NAIMA
NORTH AMERICAN INSULATION MANUFACTURERS ASSOCIATION

VIA OVERNIGHT MAIL AND ELECTRONIC MAIL

September 18, 2006

Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
79 Alexander Drive
Building 4401, Room 3118
P.O. Box 12233
Research Triangle Park, North Carolina 27709

RE: NAIMA's Comments on NTP's Proposed Review Process

Dear Dr. Jameson:

INTRODUCTION

The North American Insulation Manufacturers Association ("NAIMA") presents the following comments in response to the National Toxicology Program's ("NTP") request for comments on the Proposed Review Process for the 12th Report on Carcinogens ("RoC"). (*See* 71 Fed. Reg. 47507 (Aug. 17, 2006) (the "Proposed Review Process")). Because NAIMA has nominated glass wool (respirable size) for delisting in the 12th RoC, it has a natural interest in the 12th RoC process. NAIMA is the association of North American manufacturers of fiber glass, rock wool, and slag wool insulation products.

NAIMA is appreciative of the opportunity to submit these comments and NAIMA thanks NTP for its efforts to improve the RoC review process. The Proposed Review Process creates a more transparent program that allows for a more comprehensive and thorough review of background documents by engaging a wider spectrum of experts and the public.

NAIMA's comments focus on the retention of important features from the previous review process and positive changes achieved through NTP's Proposed Review Process. For certain parts of the process, NAIMA offers suggestions on how to improve the process or clarify the meaning of particular steps that may be ambiguous. These comments are designed to further increase transparency and reinforce the scientific credibility of the ultimate decision.

COMMENTS ON THE PROPOSED REVIEW PROCESS

NAIMA applauds the NTP for preserving the open process that allows nominations to originate from both public and private sectors. By inviting the public to nominate scientists to serve on an expert panel for each specific candidate substance, the NTP has significantly increased the likelihood that experts with first hand experience and genuine expertise on the toxicology of a specific substance are included in the peer review of the background document and the recommendation of listing status, thus enhancing its scientific credibility. Previously, many recognized experts with significant contributions to the peer-reviewed literature and practical

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experience may not have been engaged in the NTP process because they were not connected with one of the government agencies typically involved with the RoC or were not known within government circles. This new process lessens the probability of excluding a truly valuable and knowledgeable resource. Permitting the public nomination of experts also bolsters the confidence of the public that high quality scientific review will be afforded the complexity of a substance's toxicological profile. Moreover, the ultimate decision will be more readily accepted knowing that some of the most important experts were not excluded but instead involved and active participants in the decision making process. Properly implemented, NTP's proposed nomination of experts should lead to a well-rounded, comprehensive, and scrupulous examination of all relevant scientific data.

NTP's Proposed Review Process also invites the public to "provide oral and/or written comments on the draft background document." NAIMA endorses NTP's inclusion of the public in the review of the background documents. NAIMA notes that the background documents provide basic information on each substance such as trade names, CAS Registry numbers, physical-chemical properties,[1] and other information that typically would be in possession of the manufacturer or producer of a substance. Moreover, many manufacturers of a substance have extensive exposure data and are responsible stewards over medical and scientific studies relating to their products.[2] Providing the public an opportunity to review the background documents makes it more likely that full scientific information and data will be included in the basic document to be relied upon by the different review groups. It is critical that the background document be as accurate and complete as possible before it is relied upon by the NTP staff, the Interagency Scientific Review Group ("ISRG"), the NIEHS/NTP Staff Review Group ("NSRG"), and the Board of Scientific Counselors ("BSC"). Including the public allows those most familiar with physical and chemical properties of a substance, along with pragmatic aspects of a substance, to provide a verification of the background document's technical correctness.

NTP is to be commended for notifying the public about the availability of the background documents in such varied ways, including notification by e-mail via NTP listserv, a Federal Register notice, announcements in NTP publications and newsletters, and the NTP website.

In creating the new step in the review process of an expert panel and an expert panel meeting – a meeting in which the public may present oral or written comments and submit comments on the expert panel's report – NTP has granted the public an open and accessible process in which to participate and observe an important phase in the Review Process.

In the midst of this transparent and easily available process, NTP has determined that its own response to the expert panel's peer review report will not be made available to the public until release of the RoC.[3] This decision seems inconsistent and incongruent with a process, which up to this point, has been straightforward and direct. In order to make the entire expert panel element of the review process consistently open, NAIMA respectfully requests that the NTP make its own response to the expert panel's report available to the public as soon as that report is

[1] These elements are described in Section 1 (Introduction) of the background documents.
[2] NTP's Proposed Review Process requires that Sections 3, 4, and 5 must come from publicly available, peer-reviewed sources. Often the producer of a product has these published resources readily available.
[3] First paragraph, last sentence under the heading "Expert Panel Meeting."

available. This is true of other reports, including the Board of Scientific Counselors' peer review report and the NTP's response to that report.

NAIMA fully supports NTP's retention of a tiered review process and allowance of public participation in the open session of the Board of Scientific Counselors. However, NAIMA seeks clarification of the statement that the "BSC then holds the peer review of draft substance profiles in closed sessions." Historically, the BSC session discussing its recommendation was closed to the public in that the public could no longer comment or actively interact with the BSC, but the public was allowed to observe the deliberations of the BSC. If this arrangement continues to be the case, NAIMA suggests clarification that "closed session" means observe but not participate. If, on the other hand, the meaning of the aforementioned sentence is that the public cannot even observe the proceedings, NAIMA respectfully urges NTP to consider reinstating the opportunity for the public to observe as spectators the BSC deliberations.[4] This arrangement keeps the process transparent and adds an element of accountability to the BSC deliberations. Moreover, those parties interested in the outcome of the BSC decision would know of the decision immediately and those interested in the BSC recommendation would not have to make inquiries of NTP. NAIMA supports the peer review of draft substance profiles by the NTP BSC.

DELISTING NOT MENTIONED IN PROPOSED REVIEW PROCESS

In the Proposed Review Process, NTP states that "[n]ominations may seek to list a new substance in the RoC or reclassify the listing status for a substance already listed."[5] Substances are listed in two classes – either known or reasonably anticipated human carcinogen. Therefore, reclassification of a listing does not seem to contemplate delisting. The language used to address nominations here and throughout the Proposed Review Process dramatically departs from previous descriptions of NTP's review process which consistently contained such phrases as "NTP solicits and encourages broad participation from groups . . . interested in nominating agents, substances . . . for listing in or delisting from the RoC,"[6] and " . . . submit a nomination for listing in or delisting from the RoC."[7] In fact, NTP's description of RoC's process was previously entitled "Report on Carcinogens: Listing and Delisting Procedures."[8]

Instead, the important concept of delisting seems to be lost from the Proposed Review Process. The only mention of delisting in the Proposed Review Process is found in footnote 5, which does not provide a full discussion or acknowledgement of delisting. NAIMA respectfully requests that the NTP incorporate, as it has in the past, the concept of dual listing and delisting procedures into the Proposed Review Process.

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[4] Preserving the public's opportunity to observe BSC's review of draft substance profiles promotes the objective of and would seem to be required by the Federal Advisory Committee Act's language that "[e]ach advisory committee meeting shall be open to the public." Pub. L. 92-463, Sec. 10(a)(1), Oct. 6, 1972, 86 Stat. 774. The BSC's Subcommittee meetings have historically been held pursuant to Public Law 92-463. *See* 62 Fed. Reg. 51674-51675 (October 2, 1997).

[5] First paragraph, second sentence under the heading "Nomination and Selection of Candidate Substances."

[6] *NTP: Current Direction and Evolving Strategies* (Research Triangle Park, North Carolina: U.S. Department of Health and Human Services, 2002), p. 22.

[7] *Ibid*.

[8] http://ntp-server.niehs.nih.gov/NewHomeRoc/ListDelistProc.html (see attached).

The preservation of the delisting option is important for a variety of reasons. The possibility of changing the status of a RoC listing through delisting encourages further research and data development. This supplemental research and study can significantly inform the scientific basis of a listing or change in listing status. The availability of substance delisting acknowledges and recognizes that scientific understanding and theories evolve over time and that the basis for listing a substance may no longer be valid as medical and scientific advances are made. The presence of a delisting provision in the RoC promotes scientific credibility and realistic risk assessments by encouraging the maximum use of scientific information, which recognizes that often important new data have been published.

Provision of such a timely procedure for delisting petitions is consistent with the requirement of the Administrative Procedure Act, which requires that "each agency shall give an interested person the right to petition for the issuance, amendment, or repeal of a rule."[9] The NTP's decision to list a substance in the RoC is a "rule." Synthetic Organic Chem. Mfrs. Assn. v. Secretary, Dep't. of Health & Human Serv., 720 F. Supp. 1244, 1249 (W.D. La. 1989); see also Rayford v. Bowen, 715 F. Supp. 1347, 1352 (W.D. La. 1989) ("Criteria are rules.").

NAIMA encourages NTP to impose deadlines or a timeframe on the newly created Proposed Review Process. While the Proposed Review Process creates a more open process with an enhanced opportunity for public participation, this new process will unavoidably add more time to completing the 12th RoC, which has already been considerably prolonged. By imposing deadlines or a timeframe, it would encourage more timely review and benefit the public by providing an objective measure by which to gauge progress.

CONCLUSION

Except for the apparently inadvertent removal of delisting from the procedure and Expert Panel addition, NAIMA believes the Proposed Review Process differs from the current procedure in relatively small but, nonetheless, significant ways. NTP's proposal seems to instill a stronger element of transparency into the process that results in a "better and fairer set of rules than it would have had had it not gone through this process." Rayford v. Bowen, 715 F. Supp. 1347, 1352 (W.D. La. 1989). NAIMA asks that NTP promptly issue final review procedures reflecting the clarifications and comments outlined above.

Sincerely,

Angus E. Crane

Angus E. Crane
Vice President, General Counsel

Enclosure

[9] 5 U.S.C. § 553(e).

Report on Carcinogens
Listing and Delisting Procedures

Nominations for listing or delisting (removing) an agent, substance, mixture, or exposure circumstance in the Report on Carcinogens (RoC) should be submitted to the National Toxicology Program (NTP) [1]. Nominations must contain a rationale for listing or delisting as either a "known human carcinogen" or a "reasonably anticipated human carcinogen." Appropriate background information and relevant data (e.g., journal articles, NTP Technical Reports, IARC listings, exposure surveys, release inventories, etc.) that support the nomination should be provided or referenced when possible.

A nomination for listing or delisting in the RoC is evaluated initially by the NIEHS/NTP Review Group (RG1), composed of senior scientists from the NIEHS/NTP staff, to determine if the information provided indicates that the nomination warrants further consideration by the NTP. If it is determined that the submitted nomination does not contain sufficient information to warrant consideration, it is returned to the original nominator who is invited to resubmit the nomination with additional justification, which may include new data, exposure information, etc. The NTP Executive Committee and the NTP Board of Scientific Counselors are informed of all nominations not accepted for review for listing or delisting in the RoC.

The NTP solicits public comments on all nominations accepted for review through announcement in the Federal Register and NTP publications. The NTP initiates an independent search and review of the literature and prepares a background document for each nomination under consideration. The background documents are prepared with the assistance of a consultant or a panel of consultants who have expertise and/or knowledge for the specific nomination that is relevant to its evaluation of carcinogenicity. Background documents are prepared according to the following general format:

1. Introduction

   Information contained in this section includes chemical identification such as synonyms, trade names, CAS Registry numbers, molecular formula, molecular structure, etc. Also included are physical-chemical properties and identification of structural analogs or metabolites.

2. Human Exposure
   Information contained in this section can include use; production; analysis; environmental occurrence including environmental release, drinking water and food content and occurrence in consumer products; environmental fate in air, water, and soil; environmental and occupational exposures; biological indices of exposure; and regulations including occupational exposure limits and "other" standards and criteria.

3. Human Studies
   Information contained in this section can include traditional cancer epidemiology investigations including case control and cohort studies as well as data from clinical studies.

4. Experimental Carcinogenesis
   Information in this section can include experimental animal investigations of potential carcinogenesis including long-term bioassays, experiments where the substance is administered in conjugation with known carcinogens or factors that modify carcinogenic effects, studies to investigate a defined precancerous lesion and experiments on the carcinogenicity of known metabolites and derivatives.

5. Genotoxicity
   Information in this section can include investigations of genetic and related effects including gene mutation and chromosomal damage

6. Other Data Relevant to Evaluation of Carcinogenicity and its Mechanisms
   Information contained in this section can include metabolism, absorption, distribution and excretion of the substance, other toxic effects, and data derived from the study of tissues or cells from humans and/or experimental animals exposed to the substance in question, which can be useful for evaluating whether a relevant cancer mechanism is operating in people.

Data used in the preparation of Sections 3 through 6 of the background document must come from publicly available, peer-reviewed sources. In special cases, the review groups listed below may be asked to provide formal peer-review for a document the NTP deems to be important to the review but has otherwise not received peer-review; such a document would need to be publicly available.

FORMAL REVIEW STEPS

Nominations under consideration by the NTP for listing in or delisting from the RoC undergo a multi-step, scientific review process that includes several opportunities for public comment. The following text briefly describes that process.

NIEHS/NTP RoC Review Committee (RG1)

The RG1, composed of senior scientists from the NIEHS/NTP staff, conducts the initial review of a nomination for listing in or delisting from the RoC and in that review, considers all public comments received in response to the announcement of the nomination. The RG1 first reviews the background document prepared for the nomination and determines if it is adequate for use in reviewing the nomination and for applying the criteria for listing in the RoC. Upon acceptance of the background document, it is then considered the final document of record. The RG1 then proceeds with scientific review of the nomination and makes a recommendation for listing or delisting in the RoC. After the background document becomes the final document of record, it is placed on the NTP RoC web site with a notice published on the NTP list-server and the NTP web site announcing its availability.

It is possible that the RG1 review of the background document for a nomination may determine that there is insufficient relevant information to apply the criteria for listing in or delisting from the RoC. In this situation, the review of the nomination stops and the NTP will inform subsequent RoC review groups and the NTP Executive Committee of this action and why further review is not warranted. The original nominator is notified of the RG1 action and is invited to resubmit the nomination with additional relevant information and justification. All nominations not reviewed beyond RG1, because of the lack of sufficient relevant information, are included in the subsequent edition of the RoC with the reason(s) why they were not considered further

NTP Executive Committee's Interagency Working Group for the RoC (RG2)

The RG2, a governmental interagency scientific review group, conducts the second review of nominations to the RoC. The RG2 assesses whether relevant information for a nomination is available and sufficient for listing in or delisting from the RoC. The RG2 reviews the original nomination and all public comments received in response to announcements of nominations accepted for review. Upon completion of its review, the RG2 provides comments and makes its recommendations for listing or delisting the nominations in the RoC.

Board of Scientific Counselors RoC Subcommittee (External Peer Review)

The third step in the review process is external scientific peer review of the nominations by a standing subcommittee of the NTP Board of Scientific Counselors ("the RoC Subcommittee"). The RoC Subcommittee serves as an independent peer review group that assesses whether the relevant information available for a nomination is sufficient for listing or delisting it in the RoC. The RoC Subcommittee reviews nominations in an open public meeting. Prior to this public review, a notice is published in the Federal Register and NTP publications announcing the meeting and the availability of the background documents and soliciting public comment on the nominations. The notice invites interested groups or individuals to submit written comments and/or address the RoC Subcommittee during the public review meeting. Upon completion of its review, the RoC Subcommittee provides comments and makes

its recommendations for listing or delisting the nominations in the RoC.

Final Public Comment

Upon completion of the reviews by RG1, RG2 and the RoC Subcommittee, the NTP publishes the nominations and the review groups' recommendations for each (to list, to delist, or not to list in the RoC), and solicits the third and final public comment and input on the nominations.

NTP Executive Committee

The recommendations of RG1, RG2 and the RoC Subcommittee and all public comments received to date are presented to the NTP Executive Committee[2] 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.

NTP Director

The NTP Director receives the independent recommendations for the nominations from RG1, RG2 and the NTP Board RoC Subcommittee, the opinion of the NTP Executive Committee and all public comments received concerning the nominations. The NTP Director evaluates this input and any other relevant information on the nominations and develops recommendations to the Secretary, Department of Health and Human Services (DHHS) regarding whether to list, delist, or not list the nominations in the RoC.

Secretary, Department of Health and Human Services (DHHS)

The NTP prepares a final draft of the RoC based on the NTP Director's recommendations and submits it to the Secretary, DHHS for review and approval. Upon approval of the RoC, the Secretary submits it to 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 a notice of the publication and availability of the latest edition of the RoC, indicating all newly listed or delisted agents, substances, mixtures or exposure circumstances in the Federal Register and NTP publications.

[1] National Toxicology Program, Report on Carcinogens
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[2] Agencies represented on the NTP Executive Committee include:
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)

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