior written public comments.

The NTP Response attempts to justify the prejudicial actions of the Subcommittee Chair on the grounds that the Subcommittee operates under the Federal Advisory Committee Act (FACA) rules, that its minutes do not represent NTP views and thus are not subject to the IQA, and that the Chair followed NTP practice in stepping down as chair to provide his comments on naphthalene and then forbearing from participating in the Subcommittee's deliberations. As discussed in earlier correspondence from the Panel, it is unacceptable to try to discount the obvious impacts of the Chairman's presentation by responding that his temporary shedding of the mantle of Chairman served to transform him into just one among a group of scientific peers.¹⁷ The OMB Guidelines emphasize "objectivity" in presentation as well as in substance; as

¹⁵ Materials related to the two public meetings are available on NTP's web site at <http://ntp-server.niehs.nih.gov/ntpweb/index.cfm?objectid=720162CF-BDB7-CEBA-FC560DF109D40A44>.

¹⁶ See Public Comments at <http://ntp-server.niehs.nih.gov/ntpweb/index.cfm?objectid=720162CF-BDB7-CEBA-FC560DF109D40A44>.

¹⁷ See NTP Response at 8-9.

such, the disseminated information -- all the more so for influential scientific information -- must be “presented in an accurate, clear, complete, and unbiased manner.”¹⁸

It is facile to suggest that, in making his case to the Subcommittee for the carcinogenicity of naphthalene, the Chairman was, at a minimum, anything less than first among equals. The highly technical nature of his presentation, along with his failure to share his information with Subcommittee members or the public before the hearing, only reinforced the impacts of his presentation. The appearance of bias is impossible to argue away, and the damage to the deliberative process was all the greater in light of the Chairman’s manifestly incorrect toxicological characterization of naphthalene as a “polycyclic aromatic hydrocarbon” (PAH), a group of chemicals whose carcinogenic potential he also depicted inaccurately. The appearance of bias and the obvious absence of transparency associated with the Chairman’s presentation tainted the Subcommittee proceedings, as did the inability of the public or the other Subcommittee members to review the newly-introduced information for accuracy, reliability, or completeness, which further compromised the proceedings. The full impact of these irregularities cannot be fully assessed in that the reasoning process itself by which the Subcommittee members arrived at their votes was not transparent or otherwise discernible, even in an open proceeding.¹⁹

The NTP Response further attempts to discount the obviously problematic Subcommittee proceedings by asserting that, as a FACA proceeding, the IQA Guidelines do not apply.²⁰ As discussed in the Request for Correction, the Panel believes that the more appropriate view is that because the RoC Subcommittee proceedings are conducted under the *imprimatur* of the NTP/NIH, the Subcommittee’s recommendations and votes were made in a public proceeding and then published, *i.e.*, disseminated, in the *Federal Register*, the Guidelines should and do apply.²¹ Finally, whether or not the RoC Subcommittee’s recommendations -- standing alone -- are subject to the Guidelines, once the NTP Director relied upon them, there is no question that they were “disseminated” by NTP and became subject to the Guidelines. For the foregoing reasons, the Panel submits that the Subcommittee proceedings are subject to correction under the Guidelines.

¹⁸ OMB Guidelines, 67 Fed. Reg. at 8453.

¹⁹ See Request for Correction at 16-19.

²⁰ See NTP Response at 8.

²¹ See Request for Correction at 7-9.

Associate Director for Communications, NIH
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Conclusion

The NTP Response, while declining to correct any of the errors noted in the Request for Correction, also takes the position that neither the RoC Subcommittee nor the RG2 meetings may be rescinded or reconvened. The Panel believes, to the contrary, that these latter steps (including the November 19, 2002, Subcommittee vote), together with the withdrawal and correction of the Background Document and the RG1 review summary, are the only measures that can assure compliance with the IQA and the applicable implementing Guidelines. Indeed, given the recent listing of naphthalene in the 11th *RoC* -- which was released despite the NTP's knowledge that this appeal was pending -- no adequate remedy is available in the absence of these steps. In addition to granting this appeal, for these reasons discussed above and in the Panel's previous correspondence, the Panel also requests rescission of the January 31, 2005, inclusion of naphthalene in the 11th *RoC* in the absence of an objective basis for its listing.

The Panel looks forward to the resolution of this appeal. If you require additional information, please contact Dr. Anne P. LeHuray at (703) 741-5630 or anne_lehuray@americanchemistry.com.

Sincerely yours,

/s/

Courtney M. Price
Vice President, CHEMSTAR

Attachments

cc: Dr. Christopher Portier, NTP
Dr. Elias Zerhouni, NIH
Dr. John R. Graham, OMB

Attachment 1

Request for Correction of Information
Pursuant to Section 515(a) of the Treasury and General
Government Appropriations Act for Fiscal Year 2001 (the
Information Quality Act)

by the
American Chemistry Council
Naphthalene Panel

Request for Correction of Information Disseminated
by the
National Toxicology Program
Related to the Nomination to List Naphthalene
in the
Report on Carcinogens

April 1, 2004

Available On-Line at
<http://aspe.hhs.gov/infoquality/request&response/14a.pdf>



April 1, 2004

Via E-Mail

National Institutes of Health (NIH)
Associate Director for Communication
Office of the Director
Building I, Room 344
9000 Rockville Pike
Bethesda, Maryland 20892

Re: Request for Correction of Information

Dear Sir/Madam:

This request for correction of information is submitted on behalf of the American Chemistry Council's Naphthalene Panel (Panel) pursuant to Section 515(a) of the Treasury and General Government Appropriations Act for Fiscal Year 2001¹ (the Information Quality Act), and the implementing guidelines issued by the Office of Management and Budget (OMB Guidelines),² the National Institutes of Health (NIH), U.S. Department of Health and Human Services (HHS) (NIH Guidelines),³ and the HHS (HHS Guidelines).⁴ The Naphthalene Panel consists of producers and users of naphthalene.⁵ The National Toxicology Program (NTP) is an agency of the HHS and is therefore subject to OMB's Guidelines, the HHS Guidelines, and the NIH Guidelines (collectively, the "Guidelines").

¹¹ 44 U.S.C. 3516 note.

² *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information by Federal Agencies*, 67 Fed. Reg. 8452 (Feb. 22, 2002), available at www.whitehouse.gov/omb/fedreg/reproducible2.pdf.

³ *Guidelines for Ensuring the Quality of Information Dissemination to the Public*, available at <http://www.hhs.gov/infoquality>.

⁴ *Guidelines for Ensuring the Quality of Information Dissemination to the Public*, available at <http://www.hhs.gov/infoquality/part1.html>. See also MEMORANDUM FOR PRESIDENT'S MANAGEMENT COUNCIL (http://www.whitehouse.gov/omb/inforeg/pmc_graham_100402.pdf), From John D. Graham, re: Agency Draft Information Quality Guidelines (June 10, 2002) at Attachment, Section V.

⁵ Panel member companies are International Tar Association, Koppers Industries, and Recochem, Inc.

The Panel seeks, pursuant to the OMB, NIH, and HHS Guidelines, correction of information disseminated by NTP. As discussed in detail below, the Panel requests:

- (i) correction of the Background Document for Naphthalene,⁶
- (ii) correction of the Summaries of the RG1 and RG2 meetings,⁷
- (iii) rescission of the RG2 meeting with regard to naphthalene and for NTP to hold a new RG2 meeting,
- (iv) rescission of the vote of the November 19, 2002, NTP Report on Carcinogens (RoC) Subcommittee meeting with regard to naphthalene, and
- (v) reconsideration of naphthalene by a new RoC Subcommittee at a future meeting in accordance with the Guidelines' requirements.⁸

If this relief is not granted, the Panel requests that NTP staff, NIH's Office of Communications and Public Liaison (OPCL), and the NTP Executive Committee undertake a comprehensive pre-dissemination review of the entire record of the listing proceeding as it relates to naphthalene, before any recommendation is made concerning listing naphthalene in the Eleventh RoC by the NTP Director.⁹ This review would involve ensuring that information relied upon and developed in making a recommendation meets the basic standard of quality under the Guidelines, including the elements of objectivity, utility, and integrity.¹⁰

NIH's Guidelines require that a petition for correction contain several substantive components. These include: a description of the specific material that is proposed for correction, the reasons why the disputed information does not comply with the OMB or NIH Guidelines and is in error, an explanation of how the petitioning party is affected by the error, and suggested recommendations for what corrective action(s) should be taken. The Panel is adversely affected by the errors described in that the NTP Draft Background Document for Naphthalene (Background Document), and the RG1 and RG2 review summaries contain incorrect information. The information that has been disseminated by NTP, and continues to be disseminated, wrongly characterizes the cancer potential of naphthalene, thereby stigmatizing naphthalene and inviting enhanced regulatory and consumer scrutiny of naphthalene and products containing naphthalene. An unwarranted listing of naphthalene resulting from these

⁶ Included as Attachment B. Available at <http://ntp-server.niehs.nih.gov/NewHomeRoc/roc11Bkgrnd2002.html>.

⁷ Included as Attachments A and C, respectively. Available at <http://ntp-server.niehs.nih.gov/NewHomeRoc/roc11Bkgrnd2002.html>.

⁸ 68 Fed. Reg. at 3033-3036.

⁹ See NIH Guidelines, Introduction before Section I, and Section I.2; OMB Guidelines Sections III.1 and 2 (67 Fed. Reg. at 8458-8459).

¹⁰ OMB Guidelines, 67 Fed. Reg. at 8459 (1st col.); NIH Guidelines (Introduction preceding Section I).

errors, as well as from the inappropriate conduct and vote of the NTP RoC Subcommittee, would unnecessarily cause greater economic harm through, at a minimum, increased costs of regulatory compliance and possible loss of market share, to the producers and users who comprise the Panel. Each of the remaining components of the required request for correction is discussed below.

I. THE RoC LISTING PROCESS

The RoC is a Congressionally mandated report prepared biennially that contains a list of substances that are believed to pose a potential hazard to human health. According to NTP, the Reports serve as “meaningful compilations of 1) the cancer data available for the listed substances in human and/or animals, 2) on the potential for exposure to these substances, and 3) on the regulations required by Federal agencies to limit exposures to these substances or exposure circumstances.” [source - <http://ntp-server.niehs.nih.gov/NewHomeRoc-WhatisRoc.html>.]

Listing in the RoC is not an academic exercise devoid of real world consequences. Listing in the RoC means a substance will be regulated more stringently, and will be perceived thereafter as a carcinogen. For example, under OSHA’s Hazard Communication Standard, substances listed in the RoC must be identified as carcinogens in material safety data sheets (MSDS). Additionally, an RoC listing can, and often does, invite a determination by the California Environmental Protection Agency that the substance may be a carcinogen for purposes of Proposition 65 pursuant to the state statute’s authoritative bodies listing mechanism, as an NTP RoC listing is considered an authoritative body for purposes of Proposition 65.¹¹ Many other adverse inferences flow from the listing of a substance in the RoC, not the least of which is the intangible, but real nonetheless, commercially damaging stigma that is associated with substances believed to cause or contribute to cancer. This stigma can and often does lead to product liability claims, diminished sales, product substitution by downstream users of the substance, and related commercial damage.

The RoC listing process itself consists of several distinct phases. Briefly stated, the process is as follows:

- Chemical nominations undergo review by two NIEHS/NTP RoC review committees. The first, Review Group (RG) 1, is composed of senior scientists from the NIEHS/NTP staff. The RG1 first reviews the Background Document and determines if it is adequate for use in reviewing the nomination. The RG1 reviews the nomination and makes a recommendation for listing or delisting in the RoC.

¹¹ These real-world regulatory consequences are the reasons why two different federal courts have held RoC listings to be judicially reviewable. *See Tozzi v. Dept. of Health & Human Servs.*, 271 F.3D 301, 310-11 (D.C. Cir. 2001); *Synthetic Organic Chemical Mfr.s Ass’n v. Dept. of Health & Human Servs.*, 720 F. Supp. 1244 (W.D. La. 1989).

- The *NTP Executive Committee's Interagency Working Group for the RoC* (RG2) consists of government scientists designated to act on behalf of the NTP Executive Committee, which consists of the heads of the government agencies that participate in the NTP¹². RG2 conducts a second review of the nomination, and assesses whether relevant information for a nomination is available for listing in or delisting from the RoC. The RG2 reviews the original nomination, and all public comments received on the nomination, and provides comments and makes its recommendation for listing or delisting. Notably, it does not revise the Background Document or review public comments received on the Background Document.
- The third step in the RoC process is an external scientific peer review of the nomination by a standing committee of the NTP Board of Scientific Counselors (the RoC Subcommittee). The RoC Subcommittee reviews nominations in a public meeting at which the public is given the opportunity (for the first time) to make brief oral presentations. Upon completion of its review, the RoC Subcommittee provides comment and makes its recommendation regarding listing or delisting the nominated substance in the RoC. Again, however, the Background Document is not revised to reflect any of these proceedings.
- The fourth step consists of publication of a third and final request for comments in the Federal Register after the reviews by the RG1, RG2, and the RoC Subcommittee have been completed.
- The recommendations of RG1, RG2 and the RoC Subcommittee and all public comments received are presented to the NTP Executive Committee for review and comment. The NTP Executive Committee reviews the information on the nominations and provides its opinion for listing or delisting them in the RoC.
- Next, the NTP Director receives the recommendations for listing, along with all public comments received during the process. The NTP Director reviews the information and makes a recommendation to the Secretary, HHS regarding whether to list, delist, or not list the nominated substance in the RoC. The NTP prepares a final draft of the RoC based on the NTP Director's recommendations and submits the draft report to the HHS Secretary. Upon approval of the RoC, the Secretary submits it to

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Agencies represented on the NTP Executive Committee are: Agency for Toxic Substances and Disease Registry (ATSDR), Consumer Product Safety Commission (CPSC), Environmental Protection Agency (EPA), Food and Drug Administration (FDA), National Center for Environmental Health of the Centers for Disease Control and Prevention (NCEH/CDC), National Institute for Occupational Safety and Health/CDC (NIOSH/CDC), Occupational Safety and Health Administration (OSHA), National Cancer Institute of the National Institutes of Health (NCI/NIH), and National Institute of Environmental Health Sciences/NIH/NIEHS/NIH).

the U.S. Congress as a final document. The submission of the RoC to Congress constitutes publication of the report and it becomes available to the public at that time. The NTP publishes in the Federal Register a notice of the availability of the latest edition of the RoC.

The naphthalene listing process is well along. The final public comment period expired in March 2003. The matter is likely now before the NTP Executive Committee for review and comment. No final recommendation by the NTP Director to the HHS Secretary whether to list naphthalene has been announced.

Panel member companies, and others, have been and continue to be significantly adversely affected by the dissemination of the erroneous and biased information that characterizes the naphthalene listing process thus far. Panel member companies will continue to be harmed if this information is not promptly withdrawn and corrected. As evidenced by the brief summary of the process set forth above, the RoC listing process is iterative. Each successive phase of the process builds upon the information extracted from the preceding phase. The Panel believes, and demonstrates below, that the very foundation of the information construct NTP has built for naphthalene in the RoC listing process - the Background Document - fails to meet the standard for quality demanded under the IQA. The Background Document is the "document of record" in the listing process. It and all other documents for which the Panel seeks correction or withdrawal as described in this petition are documents that contain "influential scientific" information as this term is defined in the Guidelines and hence are subject to a particularly rigorous standard of quality. This standard has not been met in naphthalene's case.

The failure of the NTP to meet the IQA requirements for quality in preparing the Background Document cannot be isolated to any discrete phase of the listing process. The essentiality of the Background Document to the successive phases of the listing process, the fact that the Background Document is never revised to reflect any of the deliberations or comments upon it, and the Background Document's failure to meet IQA information quality standards, mean the entire naphthalene listing record is contaminated and utterly incapable of informing the judgment of the NTP Director for purposes of making a recommendation to list or not list naphthalene in the RoC. As with the fruit of the poisonous tree, no final decision resulting from this poisoned process can be free of taint.

It is for this reason the Panel believes the best and only appropriate solution for these IQA shortcomings is for the NTP to start over the listing process for naphthalene. Alternatively, if this relief is not granted, the Panel requests that NTP staff, NIH's OPCL, and the NTP Executive Committee engage in a well-defined process of pre-dissemination review of the entire naphthalene record to ensure that the shortcomings described below are remedied so the

IQA standard of data quality can be met before the NTP Director makes its recommendation to the Secretary of the Department of Health and Human Services.¹³

II SUMMARY OF INFORMATION FOR WHICH CORRECTION IS BEING SOUGHT IN ACCORDANCE WITH THE GUIDELINES

A. Background Document

The Panel seeks correction of significant errors or omissions in the Background Document (Attachment B). The Background Document is “influential scientific” information that has been, and continues to be, disseminated by the NTP within the meaning of the Guidelines. Background documents are prepared by the NTP after an independent search of the literature and must be prepared according to a specific format set forth in the NTP’s listing and delisting procedures for the NTP’s RoC. Among other requirements, background documents must contain a summary of any information relating to human studies of carcinogenicity, experimental carcinogenesis, genotoxicity, and other data relevant to evaluation of carcinogenicity and its mechanisms, and the data used to prepare these sections must come from peer reviewed sources.¹⁴ The Background Document must contain accurate summaries of information on these topics relating to naphthalene to satisfy IQA information quality standards.

The primary contributors to the Background Document are identified as NIEHS/NTP staff, including Dr. C.W. Jameson, Head, Report on Carcinogens, Environmental Toxicology Program. According to NTP Director Dr. Kenneth Olden, the Background Document “is the document of record” for all three scientific peer reviews in the RoC review process and “will remain the document of record.”¹⁵ Moreover, the Background Document has been and continues to be posted on NTP’s website.

The Background Document represents the views of the NTP of the facts pertinent to naphthalene’s evaluation. Accordingly, the Background Document is influential information that has been disseminated, is subject to a rigorous standard of information quality, and is, therefore, subject to the correction actions of the Guidelines.

¹³ To its credit, NTP recently solicited comments on the current RoC process and possible ways to improve it. (68 Fed. Reg. 67692, Dec. 3, 2003). ACC submitted comments on January 30, 2004 that recommend NTP replace the current process with a new one modeled closely on that followed by NTP’s Center for the Evaluation of Risks to Human Reproduction (CERHR). The Panel submits that adoption of the CERHR process would go a long way toward ensuring that future RoC nominations meet the requirements of the IQA, and should reduce the number of IQA challenges received regarding RoC matters.

¹⁴ Report on Carcinogens Listing and Delisting Procedures available at <http://ntp-server.niehs.nih.gov/NewHomeRoc/ListDelistProc.html>.

¹⁵ Letter from K. Olden, Director NTP, to C. Price, Vice-President ACC, dated March 11, 2003. Included as an Attachment to Attachment H.

The Panel is seeking correction of a number of significant errors and omissions in the Background Document discussed below, including many that are identified in the Panel's comments to NTP (Attachments E, F, G and H).

B. RG1 and RG2 Summary Reports and RG2 Meeting

The RG1 (Attachment A) and RG2 (Attachment C) summary reports are lacking any detail regarding what transpired at the closed RG1 and RG2 meetings, and the Panel is seeking correction of this deficiency. These summaries, apparently prepared by NTP staff, are represented by NTP as summaries of the RG1 and RG2 discussions and recommendations, and have been and continue to be disseminated on the NTP website. These summaries contain influential scientific information that is critical to naphthalene's evaluation in successive phases of the listing process. Accordingly, both the RG1 and the RG2 summaries are "influential scientific" information that has been disseminated and therefore subject to the correction actions of the Guidelines.

If the Eleventh RoC (or any subsequent RoC) discusses naphthalene, by necessity that document will depend crucially on the process steps that led up to its issuance. Those steps include the RG2 review meeting that occurred on October 2, 2002. The critical shortcomings in the Background Document that served as the basis for the meeting's discussions mean that the meeting itself was itself inherently flawed. Certainly the meeting summary does nothing to indicate that the participants dealt with or even recognized the problems with the Background Document identified in the prior comments of the Panel and others. The result is that any RoC based on the flawed RG2 meeting will embody the same flaws and thus will not meet IQA quality standards. The RG2 meeting thus should be rescinded and reconducted with an adequate Background Document.

Moreover, all future RoCs (as well as the Tenth) are subject to the IQA's predissemination review requirements, since they have been or will have been issued after October 1, 2002.¹⁶ Those requirements, as expressed in the OMB and NIH Guidelines, are that agencies "shall treat information quality as integral to every step of an agency's development of information, including creation, collection, maintenance, and dissemination."¹⁷ Any future RoC discussion of naphthalene that is based on the current proceedings will fail to have met those requirements, since the process NTP has followed thus far clearly cannot be described as ensuring the quality, pre-dissemination, of that document. (Indeed, the process is more certain to ensure its lack of quality.) For this reason as well, the RG2 meeting needs to be rescinded and properly reheld.

¹⁶ OMB Guidelines, 67 Fed. Reg. at 8459; NIH Guidelines, at beginning of Section II; HHS Guidelines, at Section D.3.

¹⁷ OMB Guidelines, 67 Fed. Reg. at 8459 (Section III.2); NIH Guidelines at introductory section preceding Section I.

The Panel is seeking correction of the RG1 review summary and the RG2 review summary, if not rescinded, in accordance with the above. The Panel is also seeking rescission of the RG2 findings and recommendations on naphthalene and a reconvening of the RG2 meeting after the Background Document is corrected.

C. NTP RoC Subcommittee Proceeding

The Panel is also seeking correction of the irregular and highly prejudicial manner in which information was distributed by the Chairman of the NTP RoC Subcommittee at the public Subcommittee meeting on November 19, 2002, without affording the members of the Subcommittee and the public an opportunity to review this information. It is also seeking correction of the bias and lack of objectivity that was introduced into the Subcommittee meeting proceedings, as well as the Subcommittee vote on the recommendation of naphthalene for listing as a result of this irregular and inappropriate introduction of new data. While the NTP RoC Subcommittee is composed of experts from the public and private sector and provides external peer review, its proceedings and conclusions, and the publication of its results, are subject to the OMB, NIH, and HHS Guidelines, and their corrective procedures on several grounds:

- The NIH Guidelines include among the NIH information covered by the OMB Guidelines “open meetings’ proceedings and minutes.” While the NIH Guidelines refer to “NIH Information” covered by the Guidelines and elsewhere state that the information must “represent our view,” the RoC Subcommittee proceedings are conducted under the *imprimatur* of NTP/NIH, the recommendations of the Subcommittee and the votes are made in a proceeding open to the public, and subsequently published in the *Federal Register* (thus disseminated), and the recommendations play a highly influential role in the final decision by the NTP Director on whether to list a chemical for listing.

Moreover, NTP should review the NTP RoC Subcommittee meeting proceedings to ensure that the NTP RoC Subcommittee meeting was conducted in accordance with procedures consistent with the objectivity, absence of bias, and other requirements of the Guidelines. NTP has authority to stop any further dissemination of the results of the proceedings if the procedures do not meet these standards.¹⁸ Failure to stop the further dissemination of the outcome of the Subcommittee

¹⁸ The NIH Guidelines correction procedures (Section VI.1) indicate that the material proposed for correction includes the presentation and mode of delivery. Moreover, the Office of Information and Regulatory Affairs (OIRA) explanation of the Information Quality Guidelines provide that an agency disseminates information where the agency has the authority to review and approve the information before release. June 10, 2002, Memo, attachment at 2, *citing* OMB Guidelines at 67 Fed. Reg. 8454, Feb. 22, 2002.

meeting and the vote, including its publication, indicate that the proceedings at a minimum represent NTP's view that the proceedings and results were conducted in a fair, objective, and unbiased manner, and that the recommendations and proceedings are worthy of the full consideration of the Executive Committee and the NTP Director. As a consequence, the NTP RoC Subcommittee proceedings and recommendations are subject to the OMB and NIH Guidelines at least with regard to whether the procedures followed were consistent with the goals and intent of the IQA and the OMB and NIH Guidelines.

- As discussed earlier, if the Eleventh RoC (or any subsequent RoC) discusses naphthalene, by necessity that document will depend crucially on the process steps that led up to its issuance. The meeting of the NTP RoC Subcommittee is the single most important step in that process after the initial issuance of the Background Document. As discussed more fully below, the legitimacy of that meeting is irrevocably clouded by the highly irregular and improper conduct of its chair. Even more so than in the case of the RG2 meeting, the RoC Subcommittee meeting was so profoundly flawed that any RoC based on it will inevitably be colored by the same flaws and thus will not meet IQA quality standards. As a result, the RoC Subcommittee meeting should be rescinded and reconducted appropriately.

Moreover, all future RoCs (as well as the Tenth) are subject to the IQA's predissemination review requirements, since they have been or will have been issued after October 1, 2002. Those requirements, as expressed in the OMB and NIH Guidelines, are that agencies "shall treat information quality as integral to every step of an agency's development of information, including creation, collection, maintenance, and dissemination."¹⁹ Thus, even if the RoC Subcommittee's recommendations and proceedings are not considered to represent NTP's view and therefore do not fall within the definition of "information" subject to the Guidelines, those recommendations and proceedings should be an essential part in the creation of any future RoC that discusses naphthalene. Any RoC that is based on the RoC Subcommittee proceedings will fail to have met those requirements, since that meeting cannot possibly be characterized as ensuring the quality, pre-dissemination, of that document. Rather, the proceedings only guarantee

¹⁹ OMB Guidelines, 67 Fed. Reg. at 8459 (Section III.2); NIH Guidelines at introductory section preceding Section I.

that its quality will be questioned. For this reason as well, the RoC Subcommittee meeting needs to be rescinded and properly reheld.

The transcript of the NTP RoC Subcommittee meeting of November 19, 2002 is included as Attachment D. As discussed below, the Panel is seeking rescission of the vote of the NTP RoC Subcommittee at the November 19, 2002, meeting with respect to naphthalene and a reconvening of that meeting, following correction of the other matters discussed above.

III. SUMMARY OF GROUNDS FOR CORRECTION UNDER THE GUIDELINES APPLICABLE TO THE INFORMATION DISSEMINATED OR DEVELOPED BY NTP FOR NAPHTHALENE

The bases for seeking correction of information subject to the OMB, NIH, and HHS Guidelines include the following:

- Lack of objectivity, both in substance (with regard to accuracy, reliability, and lack of bias) and presentation (with regard to presentation in a clear, complete, and unbiased manner).²⁰ The information is “highly influential” scientific information, as defined in the Guidelines, and the information must:
 - Meet heightened requirements for transparency and, if applicable, reproducibility; and
 - Satisfy certain requirements in the Safe Drinking Water Act (SDWA), as applicable, such as: (1) use “the best available science and supporting studies conducted in accordance with sound and objective scientific practices, including peer reviewed studies when available”; (2) use “data collected by accepted methods or best available methods”; and (3) be comprehensive, informative, and understandable.²¹
- Lack of utility in terms of usefulness of the information to its intended uses, including the public.²²

²⁰ HHS Guidelines Section A, D.2.D.4: NIH Guidelines, Introduction, Section V.2.a. and VII; OMB Guidelines, 67 Fed. Reg. at 8453, 8459.

²¹ HHS Guidelines Section I.D. 4.g; NIH Guidelines, Section V.2.d and VII; OMB Guidelines, 67 Fed. Reg. at 8457-8458, 8460 (col. 2).

²² OMB Guidelines, 67 Fed. Reg. at 8459; HHS Guidelines, Section D.2.b. Both Guidelines specify that in assessing usefulness of information, the agency must consider the uses of the information not only from the perspective of the agency but also from the (Footnote continued on the next page . . .)

IV. SPECIFIC CORRECTIONS REQUESTED AND BASES UNDER THE GUIDELINES

A. Requested Corrective Action for Background Document

It is important that the Background Document satisfy the Guidelines for a number of reasons:

- The Background Document contains a broad range of information on naphthalene, including not only toxicological data, but also information concerning human exposure and environmental occurrence, that may be relied upon and used by consumers and the general public. The fact that NTP may also post on its website public comments on the Background Document does not negate the fact that the Background Document is, and is likely to be read as, a stand-alone document expressing the current views of the NTP.
- The Background Document, as stated by NTP Director Olden, is the “document of record” for all three scientific peer reviews and “will remain the document of record.” Accordingly, satisfaction of the requirements of the Guidelines is necessary to ensure that the three scientific peer review groups are presented with a complete and unbiased document with which to work. Given that the starting point for discussion during the three peer review meetings is the Background Document, lack of objectivity and utility of that document can only taint the entire review process.

The Background Document fails to meet requirements for objectivity both in substance, with regard to accuracy, reliability, completeness, and lack of bias, and in presentation. Further, the Background Document constitutes “influential scientific” information as defined in the Guidelines, in that dissemination of the document will and does have a clear and substantial impact on important public policies or important private sector decisions.²³ This is evidenced by the fact that the Background Document is the “document of record” in the review of whether naphthalene should be included in the *RoC*, which the NIH Guidelines describe as “[o]ne of our most visible publications,” and the fact that the public may be expected to use and rely upon the information contained within it, as discussed above. Accordingly, the document is subject to a particularly high degree of transparency and the data and studies described therein are subject to requirement of reproducibility by third parties.

perspective of the public. When transparency of information is relevant for assessing the information’s usefulness from the public’s perspective, “the agency must take care to ensure that transparency has been addressed in its review of the information.”

²³ OMB Guidelines, 67 Fed. Reg. at 8460 (col. 3 (#9)); NIH Guidelines at Section VII.

Moreover, the document must satisfy certain requirements of the SDWA, as applicable, including in particular use of “the best available science and supporting studies conducted in accordance with sound and objective scientific practices, including peer reviewed studies when available” and constitute information that is “comprehensive, informative, and understandable.”²⁴ The Background Document fails to meet these standards.

Finally, as detailed below, the Background Document fails to meet the requirement of “utility” both because it is not sufficiently reliable and transparent for public use or for use by the scientific peer review groups.

To satisfy these deficiencies, NTP must withdraw the Background Document from NTP’s website and call for its withdrawal from any other agency’s website and cease any further dissemination of the document until the document is revised to address, at a minimum the following matters:²⁵

- **Page 21:** To satisfy the objectivity requirement and avoid the possibility of any inaccurate inferences being made, the Background Document should explain in detail why the three-decades old East German reports of the health effects observed in tar distillation workers, Wolf (1976, 1978) as cited in NTP (1992) and (2000), can fairly be construed as evidence of carcinogenicity in humans. In so doing, it should explain how it overcomes the analyses by other authoritative bodies cited in the Panel’s October 2, 2002, comments to NTP (Attachment F) and the confounding factors and other deficiencies in those studies described in the October 2, 2002, Comments.²⁶ The discussion of these reports should also incorporate additional comments and correct misleading and incorrect descriptions of the Wolf studies made by NTP in its reports on naphthalene, as discussed in the Panel’s March 24, 2003, comments to NTP (Attachment H).²⁷
- **Pages vi, 27, 31, 53:** To avoid misleading implications, which would violate the objectivity requirements, the Background Document should clarify the meaning of its terminology in referring to the “carcinogenicity”

²⁴ HHS Guidelines at Section I.D. 4.g; NIH Guidelines at Sections V.2.d, VII; OMB Guidelines, 67 Fed. Reg. at 8457-8458, 8460 (col. 2).

²⁵ Page numbers refer to page numbers in the Background Document.

²⁶ See Attachment F: Comments of the Naphthalene Panel on Draft August 26, 2002, Draft Report on Carcinogens Background Document for Naphthalene (Oct. 2, 2002) at 5, 9-11 (Oct. 2, 2002, Comments).

²⁷ See Attachment H: Letter to Dr. C.W. Jameson, NTP, from C. Price, ACC, March 24, 2003.

of naphthalene in mice and rats in several places. It should explain that the NTP Technical Report on the mouse study made a finding of “some evidence” of carcinogenicity in mice based on increases in *benign* tumors only under the criteria used by NTP only for individual studies. Similarly, it should explain that a finding of “clear evidence” of carcinogenic activity in rats was made by the NTP rat bioassay on naphthalene only with respect to male rats and only under the criteria used by NTP for individual studies. To eliminate additional incorrect implications, the Background Document should clearly explain the meaning of the conclusions reached in the individual NTP reports, as explained in those reports, that “the actual determination of risks to humans from chemicals found to be carcinogenic in laboratory animals requires a wider analysis that extends beyond the purview of these studies.”²⁸ Finally, while the criteria for listing in the RoC are set out at the beginning of the report, it would avoid confusion to the general public to state, when discussing individual bioassays, that a listing based on a finding of “reasonably anticipated to be a human carcinogen” must be considered on the weight of the evidence as set forth in the listing criteria.

- While the purpose of the Background Document is not to reach conclusions as to whether naphthalene meets the RoC listing criteria, but rather to summarize the available relevant scientific literature, to satisfy both the “utility” and objectivity requirements the document should set forth certain information that would enable the scientific review groups to better evaluate whether naphthalene meets the RoC listing criteria. These include the following information from the Panel’s September 24, 2001, comments to NTP (Attachment E)²⁹ as well as its March 24, 2003 comments (Attachment H):
 - As concluded by EPA in the Integrated Risk Information System (IRIS) file on naphthalene, “An inhalation unit risk estimate for naphthalene was not derived because of the weakness of the evidence (observations of predominant benign respiratory tumors in mice at high dose only) that naphthalene may be carcinogenic in humans.”³⁰ The single alveolar/bronchiolar carcinoma observed among the high

²⁸ See NTP Rat Study on Naphthalene at 8.

²⁹ See Attachment E, Comments of the Naphthalene Panel on Call for Public Comment on 16 Substances, Mixtures and Exposure Circumstances Proposed for Listing in the Report on Carcinogens, Eleventh Edition, 66 Fed. Reg. 38430 (Sept. 24, 2001) at 4.

³⁰ IRIS Substance File for Naphthalene at Section II.C.

dose female mice cannot legitimately be considered together with the benign lung tumors, and the NTP mouse study cannot be considered to have caused an increase in benign and malignant tumors combined. The Background Document should note that the mouse is more susceptible to the pulmonary toxicity of naphthalene than other species, calling into question the relevance of the mouse tumors to human health.

- The reasons that the rat nasal cavity tumors cannot be considered to be increased to an “unusual degree.”³¹
- The reasons as to why anatomical, physiological, and metabolic differences between rats and humans raise substantial questions as to the relevance of the rat nasal tumors to humans, as discussed in the October 2, 2002, Comments.³² The Background Document should also discuss that there is no convincing relevant evidence that naphthalene acts through mechanisms indicating it would likely cause cancer in humans, for the reasons discussed in the March 24, 2003, Comments.³³
- **Pages 27-30 (Section 4.2.1):** To satisfy the objectivity requirements of accuracy and completeness, as well the requirement for utility, this section should not only include the discussion from the September 24, 2001, Comments referenced above with regard to rat nasal tumors, but should also explain in greater detail that cell proliferation is a potentially important mechanism for the development of nasal tumors in rats exposed to naphthalene, as explained in Section III.C of the October 2, 2002, Comments.
- **Pages 33-38 (Section 5):** To satisfy the objectivity requirements with regard to completeness and a balanced discussion, the SDWA requirements to include the best available science and supporting studies, including peer reviewed studies when available, and the utility requirements as they pertain to the public and the various review groups and decision-makers, the section on genotoxicity should discuss the additional genotoxicity studies identified in the October 2, 2002,

³¹ See Comments of September 24, 2001 (Attachment E) and March 24, 2003 (Attachment H).

³² See Comments of October 2, 2002 (Attachment F) and March 24, 2003 (Attachment H).

³³ March 24, 2003, Comments (Attachment H) at [10-14].

Comments at pages 10-11 and in a recent publication by Schreiner (2003)³⁴, including in particular the standard *in vivo* studies that are described. Further, the Background Document, in both Section 5 and in the Executive Summary, should state either that available data strongly support the conclusion that naphthalene is not genotoxic or that the vast majority of genotoxicity tests on naphthalene indicate that naphthalene is not genotoxic.

- To meet the objectivity requirements with regard to accuracy and completeness, the SDWA requirements noted above, and the utility requirements, the Background Document should discuss in detail, drawing from the March 24, 2003, Comments (Section 1.5), the grounds for believing that naphthalene does not belong to a well-defined, structurally-related class of substances whose members are listed in a previous *RoC* as either known to be a human carcinogen or reasonably anticipated to be a human carcinogen.
- Outdated and incorrect information in the Background Document on production, exposure, use, and environmental fate of naphthalene should be corrected as discussed in the October 2, 2002, Comments.
- To satisfy better the requirements of objectivity, with regard to completeness and transparency, as well as utility, the Background Document should be corrected to avoid misunderstanding the integrated toxicology data, including data demonstrating that observed toxic and metabolic effects relevant to the tumorigenic process are species-specific, and data regarding the relevance of laboratory animal responses for extrapolating to humans, as discussed in the Panel's October 2, 2002, Comments³⁵ and other comments submitted by the Panel.³⁶
- The Background Document should include summaries of any scientific data meeting the SDWA standards, as adapted in the HHS Guidelines, that either RG2 or the NTP *RoC* Subcommittee intends to discuss in any repeat meetings that are held pursuant to this correction request. It should also correct any factual errors or omissions that were noted by RG1 and then subsequently by RG2.

³⁴ Schreiner, C.A. (2003). Genetic Toxicity of Naphthalene: A Review. *Journal of Toxicology and Environmental Health*, Part B, 6:161-183.

³⁵ October 2, 2002, Comments at Section III.B.

³⁶ See, e.g., March 24, 2003, Comments (Attachment H) at 10-16; September 24, 2001, Comments at 3-8.

B. Requested Correction of the RG1 and RG2 Review Summaries and of the RG2 Proceedings

Both the RG1 and the RG2 summary reports fail to meet the requirements for objectivity, both in substance with regard to completeness, and in presentation (with regard to presentation in a clear and complete manner). Moreover, the RG1 and RG2 review summaries constitute “influential scientific” information because they, like the Background Document, when disseminated will and do have a clear and substantial impact on important policies or important private sector decisions. The RG1 and RG2 recommendations and findings are considered by the NTP Director in determining whether to list naphthalene in the *RoC*, particularly since the Background Document is never revised to reflect the points they consider. Further, the public may be expected to use and rely upon the information in the RG1 and RG2 summary reports. Accordingly, these documents are required to have a particularly high degree of transparency and are subject to the SDWA requirements of comprehensiveness and informativeness.

The RG1 and RG2 summary documents fail to meet these as well as the utility requirements. The RG1 review summary fails to provide a detailed analysis of the key issues that led RG1 to make its recommendation. It does not explain how the nasal tumors in the rats satisfy the *RoC* listing requirements and why NTP’s mouse study should be considered at all. Nor does it explain how RG1 concluded that the anatomical, physiological, and metabolic differences between rats and humans are not sufficient to rule out the relevance of the rat and mouse tumors to humans.

The RG2 summary review similarly fails to explain how each of the two groups in the split vote reached their respective recommendations.

Moreover, the RG2 proceeding was subject to the pre-dissemination review requirements, as discussed above. The fact that it was provided with a flawed and incomplete Background Document as the primary basis for its review and recommendation establishes by definition that it failed to consider, use, or integrate the best available science and supporting studies, including peer reviewed studies, with respect to mechanism and genotoxicity.

The RG1 review summary and the RG2 review summary (if not rescinded), should be revised to correct the deficiencies described above. In addition, the RG2 findings and recommendations with regard to naphthalene should be rescinded and a new RG2 meeting convened, after preparation of a corrected Background Document.

C. Requested Correction of the NTP RoC Subcommittee Proceedings

The NTP RoC Subcommittee proceedings at a minimum represent NTP's view that the proceedings, including the meeting, the vote, and the publication of the Subcommittee's recommendation, were conducted in an objective, fair, unbiased manner, that the deliberations were transparent, and that the proceedings otherwise satisfied the requirements of the Guidelines, including those for pre-dissemination review. Indeed, the publication of the results of the Subcommittee vote and NTP's moving forward with the RoC listing procedures further indicate that the NTP believes that the recommendations and proceedings of the Subcommittee are worthy of the full consideration of the Executive Committee and the NTP Director. Therefore, the Panel is seeking correction of proceedings in the NTP RoC Subcommittee meeting on the grounds that it was conducted in a highly irregular manner that resulted in its failure to satisfy any of these requirements.

Moreover, as in the case of the Background Document and the RG1 and RG2 summary reports, the Subcommittee proceedings constitute "influential" scientific information and therefore are subject to a particularly rigorous degree of pre-dissemination review and a particularly high level of transparency. The Subcommittee meeting is the last of the three scientific review group meetings before all the recommendations and other relevant materials are provided to the NTP Executive Committee and the NTP Director. The Subcommittee meeting and its recommendation carry particularly significant weight in the RoC review process because the Subcommittee is the last of the three scientific review groups and because it is the only one of the scientific review groups that conducts an external peer review open to the public and which allows for consideration of public comments submitted prior to its proceedings. Accordingly, the proceedings and the Subcommittee's recommendations will have a clear and substantial impact on important public policies (*i.e.*, the decision on whether to list naphthalene in the RoC), which in turn will have a clear and substantial impact on important public sector decisions.³⁷

The primary violation of the Subcommittee's proceedings with respect to the Guidelines' requirements for objectivity, transparency, and utility originate from the highly irregular and prejudicial step taken by the Chairman of the Subcommittee, of temporarily stepping down as Chairman during the Subcommittee's meeting to present a highly technical presentation on naphthalene that included new information³⁸ that apparently had neither been shared prior to the meeting with the Subcommittee members, nor made part of the public record

³⁷ OMB Guidelines, 67 Fed. Reg. at 8460 (col. 3 (#9)); NIH Guidelines at Section VII.

³⁸ Transcript, November 19, 2002, at 74-75 and 100-101.

by NTP prior to, during, or since the meeting. Substantively, the new information presented by the Chairman to the Subcommittee during its deliberations, which appears to have significantly influenced the Subcommittee vote, included categorically incorrect statements regarding a class of chemicals known as “polycyclic aromatic hydrocarbons” (PAHs), which the Chairman asserted to include naphthalene.

For example, the Chairman argued that naphthalene belongs to the class of chemicals known as PAHs which, he stated, are “known carcinogens.” It is well known, however, that the toxicological categorization of naphthalene as a PAH is unusual in the scientific community, and that it is inaccurate and scientifically indefensible to state categorically that all PAHs are “known carcinogens.” The International Agency for Research on Cancer (IARC) has expressly addressed these issues. Volume 32 of the *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans* discusses the carcinogenicity data on 42 PAH compounds. Following the Preamble, IARC’s scientists state that “only condensed aromatic hydrocarbons and aza arenes with three or more rings are considered” in their review of PAHs and heterocyclics that have been tested for carcinogenicity³⁹ and that occur in the environment. More importantly, it is well known that the classification of PAHs is disputed. Although it is true that 15 or so PAHs are considered as known experimental or animal carcinogens, and several are considered to be human carcinogens, many others are not considered carcinogenic at all. Anthracene, fluoranthene, 1-methylchrysene, and pyrene are examples of PAHs that have been evaluated for carcinogenicity and are considered not carcinogenic by IARC, NTP, and the U.S. Environmental Protection Agency (EPA).⁴⁰ There is no information, moreover, regarding toxicological categorization of naphthalene as a PAH in any of the nomination or background materials presented by NTP in support of the nomination of naphthalene to the RoC.⁴¹

The presentation of such highly technical data to the Subcommittee members on the very day of the meeting, and the failure to make such information available to the public in advance of the meeting, did not allow the Subcommittee (or any interested party) sufficient time

³⁹ Although the NTP bioassays on naphthalene were not completed until after publication of IARC Volume 32 in 1983, at least three independent cancer bioassays and one cell transformation assay on naphthalene were published at the time of the IARC review. Included in that Monograph are reviews on a number of PAH compounds with less experimental data available than that for naphthalene in 1983.

⁴⁰ See EPA’s IRIS documents for these chemicals, available online at <http://www.epa.gov/iris/>.

⁴¹ Other highly influential information newly introduced by the Chairman, on the day of the meeting, included information on alternative metabolic pathways and unsubstantiated statements concerning the presence of naphthalene as a component of “urban air pollution” as reasons for listing naphthalene. See, e.g., March 24, 2003 Comments (Attachment H) at 16-18 ; Transcript, November 19, 2002 (Attachment D) at 100-101.

meaningfully to review the new information, confirm its accuracy, and evaluate its relevance to the listing of naphthalene. Nevertheless, the Subcommittee appeared to accept the statements of the Chairman at face value. Subcommittee members almost certainly afforded the unreviewed information and remarks considerably more weight and deference than would otherwise be the case because the presenter was, in fact, was Chairman of the Subcommittee, despite his attempt to state otherwise solely for the purpose of introducing his remarks. Similarly, the public, including the Panel, was denied any opportunity to comment on the new information and bring to the attention of the Subcommittee the flaws in the information and its lack of relevance.

Accordingly, since the Subcommittee was denied advance access to the full record considered by the Subcommittee, the purpose of the Subcommittee proceedings to conduct a meaningful external peer review was denied. This purpose was also compromised by the inability of the public, including the Panel, to comment on the newly introduced, and highly material, information. As a result, the proceedings and recommendation of the Subcommittee lacked objectivity both in substance, with regard to accuracy, reliability and bias, and in presentation (*i.e.*, in that the presentation of the new information and the deliberations on that information were not made in a clear and unbiased manner).

Moreover, the Subcommittee proceedings and vote fail to meet the rigorous standards of transparency applicable to “influential” scientific information. This follows not only from the fact that the reasoning of the Subcommittee in making its vote was not explicit, but also because the reasoning process was undoubtedly compromised by the last minute introduction of highly material information by the Subcommittee Chairman. The proceedings also failed the transparency test because the introduced materials included highly material information, such as information on metabolic pathways, which, during his presentation, the Chairman was unable to show even to the Subcommittee. In addition, during the proceedings the Chairman provided materials to the Subcommittee that were not made available to members of the public attending the meeting, let alone the general public, and discussed research results, apparently from his laboratory, and which, though said to have been published, were not provided to the Subcommittee and which were not identified by reference.⁴²

Further, the information introduced to the Subcommittee after the public comment period violates the requirements of the SDWA, applicable to “influential” scientific information, as discussed above, to use the best available science and supporting studies conducted in accordance with objective scientific practices, including peer reviewed studies when available. Because of the manner in which the information was introduced, it was impossible to verify if the studies discussed met these requirements. Clearly other information for which no documentation could be provided did not meet these standards.

⁴² The citations later provided to the Panel by K. Olden (letter of Jan. 27, 2003) were: Flowers-Geary *et al.*, 1996; McCoull *et al.*, 1999; Penning *et al.*, 1999; Yu *et al.*, 2002. These references were discussed in the Panel’s comments of March 24, 2003 (Attachment H).

It should be noted that the recommendations and other findings of the Subcommittee are not subject to the presumption of objectivity for data and analytical results that have been subjected to formal, independent peer review that is provided by the Guidelines.⁴³ To meet the requirements for such presumption, the peer review must meet the criteria recommended by OMB-OIRA to the President's Management Council, which among other criteria requires that peer reviews be conducted in an open and rigorous manner.⁴⁴ As discussed above, the Subcommittee proceedings were not conducted in a transparent manner and therefore by definition are not entitled to a presumption of objectivity. In any event, any such presumption of objectivity can be rebutted and to claim such a presumption in the case at hand is not warranted by any interpretation of the transcript (Attachment D).

Finally, the Subcommittee proceedings fail to meet the Guidelines' requirement for utility from the perspective of both NTP and the public. Clearly, proceedings and recommendations that emanate from such proceedings that are not objective, not transparent, and that are strongly influenced by bias do not serve the objective of making a RoC listing decision that is sound scientifically and free from bias. Such proceedings also fail to satisfy the utility criteria by not allowing for public access to ensure improvement of overall quality of the recommendation.⁴⁵

Because the NTP RoC Subcommittee proceedings occurred after October 1, 2002, they were subject to the pre-dissemination review requirements of the Guidelines. Under this review process, it was NTP's obligation to review the integrity of the Subcommittee meetings and their compliance with the Guidelines' requirements. For the reasons discussed above, NTP, if it had properly reviewed the proceedings, could only conclude that the Subcommittee proceedings did not meet these requirements. Accordingly, NTP should have announced proactively that the Subcommittee meeting would be repeated, after ensuring that all material information, including the updated Background Document, was made available to the Subcommittee members and the public in advance. At the same time, NTP should have negated the vote of the November 19, 2002, Subcommittee meeting. The Panel has made this request in previous correspondence with NTP. The Panel believes that, under the IQA, NTP is obligated to correct the substantial and highly prejudicial flaws of the November 19, 2002, Subcommittee meeting by taking precisely these measures.

V. CONCLUSION

For the reasons discussed above, the November 19, 2002, RoC Subcommittee meeting on naphthalene was conducted in a manner that violated the Information Quality Act and the implementing OMB, HHS, and NIH Guidelines. Moreover, the Background Document

⁴³ OMB Guidelines, 67 Fed. Reg. at 8459; HHS Guidelines, Part I.D.2.c.

⁴⁴ *Id.*

⁴⁵ NIH Guidelines at Introduction, Section VII; OMB Guidelines, 67 Fed. Reg. at 8456-57, 8460.

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does not satisfy the standards of the OMB, HHS, and NIH Guidelines applicable both to disseminated information and to information that is integral to key steps of NTP's development of disseminated information. Similarly, the RG 1 and RG2 review summaries fail to meet the requirements for objectivity both in substance (with regard to completeness) and in presentation (with regard to presentation in a clear and complete manner), as well as the requirements for utility. Moreover, the fact that RG2 was provided with a flawed and incomplete Background Document as the primary basis for its review and recommendation, very shortly before its meeting, establishes by definition that RG2 failed to consider, use, or integrate the best available science and supporting studies in its deliberations, and therefore violated the pre-dissemination review requirements under the Guidelines.

The best and only appropriate solution to these violations is for NTP to rescind the November 19, 2002, vote of the RoC Subcommittee on the listing of naphthalene, rescind the RG2 review summary, withdraw the Background Document from NTP's website and otherwise cease dissemination of that document, correct the Background Document so that it comports with the OMB, NIH, and HHS Guidelines, make the corrected document publicly available, and arrange for repeats of the RG2 and NTP RoC Subcommittee meetings that comport with the OMB, NIH, and HHS Guidelines, to be held after issuance of the corrected Background Document. NTP should also correct the RG1 and, if not rescinded, the RG2 review summaries to provide the necessary detail to satisfy the objectivity and utility requirements.

Alternatively, if this remedy is not granted, the Panel requests that NTP staff, NIH's OPCL, and the NTP Executive Committee engage in a well-defined process of pre-dissemination review of the entire naphthalene record with regard to the data quality standards under the NIH, OMB, and HHS Guidelines before the NTP Executive Committee makes its recommendation to the NTP Director.

If you seek additional information, please contact Dr. Anne P. LeHuray at (703) 741-5630 or anne_lehuray@americanchemistry.com

Sincerely yours,

Courtney M. Price
Vice President, CHEMSTAR

cc: John D. Graham, Ph.D., OIRA, OMB
Elias A. Zerhouni, M.D., Director, NIH
Alex M. Azar II, Esquire, General Counsel, HHS
Kenneth Olden, Ph.D., Director, NTP

Associate Director of Communications, NIH
April 1, 2004
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Mr. Lou Rozier, Office of the Director, NIEHS
Naphthalene Panel Members

American Chemistry Council
Naphthalene Panel

Request for Correction of Information

Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Index of Attachments

Hard copies of Attachments are included in the hard copy submission. For the electronic submission, links to the Attachments are provided.

- Attachment A Review Summary of the National Institute of Environmental Health Sciences (NIEHS/NTP) RoC Review Committee (RG1) [dated June 10, 2002].
<http://ntp-server.niehs.nih.gov/NewHomeRoc/roc11Bkgrnd2002.html>
- Attachment B Draft Report on Carcinogens Background Document for Naphthalene 26 August 2002.
<http://ntp-server.niehs.nih.gov/NewHomeRoc/roc11Bkgrnd2002.html>
- Attachment C NTP Executive Committee Working Group for the Report on Carcinogens – RG2 [dated October 2, 2002].
<http://ntp-server.niehs.nih.gov/NewHomeRoc/roc11Bkgrnd2002.html>
- Attachment D Condensed Transcript, National Institute of Environmental Health Sciences, National Toxicology Program (NTP), Board of Scientific Counselors, Report on Carcinogens (ROC) Subcommittee Meeting, November 19, 2002. Available on NTP's web site as an attachment to the Panel's March 2003 comments (see Attachment H).
<http://ntp-server.niehs.nih.gov/newhomeroc/roc11naphthalene.html>
- Attachment E Comments of the Naphthalene Panel on July 24, 2001, Call for Public Comment on 16 Substances, Mixtures and Exposure Circumstances Proposed for Listing in the Report on Carcinogens, Eleventh Edition, 66 Fed. Reg. 38430 (Sept. 24, 2001) at 4. <http://ntp-server.niehs.nih.gov/newhomeroc/roc11naphthalene.html>
- Attachment F Comments of the Naphthalene Panel in response to the release of the Draft Background Document [submitted October 2, 2002].
<http://ntp-server.niehs.nih.gov/newhomeroc/roc11naphthalene.html>
- Attachment G Comments of the Naphthalene Panel in response to the release of the RG2 Review [submitted November 4, 2002].
<http://ntp-server.niehs.nih.gov/newhomeroc/roc11naphthalene.html>
- Attachment H Comments of the Naphthalene Panel in response to the Call for Public Comments on 10 Nominations in January 22, 2003 Federal Register [submitted March 24, 2003].
<http://ntp-server.niehs.nih.gov/newhomeroc/roc11naphthalene.html>

American Chemistry Council

Naphthalene Panel

Request for Correction of Information

Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Attachment A

Review Summary of the National Institute of Environmental Health Sciences (NIEHS/NTP) RoC Review Committee (RG1)

Date: 10 June 2002

(available at <http://ntp-server.niehs.nih.gov/NewHomeRoc/roc11Bkgrnd2002.html>)

American Chemistry Council
Naphthalene Panel
Request for Correction of Information
Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Attachment B

Draft

Report on Carcinogens
Background Document
for Naphthalene

26 August 2002

(available at <http://ntp-server.niehs.nih.gov/NewHomeRoc/roc11Bkgrnd2002.html>)

American Chemistry Council

Naphthalene Panel

Request for Correction of Information

Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Attachment C

NTP Executive Committee Working Group for the Report on Carcinogens – RG2

Review Date: 2 October 2002

(available at <http://ntp-server.niehs.nih.gov/NewHomeRoc/roc11Bkgrnd2002.html>)

American Chemistry Council

Naphthalene Panel

Request for Correction of Information

Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Attachment D

Condensed Transcript

National Institute of Environmental Health
Sciences

National Toxicology Program (NTP)

Board of Scientific Counselors

Report on Carcinogens (ROC) Subcommittee Meeting

Date: 19 November 2002

American Chemistry Council

Naphthalene Panel

Request for Correction of Information

Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Attachment E

Comments of the Naphthalene Panel

on the

Nomination of Naphthalene

for

Possible Listing in the Report on Carcinogens

Submission Date: 24 September 2001

American Chemistry Council

Naphthalene Panel

Request for Correction of Information

Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Attachment F

Comments of the Naphthalene Panel

on the

Draft Background Document

Submission Date: 2 October 2002

American Chemistry Council

Naphthalene Panel

Request for Correction of Information

Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Attachment G

Comments of the Naphthalene Panel

on the

Release of the RG2 Review

Submission Date: 4 November 2002

American Chemistry Council

Naphthalene Panel

Request for Correction of Information

Pursuant to Section 515(a) of the Treasury and General Government
Appropriations Act for Fiscal Year 2001 (the Information Quality Act)

Attachment H

Comments of the Naphthalene Panel
in response to the
Call for Public Comments on 10 Nominations
in
January 22, 2003 Federal Register

Submission Date: 24 March 2003

Attachment 2

Letter from
Christopher J. Portier, Ph.D.
to
Courtney M. Price
dated
January 18, 2005

Available On-Line at
<http://aspe.hhs.gov/infoquality/request&response/14b4.pdf>

**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

**National Toxicology Program
P.O. Box 12233
Research Triangle Park, NC 27709**

January 18, 2005

Courtney M. Price
Vice President, CHEMSTAR
American Chemistry Council
1300 Wilson Boulevard
Arlington, VA 22209

Dear Ms. Price:

I am responding to your Request for Correction of Information ("the Request") dated April 1, 2004 and submitted on behalf of the American Chemistry Council's Naphthalene Panel (the Panel) pursuant to Section 515(a) of the Treasury and General Government Appropriations Act for Fiscal Year 2001¹ (the Information Quality Act or IQA) and the guidelines issues by the Office of Management and Budget (OMB Guidelines),² the National Institutes of Health (NIH) of the U.S. Department of Health and Human Services (HHS) (NIH Guidelines)³ and the HHS (HHS Guidelines)⁴. The Request concerns the background document on naphthalene and the scientific review of naphthalene for possible listing in the 11th Report on Carcinogens (RoC).⁵

¹ 44 U.S.C. 3516 note.

² *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility and Integrity of Information by Federal Agencies*, 67 Fed. Reg. 8452 (February 22, 2002), available at <http://www.whitehouse.gov/omb/fedreg/reproducible2.pdf>.

³ *Guidelines for Ensuring the Quality of Information Dissemination to the Public*, available at <http://www.hhs.gov/infoquality>.

⁴ *Guidelines for Ensuring the Quality of Information Dissemination to the Public*, available at <http://www.hhs.gov/infoquality/part1.html>.

⁵ We note that the Panel submitted written comments on the nomination and/or review of naphthalene on September 24, 2001, October 2, 2002, November 4, 2002, and March 24, 2003. As is our process, the NTP posted the Panel's comments along with those of other persons/groups who commented on naphthalene on the RoC web site (<http://ntp.niehs.nih.gov/index.cfm?objectid=ADAEC564-F1F6-975E-76C24D4639BD3613>) and provided them, as submitted, to the applicable review groups for their consideration. Specifically, the RG1, which met June 10, 2002, and the RG2, which met on October 2, 2004, received and was tasked with reviewing your comments dated September 24, 2001. The RoC Subcommittee met November 19, 2002 and received and was tasked with reviewing the comments you submitted September 24, 2001, October 2, 2002, and November 4, 2002. Finally, the NTP Executive Committee met August 21, 2003 and received and was tasked with reviewing all four sets of your comments. As to the concerns raised now about the process for the November 19th RoC Subcommittee meeting, the Panel previously raised them in separate letters dated November 27, 2002 and March 3, 2003, from Ms. Courtney M. Price, to Dr. Kenneth Olden. The NTP has responded to these points, in separate letters dated January 27, 2003 and March 11, 2003, respectively, to Ms. Price from Dr. Olden.

Page 2 – Courtney M. Price

Specifically, the Panel requests that the agency correct three documents: the Background Document for Naphthalene and the Summaries of the NIEHS/NTP RoC Review Group (RG1) and NTP Executive Committee Interagency Working Group for the RoC (RG2) meetings. Additionally, based generally on your contention that the Background Document for Naphthalene is flawed, and thus all activity involving it represents “fruit of the poisonous tree,” you have asked that the agency “rescind” the RG2 meeting with regard to naphthalene (and hold a new RG2 meeting) and the vote of the November 19, 2002 NTP Board of Scientific Counselors RoC Subcommittee (RoC Subcommittee) meeting and re-convene a new RoC Subcommittee to reconsider naphthalene at a future meeting.

In the alternative, you have asked that the NTP staff, NIH’s Office of Communications and Public Liaison (OCPL), and the NTP Executive Committee “undertake a comprehensive pre-dissemination review of the entire record of the listing proceeding as it relates to naphthalene before any recommendation is made concerning listing naphthalene in the Eleventh RoC by the NTP Director.”⁶

Before I respond to your concerns, I would like to briefly summarize the process used for the review of nominations to the 11th RoC.

Process for Reviewing Nominations to the 11th RoC

The review of all nominations to the 11th RoC, including naphthalene, followed a formal, multi-step process that solicited and incorporated public comment. Initially, the NTP published a notice in the Federal Register (July 24, 2001) and in the NTP newsletter that announced the nominations to the 11th RoC selected for review and solicited public comments on them. In addition, the NTP invited the public to submit relevant information on their carcinogenicity, production, use, and human exposure and also asked for the identification of any scientific issues related to the listing that should be addressed during the reviews. The NTP next initiated preparation of the background document on each nomination, which summarized the relevant scientific information relating to its human exposure and carcinogenic potential. The background document is intended to provide concise, comprehensive, and unbiased summaries of all relevant information found in the peer-reviewed scientific literature. The information contained within the background document is factual and includes no opinion or views from the NTP regarding what the data mean. The background document for naphthalene was made available to the public on the NTP website on August 26, 2002.

The formal review of nominations to the 11th RoC also included evaluation by two federal scientific review groups (RG1 and RG2) and a standing subcommittee of the NTP Board of Scientific Counselors (RoC Subcommittee)-a federally chartered advisory group. Prior to

⁶ We note some confusion about the meaning of this alternative request as we are uncertain about what is meant by the phrase “pre-dissemination review of the entire record of the listing proceeding.” However, please be advised that all applicable pre-dissemination review standards will be met for dissemination of the 11th RoC.

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initiation of scientific review of the nominations, the RG1 reviewed the background document on each nomination to determine if it was adequate for use in reviewing the nomination and applying the criteria for listing in the RoC. After RG1's acceptance of the background document, it was considered the document of record for the nomination and made available on the NTP RoC web site. As the document of record, the background document did not change during the review process; however, any comments received on it were added upon receipt to the record for that nomination, which was and remains publicly available, and became part of the review package provided to the review committees.

After acceptance of the background document, the scientific review of the nomination by the three groups began. Each review group met independently and reviewed the relevant data on the carcinogenicity and the exposure of U.S. residents to the nominated substances. An integral part of the review process was the solicitation and consideration of public comments during this review process. Public comments were solicited three times. Comments received during the course of a review became part of the public record, were provided to the scientific review committees as part of the review package for consideration in evaluating each nomination, and, upon receipt, were posted on the NTP RoC web site. Note that the sequential nature of this process resulted in comments accumulating throughout the reviews. Each scientific review committee assessed whether the information was sufficient to apply the criteria for listing and made a formal recommendation to the NTP regarding whether to list or not list the nomination in the 11th RoC. The NTP published the RoC Subcommittee's recommendation on naphthalene in the Federal Register (68FR3033) and invited public comments at that time on it as well as the recommendations of RG1 and RG2.

Following completion of the scientific review, the NTP provided the review packages and the recommendations of the three scientific review committees to the NTP Executive Committee for evaluation and recommendations regarding listing the nominations in the 11th RoC. The NTP Director then received the recommendations of the three review groups and the Executive Committee along with the review packages for each nomination. The NTP Director, in turn, evaluated this information, formulated a recommendation regarding listing of each nomination, and submitted these recommendations in the form of a draft 11th RoC to the Secretary, HHS, for review and approval. The Secretary will issue the 11th RoC after reviewing and approving these recommendations.

Request for Correction of the Background Document

In the Request, you assert that the NTP's policy of relying on a finalized background document as the "document of record" for review purpose does not meet the information quality guidelines. You also claim, based on comments that you previously submitted during the nomination review process (i.e., on September 24, 2001, October 2, 2002 and March 24, 2003), that the text of the Background Document fails to satisfy the applicable information quality guidelines.

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The Background Document is a reference document that compiles and summarizes publicly available, relevant information from both positive and negative studies on a nomination. It serves as a resource that the review groups can use in applying the RoC criteria for review of the nomination and in formulating their opinion on whether to recommend listing the nomination in the RoC. As described in the Introduction of the 10th RoC, “[t]he BD [Background Document] emphasizes information concerning the carcinogenicity and related toxicological evidence for the substance nominated. The document may also include information on exposure provided by study reports and monographs.”⁷

First, with regard to your concern about the NTP’s policy decision not to revise the Background Document of record on a nomination after it is finalized, please be aware that NTP follows this policy to ensure that all review groups are provided the same background document for their review of a nomination. This policy ensures that the review groups receive the same baseline toxicology and carcinogenicity information on the nominations in order to (1) prevent confusion among the groups and the public regarding what background information is being considered in the reviews, (2) reduce the potential for error in the dissemination of information on the nominations to the review groups, (3) ensure the adequacy of the scientific literature considered by the three scientific review groups in their evaluation of the nominations, and (4) help maintain the integrity of the review process. But, additionally, to address any concerns about the document and to ensure that all comments and expressed concerns are also available, the NTP provides the review groups with submitted public comments. In this way, NTP aims to ensure that reviewers can evaluate the scientific information and reach their own conclusions regarding the comments’ validity and the adequacy of information to support a nomination. In the case of the Background Document for Naphthalene, we do not believe that this policy choice compromised the quality of the information it contained.⁸

As you are aware, the NTP has held public meetings (most recently October 1999 and January 2004) to consider public comments received on the RoC review process and listing criteria and has conducted its own internal evaluation of the process used for the review of nominations to the 10th and 11th RoCs. Based upon this input, the NTP has made some revisions to the procedures for preparing background documents and reviewing nominations for future RoCs.⁹ For example, in response to requests for earlier public accessibility of the

⁷ 10th RoC, Introduction available at <http://ehp.niehs.nih.gov/roc/toc10.html>.

⁸ We note, however, that policy choices are not subject to challenge under the information quality guidelines. In this case, you have asserted, without reference, that this policy choice, in and of itself, represents a failing. We disagree because the agency concurrently makes all comments available and it clearly explains that once the RG1 determines that the background document is adequate for reviewing the nomination, it is considered the document of record. Nomination and Review Process – 11th RoC available at <http://ntp-server.niehs.nih.gov/ntpweb/index.cfm?objectid=B2580696-F1F6-975E-726E312CCF078AAE> or from Dr. C.W. Jameson, Report on Carcinogens, NIEHS/NIH, PO Box 12233, MD EC-17, Research Triangle Park, NC 27709.

⁹ The NTP response to comments received at those meetings are posted on the NTP RoC web site at <http://ntp-server.niehs.nih.gov/ntpweb/index.cfm?objectid=720162CF-BDB7-CEBA-FC560DF109D40A44>.

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background documents, the NTP now places background documents accepted as the “documents of record” for nominations to the RoC on the NTP web site at least 30 days prior to initiation of the scientific review process for their possible listing in or removal from the RoC. Any comment received on a background document becomes part of the public record and, upon receipt, is added to the review package that is distributed to the formal review committees. So, as indicated above, the NTP makes every effort to ensure that reviewers can evaluate the scientific information and reach their own conclusions regarding the validity of any comments received and the adequacy of the information in their evaluations.

Second, with respect to the specific text of the Background Document for Naphthalene, we believe that it satisfies the applicable information quality guidelines.¹⁰ Regarding the “objectivity” criterion, the Background Document for Naphthalene is an unbiased presentation of information on peer-reviewed studies with both positive and negative findings. According to the OMB Guidelines, “[i]f the data and analytic results have been subjected to formal, independent, external peer review, the information may generally be presumed to be of acceptable objectivity.”¹¹ The Background Document only discusses carcinogenicity and toxicology information from publicly available, peer-reviewed sources. On pages 11-15 of the Request you raise specific issues with regard to study findings presented in the Background Document to Naphthalene. I will point out that the NTP will only respond to issues you raise that question the accuracy of factual information. I will not respond to other issues where you ask the NTP to formulate and assert its opinion regarding the interpretation of study findings presented in the Background Document for Naphthalene, because it would be inappropriate to do so. In background documents, the NTP declines to draw conclusions about the data described or include interpretative information and evaluation like you have requested, because, in the NTP’s view, to do so could introduce bias. Instead the NTP rests such judgment with the scientists reviewing these documents and the attendant comments submitted on them by the public.

- On page 11 of your Request you state: “[p]age 21:...the Background Document should explain in detail why the three-decades old East German reports of the health effects observed in tar distillation workers, Wolf (1976, 1978) as cited in NTP (1992) and (2000), can fairly be construed as evidence of carcinogenicity in humans...The discussion of these reports should also incorporate additional comments and correct misleading and incorrect description of the Wolf studies made by NTP in its reports on naphthalene...” The NTP believes that the descriptions of the Wolf studies (1976, 1978) in the Background Document are correct. Furthermore, the Background Document clearly states on page 21, “[t]he available evidence are insufficient for evaluation of naphthalene in humans.” The NTP does not believe that the Wolf (1976, 1978) studies provide clear evidence of carcinogenicity in humans and would refer you to the final

¹⁰ According to the OMB Guidelines, 67 Fed. Reg. at 8459, Section V., “[u]tility’ refers to the usefulness of the information to the intended users.” “Objectivity” focuses on “whether disseminated information is being presented in an accurate, clear, complete, and unbiased manner” and whether it is “accurate, reliable, and unbiased.”

¹¹ OMB Guidelines, 67 Fed. Reg. at 8459, Section V.3.b.i.

sentence of Section 3 Human Cancer Studies contained on page 21 of the Background Document that states “[t]he available data are insufficient for evaluation of the carcinogenicity of naphthalene in humans.” The other issues you raise request the NTP to draw conclusions or include interpretative information and evaluation in the Background Document on Naphthalene and it is the NTP’s policy not to do so.

- On pages 12 - 14 of your Request you state: “[p]ages vi, 27, 31, 53:...the Background Document should clarify the meaning of the terminology in referring to the “carcinogenicity of naphthalene in rats and mice in several places...The Background Document should also discuss that there is no convincing relevant evidence that naphthalene acts through mechanisms indicating it would likely cause cancer in humans....” The issues you raise request the NTP to draw conclusions or include interpretative information and evaluation in the Background Document on Naphthalene and it is the NTP’s policy not to do so.
- On page 14 of your Request you state: “[p]ages 27-30 (Section 4.2.1):...this section should not only include the discussion from the September 24, 2001, comments referenced above with regard to rat nasal tumors, but should explain in greater detail...” The issues you raise request the NTP to draw conclusions or include interpretative information and evaluation in the Background Document on Naphthalene and it is the NTP’s policy not to do so.
- On page 14, you state: “[p]ages 33-38, (Section 5): the section on genotoxicity should discuss the additional genotoxicity studies identified in the October 2, 2002, Comments at pages 10-11 and in a recent publication by Schreiner (2003), including in particular the standard *in vivo* studies that are described...Further,...naphthalene is not genotoxic.” In the Background Document on Naphthalene, the NTP describes the data that indicates, in general, naphthalene is not mutagenic in bacteria or mammalian cell systems, but was genotoxic in some, but not all, test systems and then goes on to describe the positive and negative genotoxicity data. After the Background Document is finalized and becomes the document of record, it remains unchanged throughout the review process. As explained above, the reason for this policy decision is to ensure that all reviewers and the public receive the same information without interjection of bias or opinion by NTP. However, the comments you submitted were posted on the NTP RoC web site and provided to all review groups so that they were aware of the studies you referenced.

The Background Document for Naphthalene received a full and complete review by RG1 prior to its posting on the NTP RoC web site and the NTP accepted public comments on it thereafter.

Additionally, the NTP believes that the “utility” criterion is satisfied. The Background Document for Naphthalene is useful for the reader. It is a public resource document that provides information from published, publicly available studies on naphthalene including its use, production, exposure, toxicology, and carcinogenicity, and it is available in both electronic and printed formats.

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The NIH Guidelines require the use of “[t]he best available science and supporting studies, particularly peer-reviewed studies, conducted in accordance with sound and objective scientific practices” in the Background Document.¹² As noted above, publicly available, peer-reviewed technical reports and scientific articles are the primary sources of data used to prepare a background document.

With regard to your suggestion that more current information might be available on the production, exposure, use, and environmental fate of naphthalene, my staff checked the references you provided and consulted with our federal agency partners to be sure that the information on naphthalene is up-to-date in its profile in the 11th RoC, should the Secretary approve its listing. In response to your request that the Background Document “correct any factual errors or omissions that were noted by RG1 and then subsequently by RG2,” I am not aware that any were identified; however, I am confident that if any errors or omissions had been identified by either group, they would have been addressed and corrections of any factual errors made in the background document.

Request for Correction of The RG1 and RG2 Review Summaries

Regarding the review summary reports from RG1 and RG2, you argue that they “fail to meet the requirements for objectivity.” We believe that the information provided in both review summaries is objective and has utility. It is accurate, clear, complete, and unbiased and should be useful to the reader. Members of the respective review groups, not NTP staff, prepare the review summaries that are approved by the respective review group prior to their dissemination. They provide a summary of each review group’s discussion and conclusions regarding the human and animal data for carcinogenicity, exposure, and other factors. They also include any recommended action and information regarding any dissenting votes. Contrary to what you state, the RG1 review summary provides details on the key issues that led RG1 to its recommendation on naphthalene. As stated in the RG1 review summary, “[t]he committee felt that the NTP two-year inhalation study in F344 rats provided strong evidence for the carcinogenicity of naphthalene in that species... The majority of the committee felt that naphthalene should be listed as *reasonably anticipated to be a human carcinogen*, based on the rare nasal tumors in rats, but supported by an increased incidence of lung adenoma in female mice.”¹³ Moreover, contrary to your suggestion that “[t]he RG2 summary review similarly fails to explain how each of the two groups in the split vote reached their respective recommendations,” the review summary for RG2 highlights the issues raised during the discussion and explains the rationale for each motion and the reason for dissenting votes. Therefore, we believe that the RG1 and RG2 review summaries meet the Guideline’s requirements for objectivity.

¹² NIH Guidelines at Section V.2.d. and Section VII.

¹³ *RG1 Review Summary Document for Naphthalene*, available at <http://ntp-server.niehs.nih.gov/index.cfm?objectid=03CA0BBE-9561-1E86-6438319191108C7E>.

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Request for Correction of the RG2 Proceedings and the NTP Board of Scientific Counselors RoC Subcommittee Proceedings

As a preliminary matter, please note that the OMB, HHS, and NIH Guidelines provide for *correction* of disseminated *information*. Thus, NTP does not agree that your request under the information quality guidelines for new processes, in the form of new meetings and new votes, is appropriate. For example, as we will explain below, your suggestion that the “proceedings” of the RoC Subcommittee, a standing subcommittee of a duly formed federal advisory committee, are wholly subject to the IQA guidelines is inappropriate. Neither the OMB Guidelines, nor the HHS and NIH Guidelines, specify that the guidelines’ administrative complaint processes provide a mechanism to request rescission or re-formation of duly constituted meetings of agency committees like the RG2 or RoC Subcommittee. Accordingly, in our view, the OMB, NIH, and HHS Guidelines do not warrant that the agency “rescind” the meetings and votes of, or re-convene, the RG2 and RoC Subcommittee.

While the IQA does not address proceedings or procedures of meetings and is not a mechanism to rescind a meeting or vote, I would like to clarify the procedures applicable to the RoC Subcommittee meeting, as the RoC Subcommittee is comprised of both federal and non-federal employees. The Federal Advisory Committee Act (FACA, PL 92-463), which sets forth procedures for federally chartered advisory committees, governs the RoC Subcommittee proceedings. The RoC Subcommittee is a standing subcommittee of the NTP Board of Scientific Counselors and follows the rules of FACA in its conduct. The RoC Subcommittee provides advice, its proceedings are held in public forums so that the deliberations are open, and there is opportunity for all interested parties to hear the discussions and provide comment if desired. The RoC Subcommittee members act as independent scientists and, as such, are free to raise scientific issues for consideration and discussion at their meetings. The meeting minutes provide a summary of the proceedings and actions, and they are publicly available on the NTP web site or from the executive secretary. However, these minutes are not subject to the IQA because they do not represent agency views.

Additionally, as you know from the letters sent to Ms. Price from Dr. Kenneth Olden on January 27, 2003 and March 11, 2003, the NTP has previously responded to the Panel’s concerns about the proceedings of the Subcommittee meeting. The NTP again reviewed the transcript of the November 2002 meeting and concluded that it was conducted properly. The meeting complied with FACA, and conflict of interest issues for members were reviewed prior to the meeting. In addition, it is the NTP’s practice for the chair to step down in situations where he/she wishes to participate in the evaluation of a nomination. As a member of the Subcommittee, Dr. Froines was permitted to provide comments; however, he stepped down as chair during the deliberations on naphthalene in order to prevent any prejudicial influence. As noted in the transcript, please be assured there was considerable discussion among the Subcommittee members regarding the scientific evidence on the metabolism of

Page 9 – Courtney M. Price

naphthalene and its carcinogenicity and regarding application of the RoC criteria. At that time, they had before them the comments that the Panel had previously submitted on September 24, 2001, October 2, 2002, and November 4, 2002.


Conclusion

In conclusion, we believe that the Background Document on naphthalene, the RG1 summary report, and the RG2 summary report satisfy the HHS and NIH Guidelines issued pursuant to the IQA. Furthermore, while the IQA is not a proper mechanism to request that the agency rescind the RG2 and RoC Subcommittee meetings, we reviewed the conduct of those meetings and found that they comply with all applicable requirements.

I would like to let you know that you may appeal our agency's decision either in writing or electronically within 30 days of receiving this response. Your request should state the reasons for your appeal. It does not need to reference a tracking numbers. The request may be sent electronically to InfoQuality@od.nih.gov or in hard copy to the Associate Director for Communications, Office of the Director, National Institutes of Health, Building 1, Room 344, 9000 Rockville Pike, Bethesda, Maryland 20892. If the appeal is sent in hard copy, please clearly mark the appeal and outside envelop with the phrase "Information Quality Appeal."

Sincerely,

/s/

 Christopher J. Portier, Ph.D.
Associate Director