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February 18, 2020

Andrew Wheeler, Administrator
U.S. Environmental Protection Agency
EPA Docket Center, Mail Code 28221T
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Attention: Docket ID No. EPA–HQ–OAR–2018–0746

Re: *National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review (Proposed Rule)*

Dear Administrator Wheeler:

The Northeast States for Coordinated Air Use Management (NESCAUM) offer the following comments on the proposed "National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review" [84 Fed. Reg. 69182-69269 (December 17, 2019)] (hereinafter the "MON RTR" proposal).

NESCAUM is the regional association of air pollution control agencies representing Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Rhode Island, and Vermont. Our member agencies have the primary responsibility in their states for implementing clean air programs that achieve the public health and environmental protection goals of the federal Clean Air Act.

The MON RTR risk analysis determined that emissions from MON sources that have implemented NESHAP requirements pose a maximum individual cancer risk of 2,000 in one-million, and that 18,000 people are subject to a cancer risk greater than 100 in one-million as a result of those emissions. Because those risks are predominantly associated with emissions of ethylene oxide (EtO), the MON RTR proposes additional measures to control EtO emissions and calculates that implementation of those measures would reduce the cancer risk associated with MON sources to 200-300 in one-million.

NESCAUM strongly supports EPA's determination that additional controls are needed to reduce MON EtO emissions. However, EPA's justification in the proposed MON RTR of a residual risk that would continue to exceed 100 in one-million after the implementation of such controls is inappropriate. Note that EPA has generally considered a risk level of 100 in one-million to be the upper end of the range of acceptable risks and that many states have set acceptable impact levels that are based on more stringent risk criteria.

The EtO cancer risks in the proposed MON RTR were calculated using the cancer inhalation unit risk estimate (URE) for EtO in EPA's Integrated Risk Information System (IRIS), which was last updated in December 2016. The proposal also discusses, and asks for comments on, the possible use of an "alternative" URE for EtO. NESCAUM strongly supports the continued use of the IRIS URE value and is concerned by EPA's consideration of alternative values as part of a regulatory action. Of particular concern is the discussion in the proposal of a considerably less stringent risk value for EtO proposed by the Texas Commission on Environmental Quality (TCEQ) in June 2019 as a possible alternative value.

In addition, the evaluation of the acute health impact of EtO emissions in the MON RTR utilizes the Acute Exposure Guideline Level (AEGL) for that substance. As acknowledged in the MON RTR proposal, AEGLs are emergency planning benchmarks designed to address once-in-a-lifetime, short-term exposures [84 Fed. Reg. 69192]. Use of such values to evaluate acute health impacts associated with potential repeated short-term exposures associated with routine emissions is not appropriate. In particular, we present data below to demonstrate that the EtO AEGL used in the MON RTR does not protect against acute public health impacts.

A more detailed discussion of NESCAUM's concerns follows. The comments address the following issues:

1. Reconsideration of the highly reviewed, recently finalized IRIS URE for EtO in the context of a residual risk analysis is highly unusual and highly inappropriate.
2. NESCAUM strongly supports EPA's proposed requirement that MON sources implement additional measures to reduce EtO emissions. However, EPA's justification of the adequacy of control requirements that do not reduce cancer risks to below 100 in one-million is inappropriate.
3. The deeply flawed EtO cancer risk level proposed by the TCEQ, which has not been peer reviewed and is no longer available for public comment, should not be considered as an alternative to the IRIS URE for use in this or future risk analyses.
4. Acute Exposure Guidelines (AEGLs) and emergency response planning guidelines (ERPGs), which are designed to protect for once-in-a-lifetime exposures, are inappropriate for use in evaluations of short-term risks associated with exposures to routine emissions. In particular, the EtO AEGL, which was used in the MON RTR, is not adequately stringent to protect the public from acute health effects.

1. Reconsideration of the highly reviewed, recently finalized IRIS URE for EtO in the context of a residual risk analysis is highly unusual and highly inappropriate.

EPA's solicitation of additional comments on the IRIS ethylene oxide URE in a residual risk analysis is highly unusual and inappropriate. As acknowledged in the MON RTR, EPA risk assessments preferentially use IRIS toxicity values, including UREs, when they are available.

EPA's reliance on IRIS values was established in EPA's 1999 "Residual Risk Report to Congress," which stated the following:

> Regardless of the endpoint of interest (acute, chronic non-cancer, or cancer effects), consensus toxicity criteria are preferred for conducting risk assessments. For chronic non-cancer and cancer criteria, the preferred source of data is EPA's IRIS. This data base provides toxicity criteria that have undergone internal peer review, and, for recent assessments, external peer review, and have been approved Agency-wide. The toxicological basis for the criterion is provided, as well as other supporting data and information regarding the uncertainty in the assessment.[1]

The EPA has used toxicity values from other authoritative bodies when an IRIS value was not available and, in those instances, has solicited comments on the appropriateness of those values. However, it is highly unusual and inappropriate to request comments on IRIS toxicity values, particularly a cancer URE that was updated as recently as December 2016, in a rulemaking action. Over an 18-year period, at least four drafts of the IRIS EtO cancer evaluation were reviewed by a wide range of "EPA scientists, interagency reviewers from other federal agencies and the Executive Office of the President, the public, and independent scientists external to the EPA."[2] EPA has presented no evidence of the availability of new information that would merit a reconsideration of this carefully vetted derivation. If such information is available, it should be submitted to IRIS for consideration and peer review.

2. NESCAUM strongly supports EPA's proposed requirement that MON sources implement additional measures to reduce EtO emissions. However, EPA's justification of the adequacy of control requirements that do not reduce cancer risks to below 100 in one-million is inappropriate.

In the RTR, EPA proposes additional control measures to reduce emissions of EtO from MON facilities. NESCAUM strongly supports EPA's requirement of additional controls to reduce EtO emissions, which would considerably reduce the risk associated with those MON sources. However, the RTR calculates that residual cancer risks, after the implementation of the additional controls, would continue to be as high as at 200-300 in one-million at some facilities. Note that the Agency considers a risk of 100 in one-million to be the upper end of the acceptable risk range and that many states have adopted acceptable impact levels based on more stringent risk criteria.

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[1] U.S. EPA, Residual Risk Report to Congress, pp. 56-57, March 1999, EPA-453/R-99-001. https://www.epa.gov/sites/production/files/2013-08/documents/risk_rep.pdf

[2] U.S. EPA, Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide (CASRN 75–21–8) in Support of Summary Information on the Integrated Risk Information System (IRIS), p. XV, December 2016. EPA/635/R–16/350Fa. https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/1025tr.pdf

The RTR justifies the acceptability of the residual impacts as follows:

> Although the post-control risks are greater than 100-in-1 million (*i.e.,* 200 to 300-in-1 million), due to the inherent health protective nature of our risk assessment methods and the uncertainties in this assessment, we believe that this risk assessment is more likely to overestimate rather than underestimate the risks. [84 Fed. Reg. 69217]

> In particular, the MON RTR states that "two aspects of uncertainty stand out as potentially contributing to the conservative (*i.e.,* health protective) nature of the final 2016 URE." Those aspects, which are discussed in more detail in a October 2019 sensitivity analysis of the URE referenced in the RTR and included in the docket for this rulemaking[3], are: (1) using a central estimate of risk rather than the upper bound confidence level used in the derivation would reduce the EtO URE by 3 times and (2) the choice of an alternative dose-response model for calculating the risk of lymphoid cancer could reduce the URE by a factor of 2-3. The RTR states that "the central estimate and an alternative dose-response model combined could result in a URE 5 times lower. This would reduce potential post-control risks to 60- to 100-in-1 million (from 200- to 300-in-1 million)." [84 Fed. Reg. 69218]

While NESCAUM acknowledges that risk assessment is not an exact science, we are concerned about EPA's reinterpretation of risk assessment values to support policy decisions. The use of conservative assumptions in cancer assessments is necessary and appropriate, due to the severity of the health impacts of that disease. Conservatism is particularly important for known human carcinogens, like EtO. Note that EPA's December 2016 final report on the derivation of the IRIS URE states that, "overall, confidence in the hazard characterization of EtO as 'carcinogenic to humans' is high." The report goes on to discuss uncertainties in the quantitative cancer URE, but states that "While there is less confidence in the lymphoid cancer unit risk estimate than in the breast cancer unit risk estimate, the lymphoid cancer estimate is considered a reasonable estimate from the available data, and overall, there is relatively high confidence in the total cancer unit risk estimate."[4]

Further, EPA's October 2019 sensitivity analysis of the EtO URE, discussed above, cautions the following:

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[3] U.S. EPA, Memorandum from Paul White, Senior Advisor, Chemical & Pollutant Assessment Division (CPAD) to Kristina A. Thayer, Director of CPAD, entitled "Sensitivity of ethylene oxide risk estimates to dose-response model selection," October 18, 2019. https://www.regulations.gov/document?D=EPA-HQ-OAR-2018-0746-0027

[4] U.S. EPA, Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide (CASRN 75–21–8) in Support of Summary Information on the Integrated Risk Information System (IRIS), pp. 1-2 – 1-5, December 2016. EPA/635/R–16/350Fa. https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/1025tr.pdf

> Note, however, the IRIS unit risk, should not be considered a worst-case analysis. Higher estimates of risk were obtained using some other models providing statistically appropriate fits to the data. While there were limitations with these models, and we have not used them in this analysis, it is likely that a comprehensive analysis of alternative models (for example considering other spline models with knots somewhat lower than the selected values) would likely include some risk estimates higher than the IRIS unit risk.[5]

The IRIS URE for EtO was developed after careful consideration of all available models and was subject to extensive internal and external scientific review. It is inappropriate for EPA to alter the URE to rationalize a *post hoc* policy decision for allowing impacts that exceed cancer risk levels generally considered acceptable by the Agency.

Note also that a recent epidemiologic assessment by the Illinois Department of Public Health (DPH) found elevated cancers in the population surrounding the Sterigenics facility in Willowbrook, Illinois.[6] The elevated cancers were Hodgkin's lymphoma in females, female breast cancer, pediatric lymphoma in females, prostate cancer, and female pancreatic, ovarian and bladder cancers. This epidemiological investigation by Illinois DPH demonstrates tumor concordance with occupational studies. The findings of pediatric lymphoma in females in this community provide strong justification to minimize the emission of EtO from this source category to the lowest achievable emission rates possible.

3. The deeply flawed EtO cancer risk level proposed by the TCEQ, which has not been peer reviewed and is no longer open for public comment, should not be considered as an alternative to the IRIS URE for use in this or future risk analyses.

NESCAUM is even more concerned about the MON RTR's discussion of a draft TCEQ document entitled "Ethylene Oxide Carcinogenic Dose-Response Assessment." According to the RTR, that document concluded that "USEPA's ethylene oxide inhalation URF [unit risk factor] is not adequately supported by scientific data" and proposed an alternative unit risk that is 3600 times less stringent than the EPA IRIS value. Note that the terms URF and URE are essentially equivalent [84 Fed. Reg. 69218].

The RTR states that "TCEQ's concerns with the EPA's URE derivation have not been peer reviewed and the public comment period closed on September 26, 2019." Note that, at the time that the proposed TCEQ document was available for public comment, that analysis did not impact jurisdictions outside of Texas. However, EPA's citation of the TCEQ risk value as a potential alternative to the IRIS URE in the MON RTR has elevated the TCEQ proposal to

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[5] U.S. EPA, Memorandum from Paul White, Senior Advisor, Chemical & Pollutant Assessment Division (CPAD) to Kristina A. Thayer, Director of CPAD, entitled "Sensitivity of ethylene oxide risk estimates to dose-response model selection," p. 6, October 18, 2019. https://www.regulations.gov/document?D=EPA-HQ-OAR-2018-0746-0027

[6] Illinois Department of Public Health. 2019. "Cancer Incidence Assessment near Sterigenics in Willowbrook, IL, 1995-2015," Division of Epidemiological Studies, March 29, 2019.

national significance and, since the TCEQ public comment period has closed, national stakeholders do not have the opportunity to comment on that TCEQ evaluation.

NESCAUM has determined, based on information obtained from the TCEQ's website, https://www.tceq.texas.gov/toxicology/ethylene-oxide, that the TCEQ's URE derivation differed from the EPA's IRIS derivation in two major areas: (1) the dose-response models used and (2) EPA's derivation was based on both lymphoid cancer incidence in males and females and breast cancer incidence in females, while the TCEQ's URE was based on lymphoid cancer mortality in males.

The TCEQ derivation dismisses models that would associate a greater than *de minimis* cancer risk level with endogenous levels of EtO in the body. NESCAUM strongly disputes this position. Carcinogenic effects are dependent on a variety of factors, including the intake route and transport of the carcinogen to target organs. The presence of endogenous EtO levels in certain body compartments is irrelevant to the evaluation of the impacts of inhaled EtO.

The issues considered in the TCEQ analysis, including the selection of a dose-response model, were carefully evaluated and documented in the development and review of the IRIS value. As discussed above, the IRIS value has been subject to an extremely extensive vetting process and EPA should not consider the flawed TCEQ derivation, which has not been peer reviewed, as a valid alternative to that value.

4. Acute Exposure Guidelines (AEGLs) and emergency response planning guidelines (ERPGs), which are designed to protect for once-in-a-lifetime exposures, are inappropriate for use in evaluations of short-term risks associated with exposures to routine emissions. In particular, the EtO AEGL, which was used in the MON RTR, is not adequately stringent to protect the public from acute health effects.

AEGLs and ERPGs are developed for accidental release emergency planning and are not appropriate for assessing the repeated short-term human exposures associated with routine emissions. Quoting from the National Academy of Sciences' "Standing Operating Procedures for Developing Acute Exposure Levels for Hazardous Chemicals,"[7] the MON RTR states that:

> AEGLs represent threshold exposure limits for the general public and are applicable to emergency exposures ranging from 10 minutes to 8 hours. They are guideline levels for "once-in-a-lifetime, short-term exposures to airborne concentrations of acutely toxic, high-priority chemicals." [84 Fed. Reg. 69192]

[7] National Academy of Sciences. 2001. "Standing Operating Procedures for Developing Acute Exposure Levels for Hazardous Chemicals," p. 2. https://www.epa.gov/sites/production/files/2015-09/documents/sop_final_standing_operating_procedures_2001.pdf

The use of the AEGL to assess the potential acute risk from EtO exposure in the MON RTR is extremely misleading and is not protective of public health. EPA's residual risk assessment, which was prepared for this rulemaking, states that "Irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape"[8] could occur at the EtO AEGL-2 level used in that analysis.

EPA has acknowledged that there is ample evidence that even a short or a single exposure to EtO may be sufficient to produce adverse reproductive and developmental effects.[9,10] Pharmacodynamic studies in humans and animals indicate that inhaled EtO is rapidly absorbed by the lungs and immediately distributed throughout the body. In animals, the distributed EtO binds to the proteins and DNA of numerous cells, including germ cells. EtO can induce dominant lethal effects in mammals, causing the failure of embryos to develop. Exposure to EtO has been associated with spontaneous abortions and pregnancy loss among hospital staff engaged in sterilization, and chromosomal aberrations in sterilizer workers.[11,12,13,14]

In consideration of the above studies, including those that link short-term, repeated high exposures to EtO to serious adverse reproductive effects in women of childbearing age, EPA should repeat the MON RTR acute health risk analysis using the most restrictive, well-documented, short-term health EtO benchmark available. Note that the Agency for Toxics Substances and Disease Registry (ATSDR) has developed an intermediate Minimal Risk Level (MRL) for EtO of 162 µg/m^3.[15] The AGEL value used to evaluate acute risk in the MON RTR (81 mg/m^3) is 500 times higher than the ATSDR MRL and 9 times higher than the National Institute of Occupational Safety and Health and California Division of Occupational Safety and Health 15-minute occupational ceiling values (9 mg/m^3).

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[8] U.S. EPA. 2019. "Residual Risk Assessment for the Miscellaneous Organic Chemical Manufacturing Source Category in Support of the 2019 Risk and Technology Review Proposed Rule," U.S. EPA Office of Air Quality Planning and Standards, Office of Air and Radiation, June 2019.

[9] U.S. EPA. 1996. "Guidelines for Reproductive Toxicity Risk Assessment," Federal Register 61(212):56274-56322.

[10] Dellarco, VL, Farland, WH, and O'Neill, JP. Introduction to the U.S. Environmental Protection Agency's genetic risk assessment on ethylene oxide. Environmental and Molecular Mutagenesis, 16(2): 83-4.

[11] Hemminki K, P Kyyronen, and ML Lindbohm. 1985. Spontaneous abortions and malformations in the offspring of nurses exposed to anaesthetic gases, cytostatic drugs, and other potential hazards in hospitals, based on registered information of outcome. Journal of Epidemiology and Community Health, 39: 141-147.

[12] Hemminki K, P Mutanen, I Saloniemi, *et al.* 1983. Spontaneous abortions in hospital staff engaged in sterilising instruments with chemical agents. British Medical Journal, 285: 1461-1463.

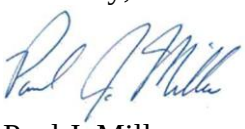
[13] Gresie-Brusin FD. 2005. Occupational exposure to ethylene oxide in women sterilising staff working in Gauteng Province, South Africa: Exposure Assessment and Association with adverse reproductive outcome. A thesis submitted to the faculty of health sciences, University of Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Doctor of Philosophy (Medicine). Accessed on-line: http://wiredspace.wits.ac.za/bitstream/handle/10539/1616/PhD%20Thesis.pdf?sequence=1

[14] Gresie-Brusin D, Kielkowski D, Baker A, Channa K and Rees D. 2007. Occupational exposure to ethylene oxide during pregnancy and association with adverse reproductive outcomes. International Archives of Occupational and Environmental Health, 80: 559-565.

[15] Agency for Toxic Substances and Disease Registry. 1990. "Toxicological Profile for Ethylene Oxide." https://www.atsdr.cdc.gov/toxprofiles/TP.asp?id=734&tid=133

NESCAUM strongly recommends that EPA continue to use the IRIS URE for EtO to evaluate cancer risk in the MON RTR and in subsequent risk analyses. If scientific data concerning EtO toxicity become available that were not considered in the IRIS deliberative process, that evidence should be presented to IRIS for evaluation and peer review and should not be part of EPA rulemaking actions. The URE should not be altered *post hoc* to rationalize policy decisions, including the evaluation of the adequacy of proposed additional control requirements in the MON RTR. Further, the MON RTR's use of emergency planning values to evaluate acute health effects associated with routine exposures is inappropriate, and the acute effects evaluation in the MON RTR should be repeated using a more appropriate short-term health benchmark.

Sincerely,



Paul J. Miller
Executive Director

cc: NESCAUM Directors
NESCAUM Air Toxics and Public Health Committee
Lynne Hamjian, Cynthia Greene, Bob Judge, EPA R1
Rick Ruvo, EPA R2