

Risk Evaluation for 1,1-Dichloroethane

Systematic Review Supplemental File:

Data Quality Evaluation Information for Human Health Hazard Epidemiology

CASRN: 75-34-3



June 2025

This supplemental file contains the data quality evaluation results for data sources that met the PECO screening criteria for the *Risk Evaluation for 1,1-Dichloroethane* and were used to characterize human health hazard. In addition, due to data gaps for 1,1-dichloroethane, EPA used 1,2-dichloroethane data as analog data for read across in the *Risk Evaluation for 1,1-Dichloroethane*. Therefore, this supplemental file also contains data quality evaluation results for data sources that met the PECO screening criteria for 1,2-dichloroethane. EPA conducted data quality evaluation based on author-reported descriptions and results; additional analyses (*e.g.*, statistical analyses performed during data integration into the risk evaluation) potentially conducted by EPA are not contained in this supplemental file. EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (also referred to as '2021 Draft Systematic Review Protocol are described in *Risk Evaluation for 1,1-Dichloroethane – Systematic Review Protocol*. Within the contents of this document, 1,1-dichloroethane may be referred to as the acronyms 1,1-DCA and 1,1-DCE. The acronyms 1,2-DCA, 1,2-DCE, and DCE refer to the chemical 1,2-dichloroethane. The acronyms 1,2-DCE refers to the chemical trans-1,2-dichloroethylene. The acronym 1,2-DCP refers to the chemical 1,2-dichloropropane.

Table of Contents

HERO ID	Reference	Page
1,1-Dichloroethau	ne	
Reproductive/Developmental		
2799700	Brender, J. D., Shinde, M. U., Zhan, F. B., Gong, X., Langlois, P. H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health 13(1):96.	6
3014082	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14.	8
Cancer/Carcinogenesis		
3014082	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14.	11
5440630	Niehoff, N. M., Gammon, M. D., Keil, A. P., Nichols, H. B., Engel, L. S., Sandler, D. P., White, A. J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.	14
Isomer: Dichloro	ethane	
Neurological/Behavioral		
18135	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.	17
Musculoskeletal		
18135	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.	21
Hepatic/Liver		
18135	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.	25
Gastrointestinal		
18135	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.	29
Other (Morbidity)		
18135	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.	33
Isomer: 1,2-Dichl	loroethane	

Neurological/Behavioral

32901

Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.

37

Table of Contents

200241	Bowler, R. M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553- 562	41
Cancer/Carcinogenesis	302.	
32901	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.	44
6570017	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).	48
200224	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.	51
5451581	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.	67
4697224	Dosemeci, M., Cocco, P., Chow, W. H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.	75
3014082	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14.	78
194820	Kernan, G. J., Ji, B. T., Dosemeci, M., Silverman, D. T., Balbus, J., Zahm, S. H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.	81
5440630	Niehoff, N. M., Gammon, M. D., Keil, A. P., Nichols, H. B., Engel, L. S., Sandler, D. P., White, A. J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.	83
1357737	Sobel, W., Bond, G. G., Skowronski, B. J., Brownson, P. J., Cook, R. R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.	86
Endocrine		
194820	Kernan, G. J., Ji, B. T., Dosemeci, M., Silverman, D. T., Balbus, J., Zahm, S. H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.	89
Reproductive/Developmental		
6570017	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).	91
200239	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.	94
194932	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.	98
2799700	Brender, J. D., Shinde, M. U., Zhan, F. B., Gong, X., Langlois, P. H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health 13(1):96.	102
3014082	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14.	104
Hepatic/Liver		
200266	Cheng, T. J., Huang, M. L., You, N. C., Du, C. L., Chau, T. T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.	107
Mortality		

6570017	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).			
200633	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.	113		
Skin and Connective Tissue				
1357737	Sobel, W., Bond, G. G., Skowronski, B. J., Brownson, P. J., Cook, R. R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.	115		
Other (sick building syndrome)				
1938385	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.	118		
Renal/Kidney				
6570017	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).	121		
4697224	Dosemeci, M., Cocco, P., Chow, W. H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.	124		
Immune/Hematological				
6570017	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).	127		
Other (Other cancers (not specified)				
6570017	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).	130		
Gastrointestinal				
6570017	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).	133		
Lung/Respiratory				
6570017	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).	136		

Study Citation: Health Outcome(s) Assessed:	 tion: Brender, J. D., Shinde, M. U., Zhan, F. B., Gong, X., Langlois, P. H. (2014). Maternal residential proximity to chlorinated solvent emis defects in offspring: A case-control study. Environmental Health 13(1):96. Reproductive/Developmental i) 						
Assessed: Reported Health Effect(s):	Health birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)						
Chemical: HERO ID:	1,1-Dichlor 2799700	oethane- Parent compound					
Domain		Metric	Rating	Comments			
Domain 1: Study Part	icipation						
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.			
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.			
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.			
Domain 2. Exposure ([•] haracterization						
Domain 2: Disposure (Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emit- ted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.			
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group			
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evalu- ated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the preg- nancy, the temporality is unknown.			
Domain 3: Outcome A	Assessment						
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diag- nosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services			
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect			
Domain 4: Potential C	Confounding / Va	ariability Control					

Study Citation:	Brender, J. I defects in of	Brender, J. D., Shinde, M. U., Zhan, F. B., Gong, X., Langlois, P. H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health 13(1):96.						
Health Outcome(s) Assessed:	Reproductiv	Reproductive/Developmental						
Reported Health Effect(s):	birth defects	(neural tube defects, limbs deficiencie	es, oral cleft defec	ts, heart defects, spina bifida, anencephaly)				
Chemical: HERO ID:	1,1-Dichloro 2799700	bethane- Parent compound						
Domain		Metric	Rating	Comments				
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non- Hispanic).				
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information				
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described				
Domain 5: Analysis								
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects				
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.				
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility				
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.				
Additional Comments:	This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,1-dichloroethane were 2.14 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.							
Overall Qualit	ty Detern	nination	High					

Study Citation: Health Outcome(s) Assessed	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14. Reproductive/Developmental				
Reported Health	breast cance	r in females			
Effect(s): Chemical: HERO ID:	1,1-Dichloro 3014082	ethane- Parent compound			
Domain		Metric	Rating	Comments	
Domain 1: Study Partici	pation Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.	
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the pur- pose of the study and analysis. Exclusion criteria were documented. Included partici- pants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.	
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.	
Domain 2: Exposure Ch	aracterization				
Domain 2. Exposure en	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.	
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.	
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.	
Domain 3: Outcome Ass	sessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.	
			Continued on nex	t page	

			continued from p	revious page		
Study Citation: Health Outcome(s)	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14. Reproductive/Developmental					
Reported Health Effect(s):	breast cance	r in females				
Chemical: HERO ID:	1,1-Dichloro 3014082	bethane- Parent compound				
Domain		Metric	Rating	Comments		
	Metric 8:	Reporting Bias	High	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3. Several significant results for ethylidene dichloride were provided in Table 3.		
Domain 4: Potential C	onfounding / Va	riability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.		
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.		
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylidene dichloride (1,1-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.		
Domain 5 [.] Analysis						
2 5man 5. 7 may 515	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.		
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylidene dichloride (1,1-dichloroethane), however, this study utilized a large co-hort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.		
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.		
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. "No apparent viola- tion of the underlying assumption of proportional hazards was detected".		
			Continued on nex	t page		

continued from previous page						
Study Citation:	Garcia, E., Hurley, S., Nelson, D. O., Hertz Environmental Health 14(1):14.	, A., Reynolds, P. (2015). Hazardous	air pollutants and breast cancer risk in California teachers: A cohort study.			
Health	Reproductive/Developmental					
Outcome(s)						
Assessed:						
Reported Health	breast cancer in females					
Effect(s):						
Chemical:	1,1-Dichloroethane- Parent compound					
HERO ID:	3014082					
Domain	Metric	Rating	Comments			
Additional Comments:	A group of 112,378 female participants fr	om the California Teacher Study col	hort were assessed for their estimated exposure to ambient air pollutants,			
	including ethylidene dichloride (1,1-dichlo	roethane), and the incidence of invasi	ive breast cancer. Air contaminant concentrations were estimated using the			
	US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,1-dichloroethane is between 1E-4 and 1E-2 (estimated from					
	Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. An increase in the hazard risk for breast cancer was observed for					
	Quintile 3 when compared with Quintile 1 (OR 1.09, 95% CI 1.00-1.18) and results were adjusted for age and race; however, this increase was not observed					
	in Quintiles 4 or 5, and the p(trend) for Quintiles 2-5 was not significant (0.19). An increase in tumor hormone responsiveness to estrogen-receptor positive					
	or progesterone receptor positive risk com	pared with all tumor types and the ri	isk among past or never hormone therapy users were also associated with			
	1,1-dichloroethane exposure.					

Overall Quality Determination

High

Study Citation: Health Outcome(s)	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14. Cancer/Carcinogenesis				
Reported Health	breast cance	r in females			
Chemical: HERO ID:	1,1-Dichloro 3014082	bethane- Parent compound			
Domain		Metric	Rating	Comments	
Domain 1: Study Partici	pation Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.	
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.	
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.	
Domain 2: Exposure Ch	aracterization				
Domain 2. Exposure en	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.	
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.	
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.	
Domain 3: Outcome As	sessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.	
			Continued on nex	t page	

			continued from p	revious page		
Study Citation: Health Outcome(s) Assessed:	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14. Cancer/Carcinogenesis					
Reported Health Effect(s):	breast cance	r in females				
Chemical: HERO ID:	1,1-Dichloro 3014082	bethane- Parent compound				
Domain		Metric	Rating	Comments		
	Metric 8:	Reporting Bias	High	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3. Several significant results for ethylidene dichloride were provided in Table 3.		
Domain 4: Potential Co	onfounding / Va	riability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.		
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.		
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylidene dichloride (1,1-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.		
Domain 5: Analysis						
2 omain 5. 7 mary 515	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.		
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylidene dichloride (1,1-dichloroethane), however, this study utilized a large co-hort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.		
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.		
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. "No apparent viola- tion of the underlying assumption of proportional hazards was detected".		
			Continued on nex	t page		

		continued from previous page				
Study Citation:	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14					
Health	Cancer/Carcinogenesis					
Outcome(s)						
Assessed:						
Reported Health	breast cancer in females					
Effect(s):						
Chemical:	1,1-Dichloroethane- Parent compound					
HERO ID:	3014082					
Domain	Metric	Rating	Comments			
Additional Comments:	A group of 112,378 female participants fi	om the California Teacher Study cohor	t were assessed for their estimated exposure to ambient air pollutants,			
	including ethylidene dichloride (1,1-dichlo	proethane), and the incidence of invasive	breast cancer. Air contaminant concentrations were estimated using the			
	US EPA NATA and the ASPEN and HEM	models. The approximate median concer	tration of 1,1-dichloroethane is between 1E-4 and 1E-2 (estimated from			
	Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. An increase in the hazard risk for breast cancer was observed for					
	Quintile 3 when compared with Quintile 1 (OR 1.09, 95% CI 1.00-1.18) and results were adjusted for age and race; however, this increase was not observed					
	in Quintiles 4 or 5, and the p(trend) for Quintiles 2-5 was not significant (0.19). An increase in tumor hormone responsiveness to estrogen-receptor positive					
	or progesterone receptor positive risk com	pared with all tumor types and the risk	among past or never hormone therapy users were also associated with			
	1,1-dichloroethane exposure.					

Overall Quality Determination

High

Study Citation: Health Outcome(s) Assessed: Reported Health	Niehoff, N. M., Gammon, M. D., Keil, A. P., Nichols, H. B., Engel, L. S., Sandler, D. P., White, A. J. (2019). Airborne mammary carcinogens and breas cancer risk in the Sister Study. Environment International 130:104897. Cancer/Carcinogenesis Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer					
Effect(s):	1 1-Dichloroe	othane- Parent compound				
HERO ID:	5440630	unane- i arent compound				
Domain		Metric	Rating	Comments		
Domain 1: Study Particip	pation		TT: 1			
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, $< 2\%$) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.		
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.		
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confound- ing variables.		
Domain 2: Exposure Ch	aracterization					
Domain 2. Exposure Ch	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."		
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.		
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later. The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.		

			. continued from previo	ous page		
Study Citation:	Niehoff, N. cancer risk i	M., Gammon, M. D., Keil, A. P., Nig n the Sister Study. Environment Inte	chols, H. B., Engel, L. S rnational 130:104897.	., Sandler, D. P., White, A. J. (2019). Airborne mammary carcinogens and breast		
Outcome(s)	Cancer/Care					
Reported Health Effect(s):	Breast cance	er diagnosis (overall), tumor characte	eristics, and estrogen rece	eptor positive (ER+) invasive breast cancer		
Chemical: HERO ID:	1,1-Dichloro 5440630	bethane- Parent compound				
Domain		Metric	Rating	Comments		
Domain 3: Outcome As	sessment					
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow- up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self- reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were ab- stracted from medical records, or self-reported.		
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.		
Domain 4: Potential Co	onfounding / Va	riability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appro- priate considerations were made for potential confounders.		
	Metric 10:	Covariate Characterization	Medium	"Most covariates were assessed by self-report at the baseline interview.""At baseline, women completed a computer-assisted telephone interview and written question- naires."Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.		
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful quali- tative information.		
Domain 5 [.] Analysis						
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.		
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).		
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.		
Continued on next page						

	continued from previous page					
Study Citation:	Niehoff, N. I cancer risk i	Niehoff, N. M., Gammon, M. D., Keil, A. P., Nichols, H. B., Engel, L. S., Sandler, D. P., White, A. J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.				
Health	Cancer/Carc	inogenesis				
Outcome(s)						
Assessed:						
Reported Health	Breast cance	er diagnosis (overall), tumor chara	cteristics, and estrogen rece	ptor positive (ER+) invasive breast cancer		
Effect(s):						
Chemical:	1,1-Dichloro	bethane- Parent compound				
HERO ID:	5440630					
Domain		Metric	Rating	Comments		
	Metric 15:	Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index cate- gories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evalu- ated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.		
Additional Comments:	This was a v limitation.	well-conducted study of a large p	rospective cohort, but the	neasurement of exposure at the census-tract rather than the individual level is a		
Overall Qualit	y Detern	nination	Medium			

Health Partone Outcome (%) Partone (%) Outcome (%) Sustainable (Comparing (%)) Perported Health muscles, rendom, and ganglia Chemical Dibloroethane ERRO (D) 18132	Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya					
HERO ID: 18135 Domain Metric Rating Comments Domain 1: Study Participation Comments Comments Domain 1: Study Participation Low Coccupational cohort study in Russian aircard manufacturing plant. The study focuses on the sort tank shop. The participation of all works in the aircard plant shops (the olimation) Include participates of all works on the sort tank shop. The participates of all works are constrained works in the aircard plant shops (the olimation) are reported. I7 glues represented the exposed and were compared to 10 mechanical shop in anchined in formation provided. The study solely perotive fusion and the vector study in a reported. If olives represented the exposed and were compared to 10 mechanical shop in anchined in anticipate are exposed. If we divergent these included in analyses or sole and were provided. The study every these included in analyses or sole and were compared to 10 mechanical shop in anchined vector show the courted stress on the courted stress and counted show are angine vectors. Though the courted stress is and in the mechanical shop in anchine vector. Show and the courted stress is and in the mechanical shop in anchine vector. Domain 2: Exposure Characterization Metric 4: Metric 4: Metric 4: Metric 4: Keurement of Exposure Vininformative Authors report quantitative exess concentration of dichorechane in air, but do not provide any and information on the method used on quantify exposure levels. Netric 4: Netric 6: Exposure Levels Low Neurolegal habit outcome ar	Health Outcome(s) Assessed: Reported Health Effect(s): Chemical:	visual-motor nuscles, ten 1,1-Dichloro	 1:31-38. Neurological/Behavioral visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia. 1. Dichloroethane, Isomer: Dichloroethane 				
Domain Metric Rating Comments Domain 1: Study Participation Metric 1: Participant Selection Low Occupational cohort study in Rossina aircrift manufacturing plant. The study focuses on or ported. The study focuses on or ported. The gluers represented the stypes of studient syness are non reported. The gluers represented the stypes of studient syness are non reported. The gluers represented the stypes of studient syness are non reported. The gluers represented the stypes of studient syness are non reported. The gluers represented the stypes of studients and synes are non reported. The study for stypes of studients and synes are non reported. The gluers represented the stypes of studients and synes are non reported. The also workers in the stammative between cases and controls is not the functions of motor apprants in upper extermities. Metric 3: Comparison Group Low Mechanics shop machinists (n=10) served as the controls. Though the controls were also workers in the stammative between cases and controls is not care provided thus, the similarity between cases and controls is not a transmitter be hands, which is distinct from the gluers (resposed). Domain 2: Exposure Characterization Metric 5: Exposure Levels Low Networkers in the same distingt exposure levels. Metric 6: Exposure Levels Low Networkers in the same distingt exposure levels. Song machina structure is the same distingt exposure levels. Domain 2: Exposure Characterization Metric 6: Exposure Levels Low <th>HERO ID:</th> <th>18135</th> <th></th> <th></th> <th></th>	HERO ID:	18135					
Domain 1: Study Participation Metric 1: Participant Selection Low Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop. The participation and the coll number of included participants across analyses are not reported. 17 gluens represented the exposed and were compared to 10 mechanical shop machinists. Metric 2: Attrition Medium Retax of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of moup parts train upper extremises. Domain 2: Exposure Characterization Metric 4: Measurement of Exposure Vininformative Authors report quantitative measures of dichoroethane in air, but do not provide any information on the soft maint stop set (seposed) and measures of dichoroethane in air, but do not provide any information when shows for mention set (seposed) and measures of dichoroethane in air, but do not provide any information on the method used to up antify exposure levels. Domain 2: Exposure Characterization Metric 5: Exposure Levels Low Neurological health outcomes are eported of thow provise space (seposed) and measures of dichoroetha	Domain		Metric	Rating	Comments		
Metric 1. Fatterpain Selection Low Occupational colors and the participation of all workers in the arcraft plant should inclusion of the soft task shop and controls from the mechanical shop) is implied. however numbers of eligible participation and the total number of included participatis across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists. Metric 2: Attrition Medium Rates of attrition cannot be determined based on the limited information provided. The study lockers and yes are not provided. The study soler peopre shows in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop machinists. Metric 3: Comparison Group Low Mechanical shop machinists. Domain 2: Exposure Characterization Metric 4: Measurement of Exposure Uninformative Metric 5: Exposure Levels Low Authors report quantitative measures of dichloroethane in air, but do not provide any informative measures of dichloroethane in air, but do not provide any informative on the method used to quantify exposure levels. Metric 6: Exposure Levels Low Neurological health studies of the shift. Metric 6: Temporality Medium The study indexes of water shifts (erg) box of the shift. Domain 3: Outcome Assessment Metric 7: Cutome Measurement or Characterization No informative Metric 7: Outcome Measurement	Domain 1: Study Partici	ipation Matria 1:	Dertiginant Solaction	Low	Occurational ask of study in Dussian singraft manufacturing plant. The study focuses on		
Metric 2: Attrition Medium Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities. Metric 3: Comparison Group Low Mechanical shop machiniss (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, autors note that controls determined the hands, which is distinct from the gluers (exposed). Domain 2: Exposure Characterization Metric 4: Measurement of Exposure Uninformative Authors report quantitative measures of dichloroethane in air, but do not provide any information on the rubed out of yourse levels. Metric 5: Exposure Levels Low Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentration of dichloroethane in olos 0.002 - 0.008." Metric 6: Temporality Medium The study reports visual-motor reaction at the end of the working day after exposure evels. Domain 3: Outcome Assessment Metric 7: Contome Measurement or Uninformative No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction at the end of the working day after exposure evels. <		metric 1.	Participant Selection	Low	the soft tank shop. The participation of all workers in the aircraft plant. The study focuses on the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.		
Metric 3: Comparison Group Low Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gures (exposed). Domain 2: Exposure Characterization Measurement of Exposure Uninformative Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels. Metric 5: Exposure Levels Low Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanics (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.058 mg/L) occurred when the rubber sheets were coated with glue. These concentrations of dichloroethane (0.08 - 0.058 mg/L) occurred with the rubber sheets exerce out of whighes. These succentrations of dichloroethane (0.08 - 0.058 mg/L) occurred with the rubber sheets exerce out of whighest the evol of the drying period 15 min later, they had decreased to 0.00 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L) octow sisual-motor reaction at the end of the working day after exposure establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radicultis. Domain 3: Outcome Assessment Uninformative No information on outcome measurement and diagnostic criteria is provided for visual-motor function, neuritis, radicultis, o		Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.		
Domain 2: Exposure Characterization Metric 4: Measurement of Exposure Uninformative Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels. Metric 5: Exposure Levels Low Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L and lever during most of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane (0.08 - 0.05 mg/L and lower during most of the shift." Metric 6: Temporality Medium The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radicultis. Domain 3: Outcome Assessment Outcome Measurement or Characterization Uninformative No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radicultits, or changes in motor function of upper extremities.		Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).		
Domain 2: Exposure Characterization Measurement of Exposure Uninformative Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels. Metric 5: Exposure Levels Low Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations of mixities conducted by gluers. "The highest concentration of dichloroethane (0.08 - 0.058 mg/L) accurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift." Metric 6: Temporality Medium The study reports visual-moor reaction at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift." Domain 3: Outcome Assessment Metric 7: Outcome Measurement or Characterization Uninformative No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.	Domain 2: Exposure Ch	naracterization					
Metric 5:Exposure LevelsLowNeurological health outcomes are reported for two groups: gluers (exposed) and me- chanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentra- tions were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had de- creased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."Metric 6:TemporalityMediumThe study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.Domain 3: Outcome Assessment Metric 7:Outcome Measurement or CharacterizationUninformative LoninformativeNo information on outcome measurement and diagnostic criteria is provided for visual- motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.	Domain 2. Exposure en	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.		
Metric 6: Temporality Medium The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis. Domain 3: Outcome Assessment Outcome Measurement or Characterization Uninformative No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities. Continued on next page		Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and me- chanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentra- tions were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had de- creased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."		
Domain 3: Outcome Assessment Metric 7: Outcome Measurement or Characterization Uninformative No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities. Continued on next page		Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.		
Metric 7: Outcome Measurement or Characterization Uninformative Continued on next page No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.	Domain 3: Outcome As	sessment					
Continued on next page	Domain 5. Outcome As	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual- motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.		
				Continued on next page			

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygien	e in the use of dichloroethan	e in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya	
Health Outcome(s) Assessed:	1:31-38. Neurologica	l/Behavioral			
Reported Health Effect(s): Chemical: HERO ID:	visual-motor muscles, ten 1,1-Dichloro 18135	reaction (simple, complex), changes in dons, and ganglia. bethane- Isomer: Dichloroethane	the function of the motor a	pparatus in the upper extremities, neuritis and radiculitis, diseases of the	
Domain		Metric	Rating	Comments	
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.	
Domain 4: Potential Co	nfounding / Va	riability Control			
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.	
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.	
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.	
Domain 5: Analysis					
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.	
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.	
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.	
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.	
Additional Comments:	Occupationa provides one are not provi and 1,2 dich	Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.			

Overall Quality Determination

Study Citation: Health Outcome(s)	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38. Neurological/Behavioral					
Assessed: Reported Health Effect(s): Chemical: HERO ID:	visual-motor muscles, tene 1,1-Dichloro 18135	isual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the nuscles, tendons, and ganglia. ,1-Dichloroethane- Isomer: Dichloroethane 8135				
Domain		Metric	Rating	Comments		
Domain 1: Study Partici	pation Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.		
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.		
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).		
Domain 2: Exposure Ch	oractorization					
Domain 2. Exposure Ch	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.		
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and me- chanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentra- tions were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had de- creased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."		
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.		
Domain 3: Outcome As	sessment					
Domain 5. Outcome As	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual- motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.		
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.		
			Continued on next page			

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygier	e in the use of dichloroethane	in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya
Health Outcome(s) Assessed: Reported Health Effect(s): Chemical: HERO ID:	1:31-38. Neurologica visual-motor muscles, ten 1,1-Dichloro 18135	l/Behavioral reaction (simple, complex), changes in dons, and ganglia. bethane- Isomer: Dichloroethane	the function of the motor ap	paratus in the upper extremities, neuritis and radiculitis, diseases of the
Domain		Metric	Rating	Comments
Domain 4: Potential Cor	nfounding / Va Metric 9:	riability Control Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
2 011111 01 1 11111 9010	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.
Additional Comments:	Occupationa provides one are not provi and 1,2 dich	l study of aircraft plant workers exposed crude comparison of prevalence of visu ded for outcomes and only case number loroethane cannot be separated in this re	I to dichloroethane via air. St ual-motor reaction impairments are reported, limiting the inview. Both chemicals have be	tudy reports number of cases of a variety of neurological conditions and nt with a control group. Otherwise, statistical analyses and comparisons formativeness of the study. Study refers only to dichloroethane, thus, 1,1 een included in evaluations.

Overall Quality Determination Uninformative

Study Citation: Health Outcome(s)	Kozik, I. V. (1:31-38. Musculoskel	(1957). [Problems of occupational hyg	iene in the use of dichloroethane in	n the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya		
Assessed: Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.					
Chemical: HERO ID:	1,1-Dichloro 18135	1,1-Dichloroethane- Isomer: Dichloroethane 18135				
Domain		Metric	Rating	Comments		
Domain 1: Study Partic	cipation Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on		
				the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.		
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.		
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).		
Domain 2: Exposure C	haracterization					
Domain 2. Exposure e	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.		
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and me- chanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentra- tions were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had de- creased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."		
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after expo- sure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.		
Domain 3: Outcome A	ssessment					
Domain 5. Outcome A	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.		
			Continued on next page			

Study Citation:	Kozik, I. V. (Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya				
Upplth	1:31-38. Museuloska	latal				
Outcome(s)	Musculoske	letal				
Assessed:						
Reported Health	changes in t	hanges in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.				
Effect(s):	8		-FF			
Chemical:	1,1-Dichloro	,1-Dichloroethane- Isomer: Dichloroethane				
HERO ID:	18135					
Domain		Metric	Rating	Comments		
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.		
Domain 1: Potential Co	nfounding / Va	riability Control				
Domain 4. 1 otentiar Co.	Metric 9.	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics		
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.		
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.		
D : 5 A I :						
Domain 5: Analysis	Matria 12.	Study Design and Mathada	Iliah	Providence levels and some share's discuss sometimes are sometimes in the maximum denisti		
	Metric 12:	Study Design and Methods	rigi	a cohort design.		
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.		
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.		
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.		
Additional Comments:	ts: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.					
Overall Quality Determination Uninformative						

Study Citation: Health Outcome(s)	Kozik, I. V. (1:31-38. Musculoskel	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38. Musculoskeletal					
Assessed: Reported Health Effect(s):	changes in th	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.					
Chemical: HERO ID:	1,1-Dichloro 18135	ethane- Isomer: Dichloroethane					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic.	ipation Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.			
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.			
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).			
Domain 2: Exposure Ch	naracterization						
Domain 2. Exposure of	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.			
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and me- chanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentra- tions were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had de- creased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."			
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after expo- sure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.			
Domain 3: Outcome As	sessment						
2 smail 5, Outcome As	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.			
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.			

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya					
Health	1:31-38. Musculoskel	1:31-38. Musculoskeletal				
Outcome(s)						
Assessed:						
Reported Health	changes in th	ne function of the motor apparatus in the	e upper extremities, diseases of	f the muscles, tendons, and ganglia.		
Effect(s):						
Chemical:	1,1-Dichloro	ethane- Isomer: Dichloroethane				
HERO ID:	18135					
Domain		Metric	Rating	Comments		
Domain 4: Potential Con	nfounding / Var	riability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.		
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.		
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.		
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.		
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.		
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.		
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.		
Additional Comments:	Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.					

Overall Quality Determination

Uninformative

Page 24 of 138

Study Citation: Health	Kozik, I. V. (1:31-38. Hepatic/Live	1957). [Problems of occupational hygic	ene in the use of dichloroethane in	n the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya
Assessed:				
Reported Health	liver and gal	l bladder diseases.		
Effect(s):				
Chemical: HERO ID:	1,1-Dichloro 18135	ethane- Isomer: Dichloroethane		
Domain		Metric	Rating	Comments
Domain 1: Study Partici	ipation			
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Ch	aracterization			
Domani 2. Exposure et	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome As	sassmant			
Domain 5. Outcome As	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4. Potential Co	nfounding / Va	riability Control		
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
			Continued on next page	

Study Citation:	Kozik, I. V. (Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya				
Health	Hepatic/Live	epatic/Liver				
Outcome(s)						
Assessed:						
Reported Health	liver and gall	l bladder diseases.				
Effect(s): Chemical: HERO ID:	1,1-Dichloro 18135	bethane- Isomer: Dichloroethane				
Domain		Metric	Rating	Comments		
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.		
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant.		
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.		
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.		
Additional Comments:	Occupationa analyses and to dichloroet	l study of aircraft plant workers expose comparisons are not provided for outc hane, thus, 1,1 and 1,2 dichloroethane	d to dichloroethane via air. Stu omes and only case numbers a cannot be separated in this rev	udy reports number of cases of liver and gall bladder diseases. Statistical are reported, limiting the informativeness of the study. Study refers only iew. Both chemicals have been included in evaluations.		

Overall Quality Determination

Study Citation:	Kozik, I. V. (Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya					
Health Outcome(s) Assessed:	1:31-38. Hepatic/Live	1:31-38. Hepatic/Liver					
Reported Health	liver and gall bladder diseases.						
Chemical: HERO ID:	1,1-Dichloro 18135	bethane- Isomer: Dichloroethane					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation						
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.			
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.			
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.			
Domain 2. Exposure Ch	aracterization						
Domain 2. Exposure of	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.			
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.			
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.			
Domain 3: Outcome As	sessment						
Domain 5. Outcome As	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.			
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed ex- traction.			
Domain 1: Potential Co	nfounding / Va	riability Control					
	Metric 9.	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics			
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.			
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.			
Domain 5: Analysis							
			Continued on next page				

Study Citation:	Kozik, I. V. (Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya					
Health	Hepatic/Live	Hepatic/Liver					
Outcome(s) Assessed:							
Reported Health Effect(s):	liver and gall	l bladder diseases.					
Chemical: HERO ID:	1,1-Dichloro 18135	bethane- Isomer: Dichloroethane					
Domain		Metric	Rating	Comments			
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.			
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant.			
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.			
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.			
Additional Comments:	Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.						
Overall Ouality Determination Uninformative							

Study Citation:	Kozik, I. V. (1:31-38.	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.					
Health Outcome(s)	Gastrointesti	Gastrointestinai					
Assessed:							
Reported Health	acute gastroi	ntestinal diseases, acute gastritis, and c	chronic gastritis.				
Effect(s):							
Chemical:	1,1-Dichloro	ethane- Isomer: Dichloroethane					
HERO ID:	18135						
Domain	· .:	Metric	Rating	Comments			
Domain 1: Study Partic	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on			
	Wettle 1.	r anteipant Serection	LOw	the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.			
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.			
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).			
Domain 2: Exposure Cl	haracterization						
Domain 2. Exposure Ci	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.			
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop com- pared to the plant. The exposure difference between groups is unclear.			
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.			
Domain 3: Outcome A	reaccmant						
Domain 5. Outcome As	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gas- trointestinal outcomes.			
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.			
Domain 4. Detertial C	mfounding 137	michility Control					
Domain 4: Potential Co	Metric 9.	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics			
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.			
			Continued on next page				
-			. 0				

Page 29 of 138

Study Citation:	Kozik, I. V. (Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya					
II a a l 4 h	1:31-38.	1:31-38.					
Health Outcomo(a)	Gastrointestinai						
Assessed:							
Assessed. Donorted Health	acuta gastroi	intestinal diseases, agute castritis, and ch	ronic asstritis				
Effect(s).	acute gastroi	intestinal diseases, acute gastritis, and er	nome gasurus.				
Chemical:	1 1-Dichloro	ethane- Isomer: Dichloroethane					
HERO ID:	18135	Senare Isomer, Diemoroculaie					
Domain		Metric	Rating	Comments			
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.			
Domain 5: Analysis							
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.			
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant.			
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.			
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.			
Additional Comments:	Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.						
Overall Quality Determination Uninformative							

Page 30 of 138

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.						
Health Outcome(s) Assessed:	Gastrointesti	Gastrointestinal					
Reported Health Effect(s):	acute gastroi	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.					
Chemical: HERO ID:	1,1-Dichloro 18135	ethane- Isomer: Dichloroethane					
Domain		Metric	Rating	Comments			
Domain 1: Study Partici	ipation						
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.			
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.			
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).			
Domain 2: Exposure Ch	naracterization						
Domani 2. Exposure et	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.			
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop com- pared to the plant. The exposure difference between groups is unclear.			
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.			
Domain 3: Outcome As	sessment						
	Metric 7:	Outcome Measurement or	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gas- trointestinal outcomes			
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.			
Domain 4: Potential Co	nfounding / Va	riability Control					
Bomani 7, 1 Otential CO	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics			
	Metric 10:	Covariate Characterization	N/A	No confounders measured.			
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.			
Domain 5: Analysis							

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya						
Health	Gastrointesti	Gastrointestinal					
Outcome(s)							
Assessed:							
Reported Health Effect(s):	acute gastroi	ntestinal diseases, acute gastritis, and chr	onic gastritis.				
Chemical: HERO ID:	1,1-Dichloro 18135	1,1-Dichloroethane- Isomer: Dichloroethane 18135					
Domain		Metric	Rating	Comments			
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.			
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant.			
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.			
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.			
Additional Comments:	Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.						

Overall Quality Determination

Study Citation: Health Outcome(s)	Kozik, I. V. (1:31-38. Other (Morb	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38. Other (Morbidity) Overall morbidity, and other diseases.					
Assessed: Reported Health Effect(s):	Overall mort						
Chemical: HERO ID:	1,1-Dichloro 18135	ethane- Isomer: Dichloroethane					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation						
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.			
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.			
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.			
Domain 2. Exposure Ch	naracterization						
Domain 2. Exposure er	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.			
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop com- pared to the plant. The exposure difference between groups is unclear.			
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.			
Domain 2: Outcome As	aggment						
Domain 5. Outcome As	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.			
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.			
Domain 4: Potential Co	nfounding / Va	riability Control					
Domain 4. I Otential CO	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.			
	Metric 10:	Covariate Characterization	N/A	No confounders measured.			
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.			
			Continued on next page				

Study Citation:	Kozik, I. V. (Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya				
Health Outcome(s)	1:31-38. Other (Morbidity)					
Assessed: Reported Health Effect(s):	Overall morbidity, and other diseases.					
Chemical: HERO ID:	1,1-Dichloro 18135	ethane- Isomer: Dichloroethane				
Domain		Metric	Rating	Comments		
Domain 5: Analysis	M (10		TT' 1			
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.		
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant.		
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.		
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.		
Additional Comments:	Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.					
Overall Quality Determination Uninformative						

Study Citation:	Kozik, I. V. (Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya					
Health Outcome(s) Assessed:	1:31-38. Other (Morb	1:31-38. Other (Morbidity)					
Reported Health	Overall mor	Overall morbidity, and other diseases.					
Chemical: HERO ID:	1,1-Dichloro 18135	bethane- Isomer: Dichloroethane					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation						
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.			
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.			
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.			
Domain 2: Exposure Cl	naracterization						
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.			
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop com- pared to the plant. The exposure difference between groups is unclear.			
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.			
Domain 3: Outcome As	resement						
Domain 5. Outcome 743	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.			
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.			
Domain 4: Potential Co	nfounding / Va	riability Control					
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.			
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.			
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.			
Domain 5: Analysis							
			Continued on next page				

Study Citation:	Kozik, I. V. (Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya					
Health Outcome(s)	Other (Morb	Other (Morbidity)					
Assessed: Reported Health Effect(s):	Overall mort	Overall morbidity, and other diseases.					
Chemical: HERO ID:	1,1-Dichloro 18135	ethane- Isomer: Dichloroethane					
Domain		Metric	Rating	Comments			
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.			
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases through- out the plant.			
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.			
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.			
Additional Comments:	Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.						

Overall Quality Determination
Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical: HERO ID:	Austin, S. G. and Environn Neurological/ Brain tumors 1,1-Dichloroe 32901	, Schnatter, A. R. (1983). A case-control nental Medicine 25(4):313-320. 'Behavioral	study of chemical	exposures and brain tumors in petrochemical workers. Journal of Occupational
Domain		Metric	Rating	Comments
Domain 1: Study Partici	pation			
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemi- cal plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through lo- cally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these "unknown" individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies

cases.

that the first scenario resulted in increased exposure estimates for controls relative to

		contin	ued from previ	ous page
Study Citation: Health Outcome(s)	Austin, S. G and Environ Neurologica	G., Schnatter, A. R. (1983). A case-control s mental Medicine 25(4):313-320. I/Behavioral	tudy of chemica	l exposures and brain tumors in petrochemical workers. Journal of Occupational
Assessed: Reported Health	Brain tumor	s		
Chemical: HERO ID:	1,1-Dichloro 32901	bethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Car- bide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee bene- fits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that em- ployees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were gener- ally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Ch	naracterization			
20man 2. Exposure er	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as "exposed" to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An "unknown" exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into "exposed" "unexposed" and "unknown"
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

Study Citation:	Austin, S. G	G., Schnatter, A. R. (1983). A case-control	l study of chemica	l exposures and brain tumors in petrochemical workers. Journal of Occupational
Health	and Environ	mental Medicine 25(4):313-320.		
Outcome(s)	ricurorogicu			
Assessed:				
Effect(s):	Brain tumor	S		
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane		
HERO ID:	32901			
Domain		Metric	Rating	Comments
Domain 3: Outcome As	ssessment			
	Metric 7: Metric 8:	Outcome Measurement or Characterization Reporting Bias	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be "confirmed" cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using "unconfirmed methods", meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
				results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Co	onfounding / Va	riability Control		
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.

Study Citation:	Austin, S. G and Environ	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.					
Health	Neurologica	Neurological/Behavioral					
Outcome(s)							
Assessed:							
Reported Health	Brain tumor	S					
Effect(s):	1.1 Diablar	athana Jaamari 1.2 Diahlaraathana					
HERO ID.	32901	Jethane- Isomer. 1,2-Diemoroethane					
	52701						
Domain	14 - 10	Metric	Rating	Comments			
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.			
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases $(n=21)$ and controls $(n=80$ in each analysis) is likely sufficient to detect an effect.			
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.			
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.			
Additional Comments:	This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative estimates limits the usefulness of this paper.						
Overall Oualit	v Deterr	nination	Medium				

Study Citation: Health Outcome(s) Assessed:	Bowler, R. M Neurological	Bowler, R. M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562. Neurological/Behavioral					
Reported Health	Wechsler Ad	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop					
Effect(s):	Color-Word Index, Symp	Test, Grooved Pegboard, Dynamomet tom Checklist-90 (SCL-90).	er, Wide Range Achievement 7	fest (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression			
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	200241						
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation Matria 1:	Participant Selection	Uninformativa	221 washing that had been averaged to 1.2 DCE in the Southern United States was ini-			
	Meure 1.	Fantcipant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern Onted States were ini- tially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were docu- mented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).			
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.			
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demo- graphically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and re- ported no prior chemical exposure.			
Domain 2: Exposure Ch	haracterization						
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.			
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysio- logical effects.			
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.			
Domain 3: Outcome As	ssessment						
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, includ- ing (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).			
			Continued on next page				

Page 41 of 138

		••	. continued from previous	s page		
Study Citation: Health Outcome(s) Assessed:	Bowler, R. M Neurologica	Bowler, R. M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562. Neurological/Behavioral				
Reported Health Effect(s):	Wechsler Ac Color-Word Index, Symr	dult Intelligence Scale III (WAIS-III), Wec Test, Grooved Pegboard, Dynamometer, ptom Checklist-90 (SCL-90).	chsler Memory Scale III (W Wide Range Achievemen	VMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop t Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression		
Chemical: HERO ID:	1,1-Dichloro 200241	bethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE- exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not pro- vided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.		
Domain 4: Potential Co	onfounding / Va	riability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.		
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.		
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work envi- ronment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.		
Demein 5. Analasia						
Domain 5: Analysis	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE- exposed workers; however, statistical methods were not comprehensive.		
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysio- logical tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.		
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.		
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.		
			Continued on next page			

	continued from previous page
Study Citation:	Bowler, R. M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health	Neurological/Behavioral
Outcome(s)	
Assessed:	
Reported Health	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop
Effect(s):	Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression
	Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	200241
Domain	Metric Rating Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing
	speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported
	in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure
	characterization among others.

Overall Quality Determination

Uninformative

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical: HERO ID:	Austin, S. G. and Environr Cancer/Carci Brain tumors 1,1-Dichloro 32901	, Schnatter, A. R. (1983). A case-control s nental Medicine 25(4):313-320. nogenesis ethane- Isomer: 1,2-Dichloroethane	tudy of chemical	exposures and brain tumors in petrochemical workers. Journal of Occupational
Domain		Metric	Rating	Comments
Domain 1: Study Particip	pation			
	Metric 1: Metric 2:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemi- cal plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through lo- cally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified. Attrition is not discussed in the study, and outcome data appear to be complete. There
		Autuon	litedulii	Author is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these "unknown" individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.
		Contir	nued on next page	ge

		conti	nued from previ	ous page
Study Citation: Health Outcome(s)	Austin, S. G and Environ Cancer/Carc	G., Schnatter, A. R. (1983). A case-control s mental Medicine 25(4):313-320. cinogenesis	study of chemica	l exposures and brain tumors in petrochemical workers. Journal of Occupational
Assessed: Reported Health	Brain tumor	S		
Chemical: HERO ID:	1,1-Dichloro 32901	bethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Car- bide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee bene- fits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that em- ployees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were gener- ally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Ch	naracterization			
20mm 2. Exposure er	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as "exposed" to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An "unknown" exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into "exposed" "unexposed" and "unknown"
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

		cor	ntinued from previo	ous page
Study Citation:	Austin, S. G and Environ	., Schnatter, A. R. (1983). A case-contro mental Medicine 25(4):313-320.	ol study of chemica	l exposures and brain tumors in petrochemical workers. Journal of Occupational
Health Outcome(s) Assessed:	Cancer/Carc	inogenesis		
Reported Health Effect(s):	Brain tumor	S		
Chemical: HERO ID:	1,1-Dichloro 32901	bethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
Domain 3: Outcome As	sessment			
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be "confirmed" cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using "unconfirmed methods", meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Co	nfounding / Va	riability Control		
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.

Domain 5: Analysis

Study Citation:	Austin, S. G and Environ	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.					
Health	Cancer/Carc	Cancer/Carcinogenesis					
Outcome(s)							
Assessed:							
Reported Health Effect(s):	Brain tumor	Brain tumors					
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	32901						
Domain		Metric	Rating	Comments			
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.			
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and con- trols (n=80 in each analysis) is likely sufficient to detect an effect.			
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.			
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.			
Additional Comments:	This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative estimates limits the usefulness of this paper.						
Overall Qualit	ty Deterr	nination	Medium				

Study Citation: Health Outcome(s) Assessed:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Cancer/Carcinogenesis				
Reported Health Effect(s): Chemical: HERO ID:	All cancer (e lymphatic an 1,1-Dichloro 6570017 Lin	xcluding non-melanoma skin cancer), diges d hematopoietic tissue cancer, other cancers ethane- Isomer: 1,2-Dichloroethane ked HERO ID(s): 6570017, 6570014	stive system can (not specified)	cer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer,	
Domain		Metric	Rating	Comments	
Domain 1: Study Partici	pation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.	
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.	
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.	
Domain 2: Exposure Ch	aracterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.	
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unex- posed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).	
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.	

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical: HERO ID:	BASF, (2005 study of emp number: 8EH Cancer/Carci All cancer (e lymphatic an 1,1-Dichloro 6570017 Lin	 BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Cancer/Carcinogenesis All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified) 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 6570017 Linked HERO ID(s): 6570017, 6570014 			
Domain		Metric	Rating	Comments	
Domain 3: Outcome As	sessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Can- cer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.	
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.	
Domain 4: Potential Co	nfounding / Va	iability Control			
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gen- der, and race.	
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gen- der, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.	
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.	
Domain 5: Analysis					
Domain J. Alialysis	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.	
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.	
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on par- ticipant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.	
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.	

Study Citation:	BASF, (2005). Letter: Subject: Supplemental study of employees assigned to a BASF Corport number: 8EHO-02-15135).	information regarding prior TSCA Se oration former chemical manufacturin	ection 8(e) submission - Preliminary results from a cancer inciden g unit in Geismar, LA that ceased operations in 1987 (EPA Cont	nce trol
Health	Cancer/Carcinogenesis			
Outcome(s)				
Assessed:				
Reported Health	All cancer (excluding non-melanoma skin can	cer), digestive system cancer, colorect	al cancer, respiratory cancer, prostate cancer, urinary system canc	cer,
Effect(s):	lymphatic and hematopoietic tissue cancer, oth	er cancers (not specified)		
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethar	ne		
HERO ID:	6570017 Linked HERO ID(s): 6570017, 65700)14		
Domain	Metric	Rating	Comments	
Additional Comments:	This occupational study examined deaths and	cancer incidence among employees w	ho worked in a chemical manufacturing unit, compared to expect	ted
	deaths among the U.S. population and expected	ed cancers among the South Louisian	a population. The study found lower death rates among employe	ees
	compared to the U.S. population. Observed can	cer incidence was generally higher than	n expected, although the study did not consistently present informati	ion
	on statistical significance. The exposure measure	surement approach was limited to ass	ignment based on job history, with no quantitative measurement	: of
	exposure. Detailed information on most aspect	s of the study design and analysis was	not provided.	
Overall Quality Determination Medium				

Study Citation: Health Outcome(s)	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716. Cancer/Carcinogenesis						
Assessed: Reported Health Effect(s):	Pancreatic ca	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma					
Chemical: HERO ID:	1,1-Dichloro 200224 Link	ethane- Isomer: 1,2-Dichloroethane ted HERO ID(s): 200224, 5447107					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.			
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.			
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.			
Domain 2: Exposure Ch	naracterization						
Domain 2. Exposure er	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is pro- vided on exposure levels, and a JEM was not used.			
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.			
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and out- come was assessed beginning at that time.			
Domain 3: Outcome As	sessment						
Domain 5. Outcome ras	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.			
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.			
Domain 4: Potential Co	nfounding / Va	rightlity Control					
Domani 4 . i otentiai Co	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar pe- riod, and interval since assignments, but distribution of these covariates was not re- ported.			
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic			
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.			
			Continued on next page	•			

Study Citation: Health Outcome(s)	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716. Cancer/Carcinogenesis				
Assessed: Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma				
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 200224 Linked HERO ID(s): 200224, 5447107				
Domain		Metric	Rating	Comments	
Domain 5: Analysis					
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.	
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.	
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.	
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin drin unit".	
Additional Comments:	None				

Overall Quality Determination

Uninformative

Study Citation: Health Outcome(s)	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716. Cancer/Carcinogenesis						
Assessed: Reported Health Effect(s):	Pancreatic ca	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma					
Chemical: HERO ID:	1,1-Dichloro 200224 Link	ethane- Isomer: 1,2-Dichloroethane ed HERO ID(s): 200224, 5447107					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation						
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.			
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.			
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.			
Domain 2: Exposure Ch	naracterization						
Domain 2. Exposure er	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is pro- vided on exposure levels, and a JEM was not used.			
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.			
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and out- come was assessed beginning at that time.			
Domain 3: Outcome As	sessment						
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.			
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.			
Domain 4: Dotantial Ca	nfounding / Vo	rishility Control					
Domani 4: Potential Co	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar pe- riod, and interval since assignments, but distribution of these covariates was not re- ported.			
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic			
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.			
Domain 5: Analysis							

		•	continued from previous pa	ge	
Study Citation:	Benson, L. C Medicine 50	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716			
Health	Cancer/Carcinogenesis				
Outcome(s)					
Assessed:					
Reported Health	Pancreatic ca	ncer, lymphatic and haematopoietic cand	cer, Leukemia, lymphosarcoma	lymphoma, multiple myeloma	
Effect(s):					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:	200224 Link	ed HERO ID(s): 200224, 5447107			
Domain		Metric	Rating	Comments	
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.	
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.	
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.	
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit".	
Additional Comments:	None				
Overall Qualit	ty Detern	nination	Uninformative		

Study Citation: Health Outcome(s)	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716. Cancer/Carcinogenesis						
Assessed: Reported Health Effect(s):	Pancreatic ca	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma					
Chemical: HERO ID:	1,1-Dichloro 200224 Link	ethane- Isomer: 1,2-Dichloroethane ed HERO ID(s): 200224, 5447107					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation						
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.			
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.			
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.			
Domain 2: Exposure Ch	naracterization						
Domain 2. Exposure er	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is pro- vided on exposure levels, and a JEM was not used.			
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.			
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and out- come was assessed beginning at that time.			
Domain 3: Outcome As	sessment						
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.			
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.			
Domain 4: Dotantial Ca	nfounding / Vo	rishility Control					
Domani 4: Potential Co	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar pe- riod, and interval since assignments, but distribution of these covariates was not re- ported.			
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic			
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.			
Domain 5: Analysis							

		•	continued from previous pa	ge	
Study Citation:	Benson, L. C Medicine 50	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716			
Health	Cancer/Carcinogenesis				
Outcome(s)					
Assessed:					
Reported Health	Pancreatic ca	ncer, lymphatic and haematopoietic cand	cer, Leukemia, lymphosarcoma	lymphoma, multiple myeloma	
Effect(s):					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:	200224 Link	ed HERO ID(s): 200224, 5447107			
Domain		Metric	Rating	Comments	
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.	
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.	
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.	
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit".	
Additional Comments:	None				
Overall Qualit	ty Detern	nination	Uninformative		

Study Citation: Health Outcome(s)	Benson, L. C Medicine 50 Cancer/Carc	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716. Cancer/Carcinogenesis					
Assessed: Reported Health Effect(s):	Pancreatic ca	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma					
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 200224 Linked HERO ID(s): 200224, 5447107						
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation						
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.			
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.			
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.			
Domain 2: Exposure Ch	naracterization						
Domain 2. Exposure er	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is pro- vided on exposure levels, and a JEM was not used.			
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.			
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and out- come was assessed beginning at that time.			
Domain 3: Outcome As	sessment						
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.			
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.			
Domain 4. Detential Co	nfounding / Vo	richility Control					
Domain 4. Potential Co	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar pe- riod, and interval since assignments, but distribution of these covariates was not re- ported.			
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic			
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.			
Domain 5: Analysis							

		•	continued from previous pa	ge	
Study Citation:	Benson, L. C Medicine 50	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716			
Health	Cancer/Carcinogenesis				
Outcome(s)					
Assessed:					
Reported Health	Pancreatic ca	ncer, lymphatic and haematopoietic cand	cer, Leukemia, lymphosarcoma	lymphoma, multiple myeloma	
Effect(s):					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:	200224 Link	ed HERO ID(s): 200224, 5447107			
Domain		Metric	Rating	Comments	
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.	
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.	
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.	
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit".	
Additional Comments:	None				
Overall Qualit	ty Detern	nination	Uninformative		

Study Citation: Health Outcome(s)	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716. Cancer/Carcinogenesis						
Assessed: Reported Health Effect(s):	Pancreatic ca	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma					
Chemical: HERO ID:	1,1-Dichloro 200224 Link	ethane- Isomer: 1,2-Dichloroethane ed HERO ID(s): 200224, 5447107					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	ipation						
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.			
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.			
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.			
Domain 2: Exposure Ch	naracterization						
Domain 2. Exposure er	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is pro- vided on exposure levels, and a JEM was not used.			
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.			
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and out- come was assessed beginning at that time.			
Domain 3: Outcome As	sessment						
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.			
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.			
Domain 4: Dotantial Ca	nfounding / Vo	rishility Control					
Domani 4: Potential Co	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar pe- riod, and interval since assignments, but distribution of these covariates was not re- ported.			
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic			
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.			
Domain 5: Analysis							

		•	continued from previous pa	ge	
Study Citation:	Benson, L. C Medicine 50	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716			
Health	Cancer/Carcinogenesis				
Outcome(s)					
Assessed:					
Reported Health	Pancreatic ca	ncer, lymphatic and haematopoietic cand	cer, Leukemia, lymphosarcoma	lymphoma, multiple myeloma	
Effect(s):					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:	200224 Link	ed HERO ID(s): 200224, 5447107			
Domain		Metric	Rating	Comments	
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.	
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.	
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.	
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit".	
Additional Comments:	None				
Overall Qualit	ty Detern	nination	Uninformative		

Study Citation: Health Outcome(s)	Citation: Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Jour Medicine 50(8):710-716. Cancer/Carcinogenesis me(s)				
Assessed: Reported Health Effect(s):	Pancreatic ca	ancer, lymphatic and haematopoietic cance	er, Leukemia, lymphosarcor	na, lymphoma, multiple myeloma	
Chemical: HERO ID:	1,1-Dichloro 200224 Link	ethane- Isomer: 1,2-Dichloroethane ed HERO ID(s): 200224, 5447107			
Domain		Metric	Rating	Comments	
Domain 1: Study Partic	ipation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.	
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.	
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.	
Domain 2: Exposure Cl	haracterization				
Domain 2. Exposure en	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is pro- vided on exposure levels, and a JEM was not used.	
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.	
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and out- come was assessed beginning at that time.	
Domain 3: Outcome As	sessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.	
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.	
Domain 4. Dotonti-1 C-	nfounding 1V-	riskility Control			
Domain 4. Potential Co	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar pe- riod, and interval since assignments, but distribution of these covariates was not re- ported.	
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic	
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.	
Domain 5: Analysis					

		•	continued from previous pa	ge		
Study Citation:	Benson, L. C Medicine 50	D., Teta, M. J. (1993). Mortality due to pa (8):710-716.	ncreatic and lymphopoietic can	cers in chlorohydrin production workers. British Journal of Industrial		
Health	Cancer/Carc	inogenesis				
Outcome(s)		0				
Assessed:						
Reported Health	Pancreatic ca	ncer, lymphatic and haematopoietic cand	cer, Leukemia, lymphosarcoma	lymphoma, multiple myeloma		
Effect(s):						
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	200224 Linked HERO ID(s): 200224, 5447107					
Domain		Metric	Rating	Comments		
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.		
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.		
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.		
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit".		
Additional Comments:	None					
Overall Quality Determination Uninformative						

Study Citation: Health Outcome(s)	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716. Cancer/Carcinogenesis							
Assessed: Reported Health Effect(s):	Pancreatic ca	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma						
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 200224 Linked HERO ID(s): 200224, 5447107							
Domain		Metric	Rating	Comments				
Domain 1: Study Partic	ipation							
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.				
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.				
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.				
Domain 2: Exposure Ch	naracterization							
Domain 2. Exposure er	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is pro- vided on exposure levels, and a JEM was not used.				
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.				
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and out- come was assessed beginning at that time.				
Domain 3: Outcome As	sessment							
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.				
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.				
Domain 4: Dotantial Ca	nfounding / Vo	rishility Control						
Domani 4: Potential Co	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar pe- riod, and interval since assignments, but distribution of these covariates was not re- ported.				
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic				
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.				
Domain 5: Analysis								

		•	continued from previous pa	ge		
Study Citation:	Benson, L. C Medicine 50	D., Teta, M. J. (1993). Mortality due to pa (8):710-716.	ancreatic and lymphopoietic can	cers in chlorohydrin production workers. British Journal of Industrial		
Health	Cancer/Carc	inogenesis				
Outcome(s)						
Assessed:						
Reported Health	Pancreatic ca	ancer, lymphatic and haematopoietic can	cer, Leukemia, lymphosarcoma	lymphoma, multiple myeloma		
Effect(s):						
Chemical:	1,1-Dichloro	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:	200224 Linked HERO ID(s): 200224, 5447107					
Domain		Metric	Rating	Comments		
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.		
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.		
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.		
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit".		
Additional Comments:	None					
Overall Quality Determination Uninformative						

Study Citation: Health Outcome(s)	Benson, L. O., Teta, M. J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716. Cancer/Carcinogenesis					
Assessed: Reported Health Effect(s):	Pancreatic ca	ancer, lymphatic and haematopoietic cance	er, Leukemia, lymphosarcor	na, lymphoma, multiple myeloma		
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 200224 Linked HERO ID(s): 200224, 5447107					
Domain		Metric	Rating	Comments		
Domain 1: Study Partic	ipation					
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.		
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.		
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.		
Domain 2: Exposure Cl	paracterization					
Domain 2. Exposure er	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is pro- vided on exposure levels, and a JEM was not used.		
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.		
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and out- come was assessed beginning at that time.		
Domain 3: Outcome As	sessment					
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.		
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.		
Demeir 4 Detential Ce		rishilita Contacl				
Domani 4: Potential Co	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar pe- riod, and interval since assignments, but distribution of these covariates was not re- ported.		
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic		
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.		
Domain 5: Analysis						

		•	continued from previous pa	ge		
Study Citation:	Benson, L. C Medicine 50	D., Teta, M. J. (1993). Mortality due to pa (8):710-716.	ncreatic and lymphopoietic can	cers in chlorohydrin production workers. British Journal of Industrial		
Health	Cancer/Carc	inogenesis				
Outcome(s)						
Assessed:						
Reported Health	Pancreatic ca	ncer, lymphatic and haematopoietic cand	cer, Leukemia, lymphosarcoma	lymphoma, multiple myeloma		
Effect(s):						
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	200224 Linked HERO ID(s): 200224, 5447107					
Domain		Metric	Rating	Comments		
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.		
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.		
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.		
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit".		
Additional Comments:	None					
Overall Quality Determination Uninformative						

Study Citation:	Carbide,, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated
Health	022189. Cancer/Carcinogenesis
Outcome(s)	
Assessed:	
Reported Health	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Effect(s):	
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5451581

Domain	Metric	Rating	Comments
Domain 1: Study Participation			
Metric 1	: Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
Metric 2	2: Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
Metric 3	: Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five- year survival period as cases. Controls survived at least to the beginning of the five- year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2. Europuna Chanastanizat	ion		
Domain 2: Exposure Characterizat Metric 4	Hon H: Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
Metric 5	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
Metric 6	b: Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the rele- vant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment			
Matria 7	. Outcome Measurement or	Madium	Case definition was based on death cortificate diagnosis; but no method validation was
Metric /	Characterization	Wearum	conducted against this well-established methods.
Metric 8	: Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).

Study Citation: Health Outcome(s)	Carbide,, Un 022189. Cancer/Carc	Carbide,, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189. Cancer/Carcinogenesis				
Assessed: Reported Health Effect(s):	Mortality fro	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma				
Chemical: HERO ID:	1,1-Dichloro 5451581	ethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
Domain 4: Potential Cor	nfounding / Va Metric 9:	riability Control Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.		
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.		
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.		
Domain 5: Analysis	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data anal- ysis included crude odds ratio and then stratified examination of odds ratios was con- ducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.		
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.		
	Metric 14: Metric 15:	Reproducibility of Analyses Statistical Analysis	Medium Low	Description was sufficient to be conceptually reproducible. Statistical model to calculate odds ratio was not described.		
Additional Comments:	This nested of chemical exp were not all (3) numbers described.	This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple themical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; 3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.				
Overall Qualit	y Detern	nination	Medium			

Study Citation:	Carbide,, Ui	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated					
Health	022189. Cancer/Carc	022189. Cancer/Carcinogenesis					
Outcome(s)							
Assessed:							
Reported Health	Mortality fro	om non-Hodgkin's lymphoma, non-lyn	nphocytic leukemia, ly	mphocytic leukemia, or multiple myeloma			
Effect(s):							
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	5451581						
Domain		Metric	Rating	Comments			
Domain 1: Study Parti	cipation						
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.			
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.			
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five- year survival period as cases. Controls survived at least to the beginning of the five- year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.			
Domain 2: Exposure (⁻ haracterization						
Domain 2. Exposure C	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.			
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.			
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.			
Domain 3: Outcome	ssassmant						
	Metric 7:	Outcome Measurement or	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods			
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).			
Domain 4: Potential C	Confounding / Va	riability Control		· · ·			
		(Continued on next pa	ge			

Study Citation: Health Outcome(s) Assessed:	Carbide,, Un 022189. Cancer/Carc	Carbide,, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189. Cancer/Carcinogenesis				
Reported Health	Mortality fro	om non-Hodgkin's lymphoma, non-lyn	nphocytic leukemia, ly	mphocytic leukemia, or multiple myeloma		
Effect(s):	1.1 Dichloro	othene Jaamer 1.2 Dickloreothene				
HERO ID:	5451581	ethane- isomer. 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.		
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.		
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.		
Domain 5: Analysis	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data anal- ysis included crude odds ratio and then stratified examination of odds ratios was con- ducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was		
	Metric 13:	Statistical Power	Low	conducted. Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2- dichlorectivelene exposure		
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.		
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.		
Additional Comments:	This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.					

Overall Quality Determination

Medium

Study Citation: Health	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189. Cancer/Carcinogenesis					
Outcome(s)		C				
Assessed:						
Reported Health	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma					
Effect(s):	1.1 Diablara	athana Jaamari 1.2 Diahlaraathana				
HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 5451581					
Domain		Metric	Rating	Comments		
Domain 1: Study Particip	pation					
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.		
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.		
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.		
Domain 2: Exposure Cha	aracterization					
Domain 2. Exposure end	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.		
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.		
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the rele- vant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.		
Domain 3: Outcome Ass	essment					
20main 5. Outcome Ass	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.		
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).		
Domain 4: Potential Con	founding / Var	iability Control		-		
	-	·	Continued on next pa	ge		

Study Citation: Health Outcome(s) Assessed:	Carbide,, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189. Cancer/Carcinogenesis			
Reported Health	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma			
Effect(s):	1.1. Dichloroethane, Isomer: 1.2. Dichloroethane			
HERO ID:	5451581			
Domain		Metric	Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data anal- ysis included crude odds ratio and then stratified examination of odds ratios was con- ducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was
				conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.
Additional Comments:	This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.			

Overall Quality Determination

Medium
Study Citation: Health	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189. Cancer/Carcinogenesis					
Outcome(s)		C				
Assessed:						
Reported Health	Mortality fro	m non-Hodgkin's lymphoma, non-ly	mphocytic leukemia, ly	mphocytic leukemia, or multiple myeloma		
Effect(s):	1.1 Diablara	athana Jaamary 1.2 Diablaraathana				
HERO ID:	5451581	ethane- isomer. 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
Domain 1: Study Particip	pation					
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.		
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.		
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.		
Domain 2: Exposure Cha	aracterization					
Domain 2. Exposure end	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.		
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.		
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the rele- vant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.		
Domain 3: Outcome Ass	essment					
20main 5. Outcome Ass	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.		
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).		
Domain 4: Potential Con	founding / Var	iability Control		-		
	-	·	Continued on next pa	ge		

Study Citation: Health Outcome(s) Assessed:	Carbide,, Un 022189. Cancer/Carc	Carbide,, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189. Cancer/Carcinogenesis				
Reported Health	Mortality fro	om non-Hodgkin's lymphoma, non-lyn	nphocytic leukemia, ly	mphocytic leukemia, or multiple myeloma		
Effect(s):	-					
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane				
HERO ID:	5451581					
Domain		Metric	Rating	Comments		
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.		
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.		
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.		
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data anal- ysis included crude odds ratio and then stratified examination of odds ratios was con- ducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.		
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.		
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.		
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.		
Additional Comments:	This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described					

Overall Quality Determination

Medium

_

Study Citation:	Dosemeci, M., Cocco, P., Chow, W. H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic				
	hydrocarbon	s. American Journal of Industrial Medicin	e 36(1):54-59.		
Health	Cancer/Carc	inogenesis			
Outcome(s)					
Assessed:					
Reported Health	renal cell car	cinoma			
Effect(s):					
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane			
HERO ID:	4697224				
Domain		Metric	Rating	Comments	
Domain 1: Study Partici	pation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).	
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors re- ferred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food- frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control sub- jects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.	
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.	
Domain 2: Exposure Ch	aracterization Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).	
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.	

		co	ntinued from previo	ous page
Study Citation: Health Outcome(s)	Dosemeci, M hydrocarbon Cancer/Carc	A., Cocco, P., Chow, W. H. (1999). Ge s. American Journal of Industrial Medic inogenesis	ender differences in a cine 36(1):54-59.	risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic
Assessed: Reported Health Effect(s):	renal cell car	rcinoma		
Chemical: HERO ID:	1,1-Dichloro 4697224	ethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome As	ssessment			
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carci- noma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Co	onfounding / Va	riability Control		
Domain 4. 1 otontiar ee	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smok- ing, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes po- tential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evalu- ated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

continued from previous page				
Study Citation:	Dosemeci, M., Cocco, P., Chow, W. H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.			
Health	Cancer/Carcinogenesis			
Outcome(s)				
Assessed:				
Reported Health	renal cell carcinoma			
Effect(s):				
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane			
HERO ID:	4697224			
Domain	Metric Rating Comments			
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with			
	renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general			
	population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal			
	cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.			

Overall Quality Determination

Medium

Study Citation: Health Outcome(s) Assessed:	Garcia, E., H Environmen Cancer/Carc	Iurley, S., Nelson, D. O., Hertz, A., tal Health 14(1):14. inogenesis	Reynolds, P. (2015).	Hazardous air pollutants and breast cancer risk in California teachers: A cohort study.
Reported Health	breast cancer	r in females		
Effect(s): Chemical: HERO ID:	1,1-Dichloro 3014082	ethane- Isomer: 1,2-Dichloroethar	ie	
Domain		Metric	Rating	Comments
Domain 1: Study Partici	pation Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Ch	aracterization			
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome As	sessment			
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
			Continued on nex	t page

		•••	continued from p	revious page		
Study Citation: Health Outcome(s) Assessed:	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14. Cancer/Carcinogenesis					
Reported Health	breast cancer	r in females				
Chemical: HERO ID:	1,1-Dichloro 3014082	ethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.		
Domain 4: Potential Co	onfounding / Va	riability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.		
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.		
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.		
D . 5 A 1 .						
Domain 5: Analysis	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.		
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large co-hort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.		
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.		
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. "No apparent viola- tion of the underlying assumption of proportional hazards was detected".		
			Continued on nex	t page		

		continued from previous page)		
Study Citation:	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14.				
Health	Cancer/Carcinogenesis				
Outcome(s)					
Assessed:					
Reported Health	breast cancer in females				
Effect(s):					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroe	thane			
HERO ID:	3014082				
Domain	Metric	Rating	Comments		
Additional Comments:	A group of 112,378 female participants fro including ethylene dichloride (1,2-dichloro US EPA NATA and the ASPEN and HEM from Figure 1). Exposures were categorize for invasive breast cancer was observed wi Quintile 1, or when further adjusted using r	om the California Teacher Study coh- ethane), and the incidence of invasive models. The approximate median co ed into 5 Quintiles, and compared aga ith Quintile 2-5 exposure estimates for nultiple comparisons.	ort were assessed for their estimated exposure to ambient air pollutants, breast cancer. Air contaminant concentrations were estimated using the concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated inst Quintile 1. No significant increase in the estimated hazard rate ratio or 1,2-dichloroethane, adjusted for age and race, when compared against		
Overall Qualit	ty Determination	High			

_

_

	study based	on death certificates from 24 U.S. states	American Iou	Kernan, G. J., Ji, B. T., Dosemeci, M., Silverman, D. T., Balbus, J., Zahm, S. H. (1999). Occupational risk factors for pancreatic cancer: A case-control attudy based on doth cartifactors from 24 U.S. attaca. American Jaureal of Judystrial Medicine 26(2):260–270.				
Health	Cancer/Carcinogenesis							
Outcome(s)	cunter, cure	in geneous						
Assessed:								
Reported Health	Death from	nancreatic cancer						
Fffect(s).	Death Hom							
Chemical:	1 1-Dichlore	ethane-Isomer: 1.2-Dichloroethane						
HERO ID.	194820	entitie isomer. 1,2 Diemoroentalie						
Domain	191020	Matric	Dating	Comments				
Domain 1: Study Partic	instion	Metric	Katilig	Comments				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported				
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.				
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.				
Domain 2: Exposure Cl	horostarization							
Domain 2. Exposure Ci	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job ma- trix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates				
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).				
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.				
Domain 3: Outcome As	sessment							
Domain 5. Outcome As	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and con- trols. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.				
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.				

Page 81 of 138

Study Citation:	Kernan, G. J	I., Ji, B. T., Dosemeci, M., Silverman,	, D. T., Balbus, J.	, Zahm, S. H. (1999). Occupational risk factors for pancreatic cancer: A case-control rnal of Industrial Medicine 36(2):260-270.					
Health	Cancer/Carcinogenesis								
Outcome(s) Assessed:									
Reported Health	Death from	pancreatic cancer							
Effect(s):	115:11								
Chemical: HERO ID:	1,1-Dichloro 194820	bethane- Isomer: 1,2-Dichloroethane							
Domain		Metric	Rating	Comments					
Domain 4: Potential Cor	nfounding / Va	riability Control							
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.					
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an ad- equate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.					
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co- exposures.					
Domain 5: Analysis									
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.					
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = $63,097$; n for controls = $252,386$).					
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.					
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.					
Additional Comments:	This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupa- tion/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.								
Overall Qualit	y Deterr	nination	High						

Study Citation:	Niehoff, N. M., Gammon, M. D., Keil, A. P., Nichols, H. B., Engel, L. S., Sandler, D. P., White, A. J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health	Cancer/Carcinogenesis
Outcome(s)	
Assessed:	
Reported Health	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Effect(s):	
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	5440630

Domain	Metric	Rating	Comments				
Domain 1: Study Participation							
Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages $35-74$ at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.				
Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.				
Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confound- ing variables.				
Domain 2: Exposure Characterization	l						
Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."				
Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.				
Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later. The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.				

		••	continued from previo	ous page		
Study Citation:	Niehoff, N. cancer risk i	Niehoff, N. M., Gammon, M. D., Keil, A. P., Nichols, H. B., Engel, L. S., Sandler, D. P., White, A. J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.				
Dutcome(s)	Cancer/Carc	Cancer/Carcinogenesis				
Reported Health Effect(s):	Breast cance	r diagnosis (overall), tumor characte	eristics, and estrogen rece	eptor positive (ER+) invasive breast cancer		
Chemical: HERO ID:	1,1-Dichloro 5440630	ethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
Domain 3: Outcome As	sessment Metric 7:	Outcome Measurement or	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-		
		Characterization		up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self- reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were ab- stracted from medical records, or self-reported.		
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.		
Domain 4: Potential Co	nfounding / Va	riability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.		
	Metric 10:	Covariate Characterization	Medium	"Most covariates were assessed by self-report at the baseline interview.""At baseline, women completed a computer-assisted telephone interview and written question- naires."Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.		
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.		
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.		
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).		
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.		
Continued on next page						

			continued from previo	bus page	
Study Citation:	Niehoff, N. I cancer risk in	Niehoff, N. M., Gammon, M. D., Keil, A. P., Nichols, H. B., Engel, L. S., Sandler, D. P., White, A. J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.			
Health	Cancer/Carc	inogenesis			
Outcome(s)					
Assessed:	_				
Reported Health	Breast cance	er diagnosis (overall), tumor charac	eteristics, and estrogen reco	eptor positive (ER+) invasive breast cancer	
Effect(s):	44.5.11				
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERO ID:	5440630				
Domain		Metric	Rating	Comments	
	Metric 15:	Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index cate- gories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evalu- ated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.	
Additional Comments:	This was a v limitation.	well-conducted study of a large pr	ospective cohort, but the	measurement of exposure at the census-tract rather than the individual level is a	
Overall Qualit	y Detern	nination	Medium		

Study Citation: Health Outcome(s)	Sobel, W., E manufacturii Cancer/Carc	Sobel, W., Bond, G. G., Skowronski, B. J., Brownson, P. J., Cook, R. R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099. Cancer/Carcinogenesis					
Reported Health	soft-tissue sa	soft-tissue sarcoma					
Effect(s):							
Chemical: HERO ID:	1,1-Dichloro 1357737	ethane- Isomer: 1,2-Dichloroethane					
Domain		Metric	Rating	Comments			
Domain 1: Study Partici	pation						
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).			
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.			
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥ 1 yr at the plant during the study period.			
Domain 2: Exposure Ch	aracterization						
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.			
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.			
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.			
Domain 3: Outcome As	sessment						
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certifi- cates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.			
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.			
Domain 4: Potential Co	nfounding / Va	riability Control					
		Cor	ntinued on next pa	ge			

	continued from previous page					
Study Citation: Health Outcome(s) Assessed:	Sobel, W., I manufacturi Cancer/Carc	Sobel, W., Bond, G. G., Skowronski, B. J., Brownson, P. J., Cook, R. R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099. Cancer/Carcinogenesis				
Reported Health	soft-tissue s	arcoma				
Effect(s):						
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane				
HERO ID:	1357737					
Domain		Metric	Rating	Comments		
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential con- founders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, for- eign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.		
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.		
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.		
Demain 5. Analasia						
Domain 5: Analysis	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the out- come of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statis- tical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).		
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.		
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.		
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.		
Additional Comments:	A case-cont	rol study of workers at a chemical produc	tion facility who wo	rked at least 1 year between January 1940-December 1979 (n-37 000) investigated		

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination

Medium

	co	ntinued from previous page	
Study Citation:	Sobel, W., Bond, G. G., Skowronski, B. J., Brown manufacturing facility. Chemosphere 16(8-9):2095-2	nson, P. J., Cook, R. R. (1987 2099.). A soft tissue sarcoma case control study in a large multi-chemical
Health	Cancer/Carcinogenesis		
Outcome(s)			
Assessed:			
Reported Health	soft-tissue sarcoma		
Effect(s):			
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane		
HERO ID:	1357737		
Domain	Metric	Rating	Comments

Study Citation: Health Outcome(s)	Kernan, G. J study based Endocrine	, Ji, B. T., Dosemeci, M., Silverman on death certificates from 24 U.S. stat	, D. T., Balbus, J., es. American Jour	, Zahm, S. H. (1999). Occupational risk factors for pancreatic cancer: A case-control rnal of Industrial Medicine 36(2):260-270.	
Assessed: Reported Health Effect(s):	Death from J	pancreatic cancer			
Chemical: HERO ID:	1,1-Dichloro 194820	ethane- Isomer: 1,2-Dichloroethane			
Domain		Metric	Rating	Comments	
Domain 1: Study Partic	cipation		TT: 1		
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.	
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.	
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.	
Domain 2: Exposure C	haracterization Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job ma- trix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.	
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).	
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.	
Domain 3: Outcome A	ecocomont				
Johan J. Outonit A	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and con- trols. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.	
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.	
Continued on next page					

Study Citation:	Kernan, G. J	J., Ji, B. T., Dosemeci, M., Silverman	, D. T., Balbus, J.	Zahm, S. H. (1999). Occupational risk factors for pancreatic cancer: A case-control		
Health Outcome(s)	study based Endocrine	study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270. Endocrine				
Assessed: Reported Health Effect(s):	Death from	pancreatic cancer				
Chemical: HERO ID:	1,1-Dichloro 194820	bethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
Domain 4: Potential Co	nfounding / Va	riability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.		
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an ad- equate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.		
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co- exposures.		
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.		
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = $63,097$; n for controls = $252,386$).		
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.		
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.		
Additional Comments:	This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupa- tion/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.					
Overall Qualit	ty Deterr	nination	High			

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s):	BASF, (2005 study of emp number: 8EF Reproductive Prostate canc	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Reproductive/Developmental Prostate cancer				
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane				
Domain	0370017 Em	Metric	Rating	Comments		
Domain 1: Study Partici	pation					
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.		
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.		
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.		
Domain 2 [.] Exposure Ch	aracterization					
2000000	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.		
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unex- posed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).		
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.		

Study Citation: I Study Citation: I Health I Outcome(s) Assessed: Reported Health I	BASF, (2005 study of emp number: 8EH Reproductive Prostate canc 1,1-Dichloroo). Letter: Subject: Supplemental info oloyees assigned to a BASF Corporatio IQ-02-15135). //Developmental	rmation regarding pr on former chemical r	ior TSCA Section 8(e) submission - Preliminary results from a cancer incidence nanufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control					
Outcome(s) Assessed: Reported Health	Prostate canc	er							
Assessed: Reported Health	Prostate canc	er							
Reported Health	Prostate canc	rer							
	1,1-Dichloro								
Effect(s):	1,1-Dichloro								
Unemical:	(F70017 T ·)	ethane- Isomer: 1,2-Dichloroethane							
HEROID:	65/001/Lin	ked HERO ID(s): 65/0017, 65/0014							
Domain		Metric	Rating	Comments					
Domain 3: Outcome Asses	ssment								
I	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Can- cer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.					
I	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.					
Domain 4: Dotantial Confe	ounding / Vor	ishility Control							
Domain 4: Potential Conic	Sunding / Var	Coverists A divetment	Iliah						
1	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gen- der, and race.					
I	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gen- der, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.					
I	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.					
Domain 5: Analysis									
Domani J. Analysis	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.					
I	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.					
I	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on par- ticipant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.					
1	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.					

Page 92 of 138

Study Citation:	BASF, (2005). Letter: Subject: Supplemental inform study of employees assigned to a BASF Corporation number: 8EHQ-02-15135).	nation regarding prior TSC 1 former chemical manufac	A Section 8(e) submission - Preliminary results from a cancer incidence turing unit in Geismar, LA that ceased operations in 1987 (EPA Control
Health	Reproductive/Developmental		
Outcome(s)			
Assessed:			
Reported Health	Prostate cancer		
Effect(s):			
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane		
HERO ID:	6570017 Linked HERO ID(s): 6570017, 6570014		
Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer	incidence among employe	es who worked in a chemical manufacturing unit, compared to expected
	deaths among the U.S. population and expected can	cers among the South Lou	isiana population. The study found lower death rates among employees
	compared to the U.S. population. Observed cancer inc	idence was generally highe	r than expected although the study did not consistently present information
	on statistical significance. The exposure measureme	ant approach was limited to	a sesignment based on job history with no quantitative measurement of
	on statistical significance. The exposure measureme	a stada da i su and an alaria	assignment based on job mistory, with no quantitative measurement of
	exposure. Detailed information on most aspects of the	e study design and analysis	was not provided.
Overall Ouali	ty Determination	Medium	
	- J		

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical:	Bove, F. J. (12(2):255-26 Reproductive Fetal growth death (>20 v (total cardiac 1,1-Dichloro	 Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266. Reproductive/Developmental Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects. 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 			
HERO ID:	200239 Link	ed HERO ID(s): 194932, 200239			
Domain		Metric	Rating	Comments	
Domain 1: Study Partici	pation		Madian		
	Metric 1:	Participant Selection	Medium	tal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 coun- ties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection bias.	
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.	
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the po- tential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.	
Domain 2: Exposure Ch	aracterization				

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical:	 Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266. Reproductive/Developmental Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects. 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 			
Domain	200239 Lini	Metric	Rating	Comments
Domain	Metric 4: Metric 5:	Measurement of Exposure Exposure Levels	Medium	Along with several other contaminants, residential drinking water exposure to 1,2- dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calcu- lated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detec- tion limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; un- known levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random. Due to the high proportion of measures below detection limits, analyses relating expo-
				sure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥ 1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
Derreiz 2: Octore - A	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Study Citation: Health Outcome(s) Assessed: Reported Health	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266. Reproductive/Developmental					
Effect(s): Chemical: HERO ID:	death (>20 (total cardiad 1,1-Dichloro 200239 Link	weeks' gestation)-Congenital anomalies: (i c, major cardiac, ventricular septum defects ethane- Isomer: 1,2-Dichloroethane ed HERO ID(s): 194932, 200239) nervous system); and (iv) any su	a (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular rveillance defect excluding chromosomal defects.		
Domain		Metric	Rating	Comments		
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.		
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables in- cluded only associations with odds ratios \geq 1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without con- fidence intervals), but no null/negative odds ratios were presented or described.		
Domain 4: Potential Co.	nfounding / Vo	rishility Control				
Johnani 4. Fotentiai Co	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.		
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.		
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was eval- uated. There was no evidence to suggest substantial confounding by this or other co- exposures.		

Domain 5: Analysis

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical: HERO ID:	 Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266. Reproductive/Developmental Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects. 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 200239 Linked HERO ID(s): 194932, 200239 				
Domain		Metric	Rating	Comments	
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.	
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small propor- tion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for ele- vated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.	
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥ 1.5 .	
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using ade- quate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.	

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2dichloroethane (as well as 1,1,1-trichloroethane; \sum [trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination

Medium

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical: HERO ID:	 Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862. Reproductive/Developmental Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects. 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 194932 Linked HERO ID(s): 194932, 200239 				
Domain		Metric	Rating	Comments	
Domain 1: Study Partici	pation Metric 1: Metric 2:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.	
	incure 2.			multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.	
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the po- tential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.	
Domain 2: Exposure Ch	aracterization				

		contin	nued from previo	bus page	
Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical: HERO ID:	 Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862. Reproductive/Developmental Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects. 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 194932 Linked HERO ID(s): 194932, 200239 				
Domain		Metric	Rating	Comments	
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2- dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were cal- culated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water sys- tems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation ex- posure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.	
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating expo- sure to health outcomes used only 2 categories for each of the three chemicals of inter- est: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene \geq 1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.	
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.	

Domain 3: Outcome Assessment

		co	ntinued from previ	ous page			
Study Citation: Health Outcome(s) Assessed:	Bove, F. J., American Jo Reproductiv	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862. Reproductive/Developmental					
Reported Health	Fetal growth	and development: -Birthweight (term b	irths), low birthweigh	nt (term births), very low birthweight, small for gestational age-Preterm birth-Fetal			
Effect(s):	death (>20	weeks' gestation)-Congenital anomalies	s: (i) nervous system	(central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular			
	(total cardia	c, major cardiac, ventricular septum defe	ects); and (iv) any su	rveillance defect excluding chromosomal defects.			
Chemical:	1,1-Dichloro	bethane- Isomer: 1,2-Dichloroethane					
HERO ID:	194932 Lini	ted HERO ID(s): 194932, 200239					
Domain		Metric	Rating	Comments			
	Metric 7: Metric 8:	Outcome Measurement or Characterization Reporting Bias	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.			
	Metric 8:	Reporting blas	Low	Models were constructed only for contaminants with associations > 1.0, and tables in- cluded only associations with odds ratios ≥ 1.5 . No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without con- fidence intervals), but no null/negative odds ratios were presented or described.			
Domain 4: Potential Co	onfounding / Va	riability Control					
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.			
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.			
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was eval- uated. There was no evidence to suggest substantial confounding by this or other co- exposures.			
Domain 5: Analysis							

		co	ntinued from previo	ous page			
Study Citation: Health Outcome(s) Assessed:	Bove, F. J., American Jo Reproductive	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862. Reproductive/Developmental					
Reported Health Effect(s):	Fetal growth death (>20 y	and development: -Birthweight (term bi weeks' gestation)-Congenital anomalies	rths), low birthweigh : (i) nervous system	at (term births), very low birthweight, small for gestational age-Preterm birth-Fetal (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular			
Chemical: HERO ID:	(total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects. 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 194932 Linked HERO ID(s): 194932, 200239						
Domain		Metric	Rating	Comments			
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.			
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small propor- tion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for ele- vated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).			
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥ 1.5 .			
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.			

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the \sum [trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination

Medium

Study Citation:	Brender, J. D., Shinde, M. U., Zhan, F. B., Gong, X., Langlois, P. H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health 13(1):96.
Health	Reproductive/Developmental
Outcome(s)	
Assessed:	
Reported Health	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Effect(s):	
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	2799700

Domain	Metric	Rating	Comments	
Domain 1: Study Participation				
Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996- 2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.	
Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.	
Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.	
Domain 2: Exposure Characterization				
Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emit- ted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.	
Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group	
Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evalu- ated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the preg- nancy, the temporality is unknown.	
Domain 3: Outcome Assessment				
Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diag- nosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services	
Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect	
Domain 4: Potential Confounding / Variability Control				

Study Citation: Health Outcome(s) Assessed: Reported Health	Brender, J. D., Shinde, M. U., Zhan, F. B., Gong, X., Langlois, P. H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health 13(1):96. Reproductive/Developmental					
Effect(s):	1 1 Dishlara	ethene. Leaven 1.2 Disklassethene				
HERO ID:	1,1-Dichloro 2799700	setnane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non- Hispanic).		
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information		
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described		
Domain 5: Analysis						
Domain 5. 7 marysis	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects		
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.		
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility		
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.		
Additional Comments:	This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.					
Overall Qualit	ty Detern	nination	High			

_

Study Citation:	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study.						
Health	Environment Reproductive	Environmental Health 14(1):14. Reproductive/Developmental					
Outcome(s)	1	I I I I I I I I I I I I I I I I I I I					
Assessed:							
Reported Health Effect(s).	breast cancer	in females					
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane					
HERO ID:	3014082						
Domain		Metric	Rating	Comments			
Domain 1: Study Particip	pation						
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.			
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the pur- pose of the study and analysis. Exclusion criteria were documented. Included partici- pants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.			
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.			
Domain 2: Exposure Ch	aracterization						
2 oniun 21 2npoonto oni	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.			
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.			
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.			
Domain 3: Outcome Ass	sessment						
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.			
			Continued on nex	t page			

		c	ontinued from p	revious page
Study Citation:	Garcia, E., H Environment	lurley, S., Nelson, D. O., Hertz, A., Re al Health 14(1):14.	ynolds, P. (2015).	Hazardous air pollutants and breast cancer risk in California teachers: A cohort study.
Health Outcome(c)	Reproductive	e/Developmental		
Assessed:				
Reported Health Effect(s):	breast cancer	r in females		
Chemical: HERO ID:	1,1-Dichloro 3014082	ethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 1: Potential Co	nfounding / Va	rightlity Control		
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
D . 5 A 1 .				
Domain 5: Analysis	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large co-hort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. "No apparent viola- tion of the underlying assumption of proportional hazards was detected".
			Continued on nex	t page

		continued from previous page				
Study Citation:	Garcia, E., Hurley, S., Nelson, D. O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health 14(1):14.					
Health	Reproductive/Developmental					
Outcome(s)						
Assessed:						
Reported Health	breast cancer in females					
Effect(s):						
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroet	thane				
HERO ID:	3014082					
Domain	Metric	Rating	Comments			
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.					
Overall Qualit	ty Determination	High				

Study Citation:	Cheng, T. J., Huang, M. L., You, N. C., Du, C. L., Chau, T. T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.						
Health	Hepatic/Liver	· · · · · · · · · · · · · · · · · · ·	, ,				
Outcome(s)							
Assessed:							
Reported Health	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).						
Effect(s):							
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane						
HERO ID:	200266						
Domain	Metric	Rating	Comments				
Domain 1. Study Part	icination						

Domain		Metric	Rating	Comments			
Domain 1: Study Pa	rticipation						
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufactur- ing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.			
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.			
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.			
Domain 2: Exposure	e Characterization						
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sam- pling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or per- sonal sampling were not reported.			
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.			
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.			
Domain 3: Outcome	Assessment						
Domain 5. Outcome	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.			
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.			
Domain 4: Potential	Confounding / Va	riability Control					
	Continued on next page						
۸ ×							

continued from previous page							
Study Citation: Health Outcome(s)	Cheng, T. J., Huang, M. L., You, N. C., Du, C. L., Chau, T. T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133. Hepatic/Liver						
Assessed: Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).						
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 200266						
Domain		Metric	Rating	Comments			
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.			
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.			
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.			
D							
Domain 5: Analysis	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest ("markers of liver damage"). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.			
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.			
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.			
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.			
Domain 6: Other (if applicable) Considerations for Diamerican Solution and Macananant (Labird et al. 2014)							
Domain 0. Other (if app	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed			
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y- glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.			
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.			
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.			
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.			
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked			

Page 108 of 138

immunosorbent assay.
		•••	. continued from previo	bus page	
Study Citation:	Cheng, T. J., Huang, M. L., You, N. C., Du, C. L., Chau, T. T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.				
Health	Hepatic/Live	er			
Outcome(s)					
Assessed:					
Reported Health	AST, ALT, C	GGT, Hepatitis B virus surface antige	n (HBsAg), and anti-he	patitis C virus antibody (anti-HCV).	
Effect(s):		-			
Chemical:	1.1-Dichloroethane- Isomer: 1.2-Dichloroethane				
HERO ID:	200266				
Domain		Metric	Rating	Comments	
	Metric 22:	Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.	
Additional Comments:	A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.				
Overall Qualit	ty Deterr	nination	Medium		

Study Citation: Health Outcome(s)	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Mortality					
Assessed:						
Reported Health	All-cause mo	ortality				
Effect(s):	1.1 Dichloro	athana Isomar: 1.2 Dichloroathana				
HERO ID:	6570017 Lin	ked HERO ID(s): 6570017, 6570014				
Domain		Metric	Rating	Comments		
Domain 1: Study Partici	pation	Wette	Rating	Comments		
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.		
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.		
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appro- priate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.		
Domain 2: Exposure Ch	aracterization					
Domain 2. Exposure en	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.		
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also com- pared to the unexposed general population.		
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.		

Page 110 of 138

Study Citation:	BASF, (2005 study of emp number: 8EF	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHO-02-15135)				
Health	Mortality					
Outcome(s)	-					
Assessed:						
Reported Health	All-cause mo	ortality				
Effect(s):						
Chemical:	1,1-Dichloro	ethane- Isomer: 1,2-Dichloroethane				
HERO ID:	6570017 Lin	ked HERO ID(s): 6570017, 6570014				
Domain		Metric	Rating	Comments		
Domain 3: Outcome Ass	sessment					
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the ex- posed population or in the comparison population; use of death certificates is implied but not stated.		
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.		
Domain 4: Potential Cor	nfounding / Va	riability Control				
Domain 4. 1 Otential Col	Metric 9.	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender		
	Weule 9.	Covariate / Kejustinent	Weddulli	Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.		
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gen- der) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.		
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.		
Domain 5. Analysis						
Domain 5: Analysis	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.		
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.		
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on par- ticipant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.		
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.		
		(Continued on next pag	ge		

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health	Mortality
Outcome(s)	
Assessed:	
Reported Health	All-cause mortality
Effect(s):	
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	6570017 Linked HERO ID(s): 6570017, 6570014
Domain	Metric Rating Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected
	deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees
	compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information
	on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of
	exposure Detailed information on most aspects of the study design and analysis was not provided
	exposure. Detailed information on most aspects of the study design and analysis was not provided.
Overall Qualit	ty Determination Medium

Study Citation:	Teta, M. J., facility Jour	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51						
Health	Mortality	nai of occupational wedenic 55(1).+5	-51.					
Outcome(s) Assessed:								
Reported Health	all cause mo	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer						
Effect(s):	mortality, bra	nortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.						
Chemical: HERO ID:	1,1-Dichloro 200633 Link	bethane- Isomer: 1,2-Dichloroethane ted HERO ID(s): 200633, 1629047						
Domain		Metric	Rating	Comments				
Domain 1: Study Partici	pation							
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.				
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.				
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.				
Domain 2: Exposure Ch	aracterization							
Domain 2. Exposure en	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.				
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.				
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.				
Domain 3: Outcome Ass	sessment							
Domain 5. Outcome rist	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.				
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.				
Domain 4: Potential Cor	nfounding / Va	riability Control						
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.				
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a vali- dated method, but there was no evidence to suggest it was an invalid method.				
Continued on next page								

Page 113 of 138

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical: HERO ID:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51. Mortality all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality. 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments	
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.	
Domain 5: Analysis	Metric 12: Metric 13: Metric 14: Metric 15:	Study Design and Methods Statistical Power Reproducibility of Analyses Statistical Analysis	High Medium Low High	This study design was appropriate for the research question. Authors utilized retro- spective occupational cohort data to determine standardized mortality rates for cancer- specific mortalities. While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates. Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided. No issues identified.	
Additional Comments:	This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.				

Study Citation: Health Outcome(s)	Sobel, W., E manufacturin Skin and Co	Bond, G. G., Skowronski, B. J., Browns ng facility. Chemosphere 16(8-9):2095-20 nnective Tissue	on, P. J., Cook, R.)99.	R. (1987). A soft tissue sarcoma case control study in a large multi-chemical
Reported Health	soft-tissue sa	rcoma		
Effect(s):	1 1 D:-11	-theme. Learners 1.2 Disklaus theme		
HERO ID:	1357737	ethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
Domain 1: Study Partici	pation			
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥ 1 yr at the plant during the study period.
Domain 2: Exposure Ch	aracterization			
r	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome As	sessment			
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certifi- cates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Co	nfounding / Va	riability Control		
		Cor	ntinued on next pa	ge

		co	ontinued from previ	ous page
Study Citation: Health Outcome(s) Assessed:	Sobel, W., I manufacturi Skin and Co	Bond, G. G., Skowronski, B. J., Brown ng facility. Chemosphere 16(8-9):2095- nnective Tissue	1son, P. J., Cook, R. 2099.	. R. (1987). A soft tissue sarcoma case control study in a large multi-chemical
Reported Health	soft-tissue sa	arcoma		
Chemical: HERO ID:	1,1-Dichloro 1357737	bethane- Isomer: 1,2-Dichloroethane		
Domain		Metric	Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential con- founders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, for- eign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
Domani J. Anarysis	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the out- come of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice refer- ence appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.
Additional Commonta	A agos contr	nal atudu of montrons at a abamical muadu	ation facility who was	wheel at least 1 years between January 1040 December 1070 (r - 27 000) investigated

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination

Medium

	•	continued from previous page	
Study Citation:	Sobel, W., Bond, G. G., Skowronski, B. J., Br manufacturing facility. Chemosphere 16(8-9):20	rownson, P. J., Cook, R. R. (1987). 095-2099.	A soft tissue sarcoma case control study in a large multi-chemical
Health	Skin and Connective Tissue		
Outcome(s)			
Assessed:			
Reported Health	soft-tissue sarcoma		
Effect(s):			
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane	e	
HERO ID:	1357737		
Domain	Metric	Rating	Comments

Study Citation: Health Outcome(s) Assessed:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504. Other (sick building syndrome)						
Reported Health Effect(s):	The statistic building syn	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only					
Chemical: HERO ID:	1,1-Dichloro 1938385	ethane- Isomer: 1,2-Dichloroethane					
Domain		Metric	Rating	Comments			
Domain 1: Study Partic	eipation Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.			
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.			
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all ex- posure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statisti- cal analysis.			
Domain 2: Exposure C	haracterization						
-	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.			
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.			
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past ("since they moved into their flats") and their association with sampling conducted during the study; thus, exposure was measured after the outcome.			
Domain 3: Outcome A	ssessment						
2 sham 5. Sutome A	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.			
			Continued on next page	•			

		••	. continued from previous	s page				
Study Citation: Health Outcome(s) Assessed:	Guo, P., Yok pollution in Other (sick l	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504. Other (sick building syndrome)						
Reported Health Effect(s):	The statistic building syn one form 3 y	al analysis considers all subjective self-r drome. The study compared two condition was completed.	eported symptoms togetheons for each studied chemi	er (not segregated by health outcome) as a group health outcome –sick cal: combined self-reported symptoms to no symptoms. Therefore, only				
Chemical: HERO ID:	1,1-Dichloro 1938385	bethane-Isomer: 1,2-Dichloroethane						
Domain		Metric	Rating	Comments				
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).				
Domain 4: Potential C	Confounding / Va	riability Control						
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.				
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).				
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.				
Domain 5 [.] Analysis								
2 5.1111 5. 7 1111 515	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.				
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.				
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.				
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.				
			~					

	•	continued from previous page				
Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian. China. International Journal of Environmental Research and Public Health 10(4):1489-1504.					
Health	Other (sick building syndrome)					
Outcome(s)						
Assessed:						
Reported Health	The statistical analysis considers all subjective self-	-reported symptoms together (not segre	egated by health outcome) as a group health outcome -sick			
Effect(s):	building syndrome. The study compared two condition	ions for each studied chemical: combin	ed self-reported symptoms to no symptoms. Therefore, only			
	one form 3 was completed.					
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane					
HERO ID:	1938385					
Domain	Metric	Rating	Comments			
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethar	ne), HCHO, and NO2 were measured in	the 59 homes of families that agreed to participate after being			
	informed of the nature of the study. Participants comp	pleted questionnaires asking about symp	otoms since they moved into the homes and the concentrations			
	of selected compounds were compared among men a	and women reporting any symptoms vs r	no symptoms. Concentrations of 1,2-dichloroethane in homes			
	of people with symptoms were higher than in homes	without. p-Dichlorobenzene was measu	red in the homes as well, but median concentration was <dl< td=""></dl<>			
	and no further analysis was made. Unacceptable du	ue to selection bias, lack of confoundin	ng control, inadequate outcome characterization, and lack of			
	temporality.					

Overall Quality Determination

Uninformative

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s):	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Renal/Kidney Urinary system cancer			
Chemical: HERO ID:	1,1-Dichloro 6570017 Lin	ethane- Isomer: 1,2-Dichloroethane ked HERO ID(s): 6570017, 6570014		
Domain		Metric	Rating	Comments
Domain 1: Study Partici	pation			
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Ch	aracterization			
2 oninin 21 2.ipoono on	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unex- posed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.

Study Citation: BASF. (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cance study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (f number: 8EHQ-Q2-15135). Health Dottome(s) Assessed: Reported Health Effect(s): Urinary system cancer Effect(s): 1.1-Dichloroethane- Isomer: 1.2-Dichloroethane Domain Metric Metric Domain 3: Outcome Assessment Metric Metric 7: Outcome Measurement or Characterization Characterization Course operation of the study did not state if or how this difference in follow-up length varied by exposure j cer cases among employees were assessed using "self-report by employees vere followed for cancer through 303, while on cancer in the South Louisiana oppulation via the registry were only ava analysis. Metric 8: Reporting Bias Medium All of the outcomes described in the introduction are reported. Numbers or versus expected cancers are reported, but SIRs and 95% confidence interve sistently reported. Domain 4: Potential Confounding / Variability Control Metric 10: Metric 11: Covariate Characterization Medium Metric 11: Covariate Characterization Medium Metric 11: Covariate Characterization	er incidence PA Control
Outcome(s) Assessed: Reported Health Urinary system cancer Effect(s): Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane HERO ID: 6570017 Linked HERO ID(s): 6570017, 6570014 Comments Domain 3: Outcome Assessment Metric Rating Comments Domain 3: Outcome Assessment Low Outcome measurement methods and follow-up length varied by exposure 1 Characterization Spouses, and fluxogh death certificates," Cancer cases in the general popul Louisiana (used as a comparison population) were assertanced through the treditoring and through death certificates," Cancer cases in the general popul Louisian population via the registry were only ava 2000; the study did not state if or how this difference in follow-up time wa analysis. Metric 8: Reporting Bias Medium All of the outcomes described in the introduction are reported. Numbers o visitently reported. Domain 4: Potential Confounding / Variability Control Metric 9: Covariate Adjustment High Comparisons of observed versus expected cancer incidence were adjusted der, and race. Metric 10: Covariate Characterization Medium The source of information on covariets that were considered in this analy der, race) was not discussed; however, based on the information came from either p records, duath records, or tumor registry records.	
Assessed: Reported Health Urinary system cancer Effect(s): Chemical: 1,1-Dichloroethane-Isomer: 1,2-Dichloroethane HERO ID: 6570017 Linked HERO ID(s): 6570017, 6570014 Domain Metric Reported Health Wetric Reported Mealth Metric Reported Mealth Metric Domain 3: Outcome Assessment Outcome Measurement or Characterization Characterization Comments Metric 7: Outcome Measurement or Characterization Metric 8: Reporting Bias Metric 8: Reporting Bias Medium All of the outcomes described in the introduction are reported. Numbers on versus expected cancers are reported, but SIRs and 95% confidence interva sistently reported. Domain 4: Potential Confounding / Variability Control Metric 10: Metric 11: Co-exposure Counfounding Medium Metric 11: Co-exposure Counfounding Low Exposure 6 information on covariates that were considered in this analy derice veince that exposure to o cals occurred in this population). Co-exposures to other chemicals were the employer's medical department (i.e., direct evidence that exposure to o cals occurred in this population). Co-exposures to other chemicals were the employer's medical department (i.e., direct evidence that exposure to o <th></th>	
Reported Healtin Umary system cancer Effect(s): Image: Comments in the system cancer Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane HERO ID: 6570017 Linked HERO ID(s): 6570014 Domain 3: Outcome Assessment Metric 7: Metric 7: Outcome Measurement or Characterization Vertice 8: Reporting Bias Metric 8: Reporting Bias Metric 9: Covariate Adjustment Metric 9: Covariate Adjustment Metric 10: Covariate Adjustment Metric 11: Co-exposure Counfounding Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposed.	
Entert(s): 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane HERO ID: 6570017 Linked HERO ID(s): 6570017, 6570014 Domain 3: Outcome Assessment Outcome Measurement or Characterization Low Outcome measurement methods and follow-up length varied by exposure j cer cases among employees were assessed using "self-report by employees spouses, and through death certificates." Cancer cases in the general popul Louisiana population were ascertained through the Tumor Registry. Employees were followed for cancer through 2003, while on cancer in the South Louisiana population via the registry were only ava 2000; the study did not state if or how this difference in follow-up time wa analysis. Domain 4: Potential Confounding / Variability Control Metric 9: Metric Otrol Comparisons of observed versus expected cancer incidence were adjusted der, and race. Domain 4: Potential Confounding / Variability Control Medium High Comparisons of observed versus expected cancer incidence were adjusted der, and race. Metric 10: Covariate Characterization Medium He source of information on covariates that were considered in this andly der, race, was not discussed; however, based on the information came from either p records, dath records, or tumor registry records. Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposed used to ansufficture bentazon. Acute exposures to other chemicals were on calab certained in this population). Co-exposures to other chemicals wer	
HERO ID: 6570017 Linked HERO ID(s): 6570017, 6570014 Domain Metric Rating Comments Domain 3: Outcome Assessment Metric 7: Outcome Measurement or Characterization Low Outcome measurement methods and follow-up length varied by exposure j eer cases among employees were assessed using "self-report by employees spouses, and through death certificates." Cancer cases in the general popul Louisiana (used as a comparison population) were ascertained through the Tumor Registry. Employees were followed for cancer through 2003, while on cancer in the South Louisiana population) were ascertained through the Tumor Registry. Employees were followed for cancer through 2003, while on cancer in the South Louisiana population via the registry were only ava 2000; the study did not state if or how this difference in follow-up time wa analysis. Metric 8: Reporting Bias Medium All of the outcomes described in the introduction are reported. Numbers ot versus expected cancers are reported, but SIRs and 95% confidence interva sistently reported. Domain 4: Potential Confounding / Variability Control Metric 9: Covariate Characterization Medium Metric 10: Covariate Characterization Medium The source of information on covariates that were considered in this analyje der, race) was not discussed; however, based on the information available to authors it is reasonable to assume that the information available to authors it is reasonable to assume that the information available to authors it is reasonable to assume that the information available to evend a cancer were exposed used to manufacture be	
Intervention Option Planked intervention Domain Metric Rating Comments Domain 3: Outcome Assessment Metric 7: Outcome Measurement or Characterization Low Outcome measurement methods and follow-up length varied by exposure for creases anong employees were assessed using "self-report by employees spouses, and through death certificates," Cancer cases in the general oppul Louisiana (used as a comparison population) were ascertained through the Tumor Registry. Employees were followed for cancer through 2003, while on cancer in the South Louisiana population via the registry were only ava 2000; the study did not state if or how this difference in follow-up time wa analysis. Metric 8: Reporting Bias Medium All of the outcomes described in the introduction are reported. Numbers of versus expected cancers are reported, but SIRs and 95% confidence interva sistently reported. Domain 4: Potential Confounding / Variability Control Metric 9: Covariate Adjustment High Comparisons of observed versus expected cancer incidence were adjusted der, and race. Metric 10: Covariate Characterization Medium The source of information on covariates that were considered in this analy der, race) was not discussed; however, based on the information available t authors it is reasonable to assume that the information available t authors it is reasonable to assume that the information actime reported. Metric 11: Co-exposure Counfounding Low Exposure assessment in this study r	
DomainMetricRatingCommentsDomain 3: Outcome AssessmentMetric 7:Outcome Measurement or CharacterizationLowOutcome measurement methods and follow-up length varied by exposure a cer cases among employees were assessed using "self-report by employees spouses, and through death certificates." Cancer cases in the general popul Louisiana (used as a comparison population) were ascertation were ascertation and user as comparison population) were ascertation were ascertated through the Tumor Registry. Employees were followed for cancer through 2003, while on cancer in the South Louisiana population via the registry were only ava 2000; the study did not state if or how this difference in follow-up time way analysis.Metric 8:Reporting BiasMediumAll of the outcomes described in the introduction are reported. Numbers of versus expected cancers are reported, but SIRs and 95% confidence interve sistently reported.Domain 4: Potential Confounding / Variability Control Metric 10:Covariate AdjustmentHigh Comparisons of observed versus expected cancer incidence were adjusted der, and race.Metric 10:Covariate CharacterizationMediumThe source of information on covariates that were considered in this analy der, race) was not discussed; however, based on the information available t authors it is reasonable to assume that the information available t eurods, death records, cent medical department (i.e., direct evidence that exposure to o erecords, death records, ot umer registry records.Domain 4: Potential 11:Co-exposure CounfoundingLowExposure assessment in this study reflected whether workers were exposed used to anaufacture bentazon. Acute exposures to other chemicals were the employer's medic	
Domain 3: Outcome Assessment Metric 7: Outcome Measurement or Characterization Low Outcome measurement methods and follow-up length varied by exposure 4 cer cases among employees were assessed using "self-report by employees spouses, and through death certificates." Cancer cases in the general popul Louisiana (used as a comparison population) were ascertained through the Trumor Registry. Employees were follow-up time wa analysis. Metric 8: Reporting Bias Medium All of the outcomes described in the introduction are reported. Numbers of versus expected cancers are reported, but SIRs and 95% confidence interve sistently reported. Domain 4: Potential Confounding / Variability Control High Comparisons of observed versus expected cancer incidence were adjusted der, and race. Metric 10: Covariate Characterization Medium The source of information on covariates that were considered in this analy der, race) was not discussed; however, based on the information available t authors it is reasonable to assume that the information available t authors it is reasonable to assume that the information available t authors it, is reasonable to assume that the information available t authors it, is reasonable to assume that the information available t authors it, is reasonable to assume that the information available t authors it, is reasonable to assume that the information available t authors it, is reasonable to assume that the information available t authors it, is reasonable to assume that the information available t authors it, is reasonable to assume that the information available t authors it is reasonable to assume that the information available t authors it is reasonable to assume that the information available t au	
Metric 7: Outcome Measurement or Characterization Low Outcome measurement methods and follow-up length varied by exposure ; cer cases among employees were assessed using "self-report by employees spouses, and through death certificates." Cancer cases in the general popul Louisiana (used as a comparison population) were ascertained through the Tumor Registry. Employees were followed for cancer through 2003, while on cancer in the South Louisiana population) were ascertained through the Tumor Registry. Employees were followed for cancer through 2003, while on cancer in the South Louisiana population) were ascertained through the Tumor Registry. Employees were followed for cancer through 2003, while on cancer in the South Louisiana population via the registry were only ava 2000; the study did not state if or how this difference in follow-up time wa analysis. Metric 8: Reporting Bias Medium All of the outcomes described in the introduction are reported. Numbers of versus expected cancers are reported, but SIRs and 95% confidence interva sistently reported. Domain 4: Potential Confounding / Variability Control High Comparisons of observed versus expected cancer incidence were adjusted der, and race. Metric 10: Covariate Characterization Medium The source of information on covariates that were considered in this analy der, race) was not discussed; however, based on the information available to assume that the information came from either pe records, death records, or tumor registry records. Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposure used to manufacture bentazon. Acute exposures	
Metric 8: Reporting Bias Medium All of the outcomes described in the introduction are reported. Numbers of versus expected cancers are reported, but SIRs and 95% confidence intervasistently reported. Domain 4: Potential Confounding / Variability Control Image: Comparisons of observed versus expected cancer incidence were adjusted der, and race. Metric 10: Covariate Characterization Medium Metric 11: Covariate Characterization Medium Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposed used to manufacture bentazon. Acute exposures to multiple chemicals were the employer's medical department (i.e., direct evidence that exposure to or cals occurred in this population). Co-exposures to other chemicals were not cals occurred in this population). Co-exposures to other chemicals were not cals occurred in this population). Co-exposures to other chemicals were not cals occurred in this population).	oup. Can- or their tion of South Louisiana information lable through addressed in
Domain 4: Potential Confounding / Variability Control Metric 9: Covariate Adjustment Metric 10: Covariate Characterization Metric 10: Covariate Characterization Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposed used to manufacture bentazon. Acute exposures to multiple chemicals were the employer's medical department (i.e., direct evidence that exposure to or cals occurred in this population). Co-exposures to other chemicals were not cals occurred in this population). Co-exposures to other chemicals were not cals occurred in this population).	observed s are incon-
Domain 4: Potential Contouring / variability Control Metric 9: Covariate Adjustment Metric 10: Covariate Characterization Metric 10: Covariate Characterization Metric 11: Co-exposure Counfounding Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposed used to manufacture bentazon. Acute exposures to multiple chemicals were the employer's medical department (i.e., direct evidence that exposure to o cals occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to one calls occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to one calls occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to one calls occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to o calls occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to o call the employer's medical department (i.e., direct evidence that exposure to o calls occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to o call the employer's medical department (i.e., direct evidence that exposure to o calls occurred in this population).	
Metric 9. Covariate Adjustment High Comparisons of observed versus expected cancer incidence were adjusted der, and race. Metric 10: Covariate Characterization Medium The source of information on covariates that were considered in this analys der, race) was not discussed; however, based on the information available t authors it is reasonable to assume that the information came from either percords, death records, or tumor registry records. Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposed used to manufacture bentazon. Acute exposures to multiple chemicals wer the employer's medical department (i.e., direct evidence that exposure to o cals occurred in this population). Co-exposures to other chemicals were not call the opportunity of the product of the employer's medical department (i.e., direct evidence that exposure to o calls occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to o calls occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to o calls occurred in this population).	
Metric 10: Covariate Characterization Medium The source of information on covariates that were considered in this analysis der, race) was not discussed; however, based on the information available to authors it is reasonable to assume that the information came from either percords, death records, or tumor registry records. Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposed used to manufacture bentazon. Acute exposures to multiple chemicals were the employer's medical department (i.e., direct evidence that exposure to or cals occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to or calls occurred in this population).	or age, gen-
Metric 11: Co-exposure Counfounding Low Exposure assessment in this study reflected whether workers were exposed used to manufacture bentazon. Acute exposures to multiple chemicals were the employer's medical department (i.e., direct evidence that exposure to o cals occurred in this population). Co-exposures to other chemicals were not call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure to one call the employer's medical department (i.e., direct evidence that exposure the employer's medical department (i.e., direct evidence that exposure the employer's medical department (i.e., direct evidence that exposure the employer's medical department (i.e., direct evidence that exposure the employer's medical department (i.e., direct evidence that exposure the employer's medical department (i.e., direct evidence that exposure the employer's medical department (i.e., direct evidence that exposure the employer's medical department (i.e., direct evidence that exposure the employer's medical department (i.e., direct evidence that exposure the employer's medical department evidence that exposure the employer's med	s (age, gen- the study sonnel
	to chemicals reported to her chemi- adjusted for.
Domain 5: Analysis	
Metric 12: Study Design and Methods High The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question. The study design chosen was appropriate for the research question.	dy reported ected deaths
Metric 13: Statistical Power Medium The study population included 251 exposed workers with no reported loss	o follow-up.
Metric 14: Reproducibility of Analyses Low The description of the analysis is limited. In particular, additional informat ticipant selection, outcome assessment methods, and details of the statistic would be needed to reproduce the analysis.	on on par- l analysis
Metric 15: Statistical Analysis High The main results of this analysis were observed versus expected cancers; S for age, gender, and race were reported for some analyses.	Rs adjusted

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health	Renal/Kidney
Outcome(s)	
Assessed:	
Reported Health	Urinary system cancer
Effect(s):	
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	6570017 Linked HERO ID(s): 6570017, 6570014
Domain	Metric Rating Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected
	deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees
	compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information
	on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of
	exposure. Detailed information on most aspects of the study design and analysis was not provided.
Overall Qualit	ty Determination Medium

Study Citation: Health Outcome(s)	Dosemeci, 1 hydrocarbor Renal/Kidne	Dosemeci, M., Cocco, P., Chow, W. H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59. Renal/Kidney				
Assessed: Reported Health Effect(s):	renal cell ca	rcinoma				
Chemical: HERO ID:	1,1-Dichloro 4697224	bethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
Domain 1: Study Partic	cipation					
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).		
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors re- ferred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food- frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control sub- jects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.		
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.		
Domain 2: Exposure C	haracterization					
Domain 2. Exposure C	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).		
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.		
		Con	tinued on next pa	nge		

Page 124 of 138

		0	ontinued from previo	ous page		
Study Citation: Health Outcome(s)	Dosemeci, M., Cocco, P., Chow, W. H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59. Renal/Kidney					
Assessed: Reported Health Effect(s):	renal cell car	rcinoma				
Chemical: HERO ID:	1,1-Dichloro 4697224	ethane- Isomer: 1,2-Dichloroethane				
Domain		Metric	Rating	Comments		
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.		
Domain 3: Outcome A	ssessment					
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carci- noma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.		
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.		
Domain 4 [.] Potential Co	onfounding / Va	riability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smok- ing, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.		
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes po- tential confounders, e.g., smoking habits. Validation was not specified.		
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evalu- ated individually and as a group.		
Domain 5: Analysis						
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.		
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.		
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.		
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.		

Study Citation:Dosemeci, M., Cocco, P., Chow, W. H. (1 hydrocarbons. American Journal of Industr Renal/Kidney	999). Gender differences in risk of renal ce ial Medicine 36(1):54-59.	ll carcinoma and occupational exposures to chlorinated aliphatic
Health Renal/Kidney		
Outcome(s)		
Assessed:		
Reported Health renal cell carcinoma		
Effect(s):		
Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroe	thane	
HERO ID: 4697224		
Domain Metric	Rating	Comments
Additional Comments: A group of 438 cases (273 men and 165 v	women) were selected from the Minnesota (Cancer Surveillance System that had been newly diagnosed with
renal cell carcinoma. Controls included 68	7 participants (462 men and 225 women) age	e- and gender- stratified that were selected from either the general
population of Minnesota (age 20-64 years)	or from the Health Care Financing Administr	ration files (age 65-85). No significant increase in the risk of renal
cell carcinoma was observed with exposure	e to 1,2-dichloroethane among men or women	separately, or for all participants exposed.

Overall Quality Determination

Medium

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s):	 BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Immune/Hematological Lymphatic and hematopoietic tissue cancer 			
Chemical: HERO ID:	1,1-Dichloro 6570017 Linl	ethane- Isomer: 1,2-Dichloroethane ked HERO ID(s): 6570017, 6570014		
Domain		Metric	Rating	Comments
Domain 1: Study Partici	pation			
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2 [,] Exposure Ch	aracterization			
2 oniun 21 2.1.poono en	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unex- posed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.

		co	ntinued from previ	ous page	
Study Citation: Health	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Immune/Hematological				
Outcome(s)					
Assessed: Reported Health Effect(s):	Lymphatic a	nd hematopoietic tissue cancer			
Chemical.	1 1-Dichloro	ethane- Isomer: 1.2-Dichloroethane			
HERO ID:	6570017 Lin	ked HERO ID(s): 6570017, 6570014			
Domain		Metric	Rating	Comments	
Domain 3: Outcome As	sessment	Wiette	Rating	Comments	
Domain 5. Outcome As	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Can- cer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.	
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.	
Domain 4. Detential Co	nfounding / Vo	richility Control			
Domain 4: Potential Co	Matria O	riability Control	Iliah		
	Meuric 9.	Covariate Aujustinent	rigii	der, and race.	
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gen- der, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.	
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.	
Domain 5: Analysis					
Domain 5: Anarysis	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.	
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.	
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on par- ticipant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.	
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.	

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health	Immune/Hematological
Outcome(s)	
Assessed:	
Reported Health	Lymphatic and hematopoietic tissue cancer
Effect(s):	
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	6570017 Linked HERO ID(s): 6570017, 6570014
Domain	Metric Rating Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected
	deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees
	compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information
	on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of
	exposure. Detailed information on most aspects of the study design and analysis was not provided.
Overall Qualit	ty Determination Medium

Study Citation: Health Outcome(s) Assessed:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Other (Other cancers (not specified))			
Reported Health Effect(s):	Other cancers	s (not specified)		
HERO ID:	6570017 Lin	ked HERO ID(s): 6570017, 6570014		
Domain		Metric	Rating	Comments
Domain 1: Study Partici	pation			
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Ch	aracterization			
2 oninin 21 2.1900.00 cm	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unex- posed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s):	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Other (Other cancers (not specified)) Other cancers (not specified)				
Chemical: HERO ID:	1,1-Dichloro 6570017 Lin	ethane- Isomer: 1,2-Dichloroethane ked HERO ID(s): 6570017, 6570014			
Domain		Metric	Rating	Comments	
Domain 3: Outcome As	sessment Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Can- cer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.	
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.	
Domain 4: Potential Con	nfounding / Va	riability Control			
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gen- der, and race.	
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gen- der, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.	
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.	
Domain 5: Analysis					
2 omain 3. 7 marysis	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.	
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.	
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on par- ticipant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.	
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.	

Continued on next page ...

Page 131 of 138

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHO-02-15135).			
Health	Other (Other cancers (not specified))			
Outcome(s)				
Assessed:				
Reported Health	Other cancers (not specified)			
Effect(s):				
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane			
HERO ID:	6570017 Linked HERO ID(s): 6570017, 6570014			
Domain	Metric Rating Comments			
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected			
	deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees			
	compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information			
	on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of			
	exposure. Detailed information on most aspects of the study design and analysis was not provided.			
Overall Quality Determination Medium				

Study Citation: Health Outcome(s) Assessed:	BASF, (2005 study of emp number: 8EH Gastrointestin). Letter: Subject: Supplemental informat loyees assigned to a BASF Corporation fo (Q-02-15135). nal	tion regarding pri ormer chemical n	or TSCA Section 8(e) submission - Preliminary results from a cancer incidence nanufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control	
Reported Health Effect(s):	Digestive sys	tem cancer, colorectal cancer			
Chemical: HERO ID:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane 6570017 Linked HERO ID(s): 6570017, 6570014				
Domain		Metric	Rating	Comments	
Domain 1: Study Partici	pation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.	
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.	
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.	
Domain 2: Exposure Ch	aracterization				
·	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.	
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unex- posed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).	
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.	

Study Citation: Health Outcome(s) Assessed: Benorted Health	BASF, (2005 study of emp number: 8EI Gastrointesti	5). Letter: Subject: Supplemental information ployees assigned to a BASF Corporation of IQ-02-15135). nal	ation regarding pri former chemical r	ior TSCA Section 8(e) submission - Preliminary results from a cancer incidence nanufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control
Effect(s):	Digestive sys	deni cancer, colorectar cancer		
Chemical: HERO ID:	1,1-Dichloro 6570017 Lin	ethane- Isomer: 1,2-Dichloroethane ked HERO ID(s): 6570017, 6570014		
Domain		Metric	Rating	Comments
Domain 3: Outcome As	sessment			
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Can- cer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Co	nfounding / Va	riability Control		
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gen- der, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gen- der, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on par- ticipant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health	Gastrointestinal
Outcome(s)	
Assessed:	
Reported Health	Digestive system cancer, colorectal cancer
Effect(s):	
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	6570017 Linked HERO ID(s): 6570017, 6570014
Domain	Metric Rating Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected
	deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees
	compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information
	on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of
	exposure. Detailed information on most aspects of the study design and analysis was not provided.
Overall Qualit	ty Determination Medium

Study Citation: Health Outcome(s) Assessed: Reported Health Effect(s): Chemical:	BASF, (2005 study of emp number: 8EF Lung/Respira Respiratory o 1,1-Dichloro). Letter: Subject: Supplemental informat loyees assigned to a BASF Corporation fo IQ-02-15135). atory ancer ethane- Isomer: 1,2-Dichloroethane	ion regarding pri ormer chemical n	for TSCA Section 8(e) submission - Preliminary results from a cancer incidence nanufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control
HERO ID:	6570017 Lin	ked HERO ID(s): 6570017, 6570014		
Domain		Metric	Rating	Comments
Domain 1: Study Partici	pation Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Ch	aracterization			
Domain 2. Exposure en	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unex- posed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.

		0	ontinued from previo	ous page	
Study Citation: Health Outcome(s)	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135). Lung/Respiratory				
Assessed:					
Reported Health	Respiratory cancer				
Effect(s):					
Unemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane				
HERU ID:	0370017 LII	IKed HERO ID(s): 0370017, 0370014			
Domain		Metric	Rating	Comments	
Domain 3: Outcome As	sessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Can- cer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.	
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.	
Domain 4. Detential Co	nfounding / Vo	rishility Control			
Domain 4: Potential Co	Matria O	Coveriete Adjustment	Ulah		
	Metric 9:	Covariate Adjustment	High	der, and race.	
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gen- der, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.	
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.	
Domain 5. Analysis					
Domain 5: Analysis	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.	
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.	
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on par- ticipant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.	
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.	

Page 137 of 138

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health	Lung/Respiratory
Outcome(s)	
Assessed:	
Reported Health	Respiratory cancer
Effect(s):	
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
HERO ID:	6570017 Linked HERO ID(s): 6570017, 6570014
Domain	Metric Rating Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected
	deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees
	compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information
	on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of
	exposure. Detailed information on most aspects of the study design and analysis was not provided.
Overall Qualit	y Determination Medium