

Appendix A

EPA has excluded or dismissed a number of key studies, reviews, responses, and presentations, with a majority having been presented in correspondence and presentations by the ACC Formaldehyde Panel to the Agency since 2011.

Important studies, reviews, or responses in peer-reviewed publications which are not referenced in the external review draft for EPA's toxicological review (789 pp) or supplemental information (1058 pp):¹

Albertini, R.J. and Kaden, D.A., 2017. Do chromosome changes in blood cells implicate formaldehyde as a leukemogen?. *Critical Reviews in Toxicology*, 47(2), pp.145-184.

Albertini, R.J. and Kaden, D.A., 2020. Mutagenicity monitoring in humans: global versus specific origin of mutations. *Mutation Research/Reviews in Mutation Research*, 786, p.108341.

Allegra, A., Spatari, G., Mattioli, S., Curti, S., Innao, V., Ettari, R., Allegra, A.G., Giorgianni, C., Gangemi, S. and Musolino, C., 2019. Formaldehyde exposure and acute myeloid leukemia: a review of the literature. *Medicina*, 55(10), p.638.

Andersen, M.E., Gentry, P.R., Swenberg, J.A., Mundt, K.A., White, K.W., Thompson, C., Bus, J., Sherman, J.H., Greim, H., Bolt, H. and Marsh, G.M., 2019. Considerations for refining the risk assessment process for formaldehyde: Results from an interdisciplinary workshop. *Regulatory Toxicology and Pharmacology*, 106, pp.210-223.

Bachand, A.M., Mundt, K.A., Mundt, D.J. and Montgomery, R.R., 2010. Epidemiological studies of formaldehyde exposure and risk of leukemia and nasopharyngeal cancer: a meta-analysis. *Critical reviews in toxicology*, 40(2), pp.85-100.*

Bosetti, C., McLaughlin, J.K., Tarone, R.E., Pira, E. and La Vecchia, C., 2008. Formaldehyde and cancer risk: a quantitative review of cohort studies through 2006. *Annals of Oncology*, 19(1), pp.29-43.*

¹ * denotes studies, reviews, or responses referenced in supplemental information but not the main text; ** denotes studies, review, or responses briefly referenced in the main text but not the supplemental information; *** denotes studies miscited in the main text but not referenced in the supplemental information.

Brüning, T., Bartsch, R., Bolt, H.M., Desel, H., Drexler, H., Gundert-Remy, U., Hartwig, A., Jäckh, R., Leibold, E., Pallapies, D. and Rettenmeier, A.W., 2014. Sensory irritation as a basis for setting occupational exposure limits. *Archives of toxicology*, 88(10), pp.1855-1879.

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Catalani, S., Donato, F., Madeo, E., Apostoli, P., De Palma, G., Pira, E., Mundt, K.A. and Boffetta, P., 2019. Occupational exposure to formaldehyde and risk of non hodgkin lymphoma: a meta-analysis. *BMC cancer*, 19(1), pp.1-9.

Chang, E.T., Ye, W., Zeng, Y.X. and Adami, H.O., 2021. The evolving epidemiology of nasopharyngeal carcinoma. *Cancer Epidemiology and Prevention Biomarkers*, 30(6), pp.1035-1047.

Checkoway, H., Boffetta, P., Mundt, D.J. and Mundt, K.A., 2012. Critical review and synthesis of the epidemiologic evidence on formaldehyde exposure and risk of leukemia and other lymphohematopoietic malignancies. *Cancer Causes & Control*, 23(11), pp.1747-1766.

Checkoway, H., Lees, P.S., Dell, L.D., Gentry, P.R. and Mundt, K.A., 2019. Peak exposures in epidemiologic studies and cancer risks: considerations for regulatory risk assessment. *Risk Analysis*, 39(7), pp.1441-1464.

Cole, P., Adami, H.O., Trichopoulos, D. and Mandel, J., 2010. Formaldehyde and lymphohematopoietic cancers: a review of two recent studies. *Regulatory Toxicology and Pharmacology*, 58(2), pp.161-166.

Cole, P., Adami, H.O., Trichopoulos, D. and Mandel, J.S., 2010. Re: Mortality from lymphohematopoietic malignancies and brain cancer among embalmers exposed to formaldehyde. *Journal of the National Cancer Institute*, 102(19), pp.1518-1519.

Cole, P. and Axten, C., 2004. Formaldehyde and leukemia: an improbable causal relationship. *Regulatory Toxicology and Pharmacology*, 40(2), pp.107-112.

Collins, J.J. and Lineker, G.A., 2004. A review and meta-analysis of formaldehyde exposure and leukemia. *Regulatory Toxicology and Pharmacology*, 40(2), pp.81-91.*

Collins, J.J., Ness, R., Tyl, R.W., Krivanek, N., Esmen, N.A. and Hall, T.A., 2001. A review of adverse pregnancy outcomes and formaldehyde exposure in human and animal studies. *Regulatory Toxicology and Pharmacology*, 34(1), pp.17-34.

Collins, J.J., Esmen, N.A. and Hall, T.A., 2001. A review and meta-analysis of formaldehyde exposure and pancreatic cancer. *American journal of industrial medicine*, 39(3), pp.336-345.*

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European Food Safety Authority, 2014. Endogenous formaldehyde turnover in humans compared with exogenous contribution from food sources. *EFSA Journal*, 12(2), p.3550.

Gaylor, D.W., Lutz, W.K. and Conolly, R.B., 2004. Statistical analysis of nonmonotonic dose-response relationships: Research design and analysis of nasal cell proliferation in rats exposed to formaldehyde. *Toxicological Sciences*, 77(1), pp.158-164.

Gentry, R., Thompson, C.M., Franzen, A., Salley, J., Albertini, R., Lu, K. and Greene, T., 2020. Using mechanistic information to support evidence integration and synthesis: a case study with inhaled formaldehyde and leukemia. *Critical reviews in toxicology*, 50(10), pp.885-918.

Golden, R., 2011. Identifying an indoor air exposure limit for formaldehyde considering both irritation and cancer hazards. *Critical reviews in toxicology*, 41(8), pp.672-721.

Golden, R. and Holm, S., 2017. Indoor air quality and asthma: has unrecognized exposure to acrolein confounded results of previous studies?. *Dose-Response*, 15(1), p.1559325817691159.

Golden, R. and Valentini, M., 2014. Formaldehyde and methylene glycol equivalence: critical assessment of chemical and toxicological aspects. *Regulatory Toxicology and Pharmacology*, 69(2), pp.178-186.

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- Heck, H.D.A. and Casanova, M., 2004. The implausibility of leukemia induction by formaldehyde: a critical review of the biological evidence on distant-site toxicity. *Regulatory Toxicology and Pharmacology*, 40(2), pp.92-106.**
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- Lu, K., Ye, W., Zhou, L., Collins, L.B., Chen, X., Gold, A., Ball, L.M. and Swenberg, J.A., 2010. Structural characterization of formaldehyde-induced cross-links between amino acids and deoxynucleosides and their oligomers. *Journal of the American Chemical Society*, 132(10), pp.3388-3399.**
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Marsh, G.M. and Youk, A.O., 2005. Reevaluation of mortality risks from nasopharyngeal cancer in the formaldehyde cohort study of the National Cancer Institute. *Regulatory Toxicology and Pharmacology*, 42(3), pp.275-283.**

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Monticello, T.M., Morgan, K.T. and Hurtt, M.E., 1990. Unit length as the denominator for quantitation of cell proliferation in nasal epithelia. *Toxicologic Pathology*, 18(1), pp.24-31.²

Mundt, K.A., Dell, L.D., Boffetta, P., Beckett, E.M., Lynch, H.N., Desai, V.J., Lin, C.K. and Thompson, W.J., 2021. The importance of evaluating specific myeloid malignancies in epidemiological studies of environmental carcinogens. *BMC cancer*, 21(1), pp.1-22.

2 Included in main text references but not in text nor in appendices.

Mundt, K.A., Gentry, P.R., Dell, L.D., Rodricks, J.V. and Boffetta, P., 2018. Six years after the NRC review of EPA's Draft IRIS Toxicological Review of Formaldehyde: Regulatory implications of new science in evaluating formaldehyde leukemogenicity. *Regulatory Toxicology and Pharmacology*, 92, pp.472-490.

Mundt, K.A., Gallagher, A.E., Dell, L.D., Natelson, E.A., Boffetta, P. and Gentry, P.R., 2018. Response to Dr. Bernard D. Goldstein's Letter to the Editor. *Critical Reviews in Toxicology*, 48(5), pp.341-343.

Nielsen, G.D., Larsen, S.T. and Wolkoff, P., 2017. Re-evaluation of the WHO (2010) formaldehyde indoor air quality guideline for cancer risk assessment. *Archives of toxicology*, 91(1), pp.35-61.

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Nielsen, G.D., Larsen, S.T. and Wolkoff, P., 2013. Recent trend in risk assessment of formaldehyde exposures from indoor air. *Archives of toxicology*, 87(1), pp.73-98.

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Pira, E., Romano, C., Vecchia, C.L. and Boffetta, P., 2017. Hematologic and cytogenetic biomarkers of leukemia risk from formaldehyde exposure. *Carcinogenesis*, 38(12), pp.1251-1252.

Pontel, L.B., Rosado, I.V., Burgos-Barragan, G., Garaycochea, J.I., Yu, R., Arends, M.J., Chandrasekaran, G., Broecker, V., Wei, W., Liu, L. and Swenberg, J.A., 2015. Endogenous formaldehyde is a hematopoietic stem cell genotoxin and metabolic carcinogen. *Molecular cell*, 60(1), pp.177-188.**

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- Rhomberg, L.R., 2015. Contrasting directions and directives on hazard identification for formaldehyde carcinogenicity. *Regulatory Toxicology and Pharmacology*, 73(3), pp.829-833.
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- Starr, T.B. and Swenberg, J.A., 2013. A novel bottom-up approach to bounding low-dose human cancer risks from chemical exposures. *Regulatory Toxicology and Pharmacology*, 65(3), pp.311-315.**
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thresholds to whole body exposures—experimental approaches evaluating chemosensory effects of chemicals. *International archives of occupational and environmental health*, 79(4), pp.308-321.

Wolkoff, P. and Nielsen, G.D., 2010. Non-cancer effects of formaldehyde and relevance for setting an indoor air guideline. *Environment international*, 36(7), pp.788-799.

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Zeller, J., Högel, J., Linsenmeyer, R., Teller, C. and Speit, G., 2012. Investigations of potential susceptibility toward formaldehyde-induced genotoxicity. *Archives of toxicology*, 86(9), pp.1465-1473.

Zeller, J., Ulrich, A., Mueller, J.U., Riegert, C., Neuss, S., Bruckner, T., Triebig, G. and Speit, G., 2011. Is individual nasal sensitivity related to cellular metabolism of formaldehyde and susceptibility towards formaldehyde-induced genotoxicity?. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, 723(1), pp.11-17.

In addition, several important studies and reviews, while briefly cited by EPA in the main text of the assessment, are summarily dismissed by the Agency (in several cases devoting a sentence or less, or a single footnote to the content). Examples include:

Gentry, P.R., Rodricks, J.V., Turnbull, D., Bachand, A., Van Landingham, C., Shipp, A.M., Albertini, R.J. and Irons, R., 2013. Formaldehyde exposure and leukemia: critical review and reevaluation of the results from a study that is the focus for evidence of biological plausibility. *Critical reviews in toxicology*, 43(8), pp.661-670.

Lu, K., Boysen, G., Gao, L., Collins, L.B. and Swenberg, J.A., 2008. Formaldehyde-induced histone modifications in vitro. *Chemical research in toxicology*, 21(8), pp.1586-1593.

Möhner, M., Liu, Y. and Marsh, G.M., 2019. New insights into the mortality risk from nasopharyngeal cancer in the national cancer institute formaldehyde worker cohort study. *Journal of Occupational Medicine and Toxicology*, 14(1), pp.1-4.

Mundt, K.A., Gallagher, A.E., Dell, L.D., Natelson, E.A., Boffetta, P. and Gentry, P.R., 2017. Does occupational exposure to formaldehyde cause hematotoxicity and leukemia-specific chromosome changes in cultured myeloid progenitor cells? *Critical Reviews in Toxicology*, 47(7), pp.598-608.