Penthouse Level
Suntec Tower 3
8 Temasek Blvd
Singapore 038988
Tel: +65 6866 3238

Methanol Institute

124 West Street South
Suite 203
Alexandria, VA 22314
Tel: 703.248.3636

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Information Quality Guidelines Staff (Mail Code 2811R)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Re: Methanol Institute Request for Correction: The Ramazzini Institute's Methanol Study

Dear Sir or Madam:

This Request for Correction of Information (RFC) is being submitted on behalf of the Methanol Institute, pursuant to Section 515(a) of the Treasury and General Government Appropriations Act for Fiscal Year 2001 (the Information Quality Act or IQA),[1] and the guidelines implementing the IQA issued by the United States Office of Management and Budget (OMB)[2] and the United States Environmental Protection Agency (EPA).[3] As discussed below, the Methanol Institute believes that the recent review of certain tissue slides by the National Toxicology Program from research conducted by the Ramazzini Institute in 1990-1992 and published in 2002 ("Ramazzini study") demonstrate that the study is highly flawed, and therefore all documents and assessments related to this study should be removed from both EPA's website[4] and the Integrated Risk Information System (IRIS) database because they do not reflect this significant new information and instead rely heavily on the Ramazzini study to support their conclusions. Further, on June 15th the Agency announced in a press release that it was placing on hold further work regarding the draft methanol IRIS assessment (and three other ongoing assessments) as the Agency "will determine whether the questions raised by NTP will require EPA to revise the assessments or take additional action to verify the data used in these

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[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 (notes).

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

[3] EPA, Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency, EPA/260R-02-008 (Oct. __, 2002) *available at* http://www.epa.gov/quality/informationguidelines/documents/EPA_InfoQualityGuidelines.pdf (EPA Guidelines).

[4] Including all relevant documents posted on www.regualtions.gov, EPA docket, EPA-HQ-ORD-2009-0398.

assessments." Given the new data review by the NTP and the EPA's acknowledgement that the data from the Ramazzini Institute requires additional verification, the Agency has an obligation under the IQA to take the action we have requested here.

Background

In January 2010, EPA released a draft toxicological assessment of methanol under IRIS that proposed to classify methanol as a "likely human carcinogen." This assessment was largely based on data derived from a methanol study produced by the Ramazzini Institute in Italy. However, a team of pathologists from the National Toxicology Program (NTP) recently completed a partial review of this study, and found significant discrepancies in the interpretation of the reported results and concluded that an independent pathology review and quality review of the pathology data and specimens were necessary to determine the accuracy of the study's overall conclusions.[5] As a result of NTP's review, on June 15, 2010, EPA announced that it would place a hold on further action for its IRIS assessment of methanol pending a full review of the Ramazzini Institute's methanol study.

The Methanol Institute applauds this quick and appropriate reaction by EPA to the NTP report, but requests that EPA take further action to prevent misinformation from being further disseminated by EPA. As discussed below, EPA must remove the draft methanol toxicological assessment and all other documents and assessments related to the Ramazzini study from both its website and the IRIS database in order to fully address the weaknesses in the study identified by the National Toxicology Program's Report and the potential deleterious effects of further disseminating flawed information. Failure to remove the assessment will compromise the objectives outlined in the EPA and OMB Guidelines of objectivity and utility. The remainder of this letter explains how the draft methanol assessment fails to meet the EPA data quality guidelines, delineates the problems associated with the underlying Ramazzini study, and sets forth corrective action requested of EPA.

Methanol Institute: An Affected Stakeholder

The Methanol Institute is the trade association for the global methanol industry. Founded in 1989 to provide information to the U.S. Congress and others in support of methanol fuel markets, the Methanol Institute's membership includes the world's leading methanol producers, technology companies, distributors, terminal operators and shippers. On behalf of its members, the Methanol Institute provides accurate and reliable technical information to its membership and regulatory authorities, and participates proactively in all scientific, regulatory, and public policy debates that affect the industry. Accordingly, the Methanol Institute participated in the recent review of EPA's draft methanol assessment by providing public comments.

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[5] U.S. Department of Health and Human Services National Toxicology Program, Memo to John R. Bucher Re. Report on visit (4/25/2010 - 4/30/2010) and assessment of the pathology procedures performed at the Ramazzini Institute (RI), Bentivoglio, Italy (June 11, 2010).

The accuracy of the information presented by EPA, particularly as it incorporates the Ramazzini study, reflects upon the scientific integrity of EPA's potential actions regarding methanol. EPA actions, such as the proposed IRIS classification of methanol as a "likely human carcinogen, can greatly influence the methanol market. The Methanol Institute and its members are thus parties highly affected by EPA's continued dissemination of the Ramazzini study's defective information.

EPA's Guidelines: The "Objectivity" and "Utility" Criteria

EPA issued its Guidelines to ensure and maximize the quality of all disseminated information, particularly with respect to the information's objectivity, utility, and integrity. A review of these guidelines makes clear that the defects in the Ramazzini study identified by the National Toxicology Program implicate EPA's criteria for objectivity and utility of disseminated information as well as its heightened standard for influential scientific information.

The EPA Guidelines "contain EPA's policy and procedural guidance for ensuring and maximizing the quality of information we disseminate" as well as specifically describing "new mechanisms to enable affected persons to seek and obtain corrections from EPA regarding disseminated information that they believe does not comply with EPA or OMB guidelines."[6] The Guidelines provide a pathway for the correction of any information disseminated by EPA that falls short of the "basic standard of quality, including objectivity, utility, and integrity,"[7] as enunciated in EPA's and OMB's Guidelines.

Like OMB, EPA defines objective information as being "presented in an accurate, clear, complete, and unbiased manner, and as a matter of substance, is accurate, reliable, and unbiased."[8] The "utility" criterion relates to "the usefulness of the information to the intended users."[9]

The EPA Guidelines adopted the quality principles in the Safe Drinking Water Act Amendments (SDWA) of 1996.[10] In the dissemination of influential scientific information regarding human health, safety, or environmental risk assessments, EPA promised to ensure the objectivity of such information disseminated by the Agency by applying the following adaptation of the quality principles found in the SDWA:

> (A) The substance of the information is accurate, reliable and unbiased. This involves the use of: (i) the best available science and supporting studies conducted in accordance with sound and objective scientific practices, including, when available, peer reviewed science and supporting studies; and (ii) data

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[6] EPA Guidelines at 3.
[7] *Id.*
[8] *Id.* at 15; OMB Guidelines § V.3, 67 Fed. Reg. at 8459.
[9] EPA Guidelines at 15; OMB Guidelines § V.2, 67 Fed. Reg. at 8459.
[10] Safe Drinking Water Act Amendments of 1996, 42 U.S.C. 300g-1(b)(3)(A) & (B)

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).

(B) The presentation of information on human health, safety, or environmental risks, consistent with the purpose of the information, is comprehensive, informative, and understandable.

EPA also acknowledges that the "influential scientific, financial, or statistical information" it disseminates "should meet a higher standard of quality."[11] Under the Guidelines, information is considered influential if "the Agency can reasonably determine that dissemination of the information will have or does have a clear and substantial impact (*i.e.*, potential change or effect) on important public policies or private sector decisions."[12] Such "influential scientific information" is subject to "a higher degree of quality (for example, transparency about data and methods)."[13] EPA has indicated that all IRIS toxicological reviews are considered "influential scientific information."

Further Disseminating the Ramazzini Report Violates EPA's Guidelines

Given the potential for the scientific information in the draft methanol toxicological review to shape EPA policy, this information unquestionably qualifies as "influential scientific information" subject to "a higher degree of quality." As outlined by the NTP report, the Ramazzini study does not meet that higher standard and because it relies so heavily on this study, the draft methanol toxicological review does not meet that higher standard as well.

The study does not comport with the "objectivity" criterion requirements of the SDWA quality principles. NTP's report recommends that an independent pathology review and quality review of the pathology data and specimens be carried out to resolve the diagnoses of certain cancers reported in the study. Considering that the NTP's review of the Ramazzini study particularly calls into question transparency about data and methods, further dissemination of the draft methanol toxicological review that relies heavily on the Ramazzini methanol study by continuing to post the assessment on EPA's website and otherwise would violate EPA's Guidelines. This decision to stop the dissemination of the methanol assessment does not require EPA to determine what the true findings of the Ramazzini study are through a full PWG or other method. This removal is simply a natural and proper consequence of EPA's previous decision to place the methanol assessment that relies so heavily on the Ramazzini study on hold based on the Report of the National Toxicology Program.

To disseminate the draft IRIS toxicological assessment based upon the Ramazzini study's pervasive deficiencies and flaws would also violate the "utility" guideline. The data on which the assessment is based fall far short of embodying "the best available science and supporting

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[11] EPA Guidelines at 19.
[12] *Id.*
[13] *Id.* at 20. *See also* OMB Guidelines §§ V.3(b)(ii) and V.9, 67 Fed. Reg. at 8460.

studies conducted in accordance with sound and objective scientific practices" and the other components of "objectivity." The further dissemination of such a flawed data is inappropriate and would be highly problematic for those that rely on the information. The assessment and all other documents and assessments related to this study should be removed from EPA websites, the regulations.gov website, and the IRIS database in order to avoid misleading the public. At a minimum, this includes:

- IRIS Toxicological Review of Methanol, December 2009
- NCEA's Proposed Charge to External Reviewers for the IRIS Toxicological Review of Methanol, December 2009
- PBPK code and supporting files

Moreover, the NTP report clearly establishes that the burden of proof has been shifted to any agency that wishes to rely in whole or in part on the Ramazzini study to support regulatory action. Unless and until the independent pathology and data quality reviews recommended by the NTP are completed and the accurate diagnoses of certain cancers are resolved, this study will not meet EPA's own Guidelines for influential scientific information and can not be used for any purpose by the Agency.

If EPA intends to rely upon these data, it must ensure that all data confirmations and pathology reviews are public and peer reviewed. As noted by the NTP, "Discrepancies between a study pathologist and a reviewing pathologist are typically resolved through use of a formal pathology peer review to verify the accuracy of the pathology data. It is recommended that the RI carry out an equivalent process to address the discrepancies identified in the methyl alcohol study."[14] In light of the "influential" nature of this information, informal communications between EPA staff and representatives from the Ramazzini Institute are not an appropriate method of validation for data used in IRIS toxicological review determinations. EPA should follow NTP's recommendations regarding data verification before further relying on the Ramazzini study. The EPA also must address the concerns raised by the NTP reviewers with regards to the study protocols used by the Ramazzini Institute in allowing animals to die spontaneously rather than terminating study animals after two years as is practiced in all other laboratories. The NTP pathologists noted that "significant autolysis of some tissues" precluded any histological diagnosis. Further, the NTP reviewers noted that the presence of inflammatory lesions in several tissues was consistent with chronic respiratory infection. The Ramazzini Institute has repeatedly denied that their rat colony suffers from such a chronic infection, while outside authoritative bodies and experts have cited this issue as a significant flaw in research by the Ramazzini Institute. The EPA must address this issue as well before using any data from the Ramazzini Institute for toxicological reviews.

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[14] NTP Memo at 5.

Conclusion: Removing the Ramazzini Study Is Essential

EPA's draft toxicological review of methanol, and all other documents and assessments related to the methanol study conducted by the Ramazzini Institute, should be removed from the IRIS database and other EPA public dissemination sources[15] immediately. Unless and until a full and independent pathology review and a quality review of the pathology data and specimens has been conducted to determine the true findings of the Ramazzini Institute's methanol study, the National Toxicology Program's Report demonstrates that EPA cannot rely on the reported findings of this study as data that meet EPA's Guidelines for influential scientific information for any purpose. Because EPA's draft toxicological review of methanol relies so heavily upon the Ramazzini Institute's methanol study, EPA cannot continue to distribute it to the public through its website or otherwise without violating the IQA. The continued dissemination of these defective data contravenes the standards of objectivity and utility outlined in both the OMB and EPA Guidelines, and poses continued harm to the Methanol Industry and its members.

The Methanol Institute respectfully requests that this request for correction be granted and the corrections implemented accordingly. We ask that this be done quickly so as to remove the risk of immediate harm to the public and the methanol industry. This action does not prejudge EPA's decisions regarding the Ramazzini study of methanol at the end of EPA's own review process, but assures that in the meantime the public is not misinformed about methanol and the basis for determining whether or not it has potential health effects.

Sincerely,

Gregory Dolan
Executive Director – Americas/Europe

[15] Including all relevant documents posted on www.regualtions.gov, EPA docket, EPA-HQ-ORD-2009-0398.