Intended for

Denka Performance Elastomer LLC, Request for Correction

Exhibit B

Date

July 15, 2021

EPIDEMOLOGICAL BASIS FOR SUPPORTING A CORRECTION OF THE CHLOROPRENE INHALATION UNIT RISK (IUR): UPDATE

RAMBOLL Bright ideas. Sustainable change.

CONTENTS

1. INTRODUCTION

The community living near the Denka Performance Elastomer facility in St. John the Baptist Parish, LA has been in a state of high alert after being identified by United States Environmental Protection Agency (USEPA) as having exceptionally high cancer risk, based on estimated, modeled chloroprene exposures used in the two most recent National-Scale Air Toxics Assessments (NATA). As discussed in Section 2, below, these USEPA risk conclusions for the community were based on the results of screening-level models that are designed to identify areas for more detailed, data-driven evaluation and targeted environmental interventions, and do not provide a definitive assessment of cancer risks (USEPA 2018). Section 3 summarizes the recent epidemiological evidence regarding the carcinogenicity of chloroprene, highlighting results from the most recent occupational epidemiology studies (Marsh et al. 2007a, 2007b, 2021). If there were an association between chloroprene exposure and cancer(s), it would be more easily detected in an occupational setting where exposures are higher than in the general population and can be reasonably well estimated.

In addition, we summarize the latest data from the Louisiana Tumor Registry (LTR) in Section 4. These data as a whole – the updated epidemiological evidence together with current data from the LTR – continue to support the position that the USEPA NATA model results, used to suggest high cancer rates in St. John the Baptist Parish, are not substantiated empirically. Despite this, some groups, in particular the University Network for Human Rights (UNHR), have attempted to promote the opposite conclusion, that cancer risks in St. John the Baptist Parish are higher than expected. Therefore, to ensure the body of epidemiological evidence is accounted for and correctly interpreted, we discuss in Section 5 the numerous scientific deficiencies in a report issued by the University Network for Human Rights (UNHR 2019) and a follow up publication (Nagra et al. 2021).

2. NATA SUMMARY

Residents living in the community near the Denka Performance Elastomer facility became concerned about cancer risks from the Denka facility's chloroprene emissions after the USEPA publicized the results of their NATA screening and interpreted them as showing the community to be at elevated cancer risk compared to other regions of the United States.[1] The NATA is conducted by USEPA about every three years to evaluate sources, levels, and potential risks of hazardous air pollutants (HAPs), or air toxics. The NATA analyses rely primarily on source emissions inventories as inputs into air dispersion models and are used to predict population-level exposures. Multiple complex models are involved in the screening that may not reflect local site conditions. Toxicity factors, such as inhalation unit risk values for cancer effects, are then applied to the results of the exposure models to predict risks at the population level. The multiple steps in the analysis incorporate conservative estimates at each level, usually resulting in overestimated risks.

USEPA has highlighted that NATA does not include information that applies to specific locations, because exposure data at the county and census-tract level are not usually available. Instead, the NATA applies models to estimate exposures at the county and census-tract level. According

[1] National Air Toxics Assessment | US EPA

to USEPA, the NATA assessment is designed as a comparative tool that should be used to evaluate relative variations in air concentrations, exposures, and risk among geographic areas rather than to identify or estimate risks in any given, specific location. These data can then be used to help communities design local assessments, improve emissions inventories, and find areas where the air toxics monitoring network could be expanded or improved. USEPA specifically notes that NATA should not be used to address epidemiological questions such as the relationship between cancer risk and proximity to certain sources. There is significant uncertainty in modeled risk estimates. USEPA highlights that the NATA results should be applied cautiously, because of these large uncertainties, which vary from location to location as well as from pollutant to pollutant.

In 2015 and 2018, USEPA published the NATA results based on 2011 and 2014 emissions data, respectively, for the United States, including Louisiana. The risk calculations presented in the 2015 report (USEPA 2015) combined estimated exposures based on emissions data with a cancer inhalation unit risk (IUR) value derived by USEPA's Integrated Risk Information System (IRIS), documented in the Toxicological Review of Chloroprene (USEPA 2010). An updated assessment based on 2014 emission data was published in 2018 that relied on the same IUR as the prior assessment (USEPA 2018). As we have previously shown, the IUR is highly inflated due to the lack of consideration of pharmacokinetic differences between species (e.g. Sax et al. 2020; Clewell et al. 2020). Because they relied on the inflated IUR, both NATA assessments reported that Louisiana residents experienced the highest cancer risks in the US and attributed these risks to chloroprene exposures. The epidemiological evidence cited by USEPA as supporting its IUR in its 2010 report (USEPA 2010) is discussed in Section 3.1, as it provides a basis for the epidemiological evidence published since 2010, which is discussed in Section 3.2.

3. EPIDEMIOLOGICAL EVIDENCE

3.1 Summary of Epidemiological Evidence Considered in the USEPA Toxicological Review of Chloroprene

Occupational epidemiological studies are relevant to the identification of health risks associated with specific exposures because occupational exposures tend to be substantially higher than environmental exposures experienced by community members. Therefore, if the exposure is truly related to the outcome, that relationship is more likely to be detected in the occupational vs. the community setting.

As summarized in the USEPA Toxicological Review of Chloroprene (USEPA 2010) and in Sax et al. (2020), the epidemiological literature on chloroprene exposure and cancer risk includes studies of occupational cohorts from several countries, published over approximately 30 years. Among the available occupational epidemiological studies, those by Marsh et al. (2007a, 2007b) represent the most comprehensive and methodologically robust based on the size of the cohort, amount of follow-up time, and completeness of exposure assessment, among other strengths (Bukowski 2009; Sax et al. 2020). The results from earlier studies conducted in the US (Pell 1978; Leet and Selevan 1982) were included in the update by Marsh et al. (2007a, 2007b).

The studies by Marsh et al. (2007a, 2007b) include a cohort of 12,430 workers from two US facilities in Louisville, KY (Plant L, n= 5507) and Pontchartrain, LA (Plant P, n=1357)) and two European facilities (Maydown, Northern Ireland; Plant M, n = 4849 and Grenoble, France; Plant G, n=717). Chloroprene production at these facilities dates back to 1942 (Plant L) and 1969

(Plant P). Two of the facilities (Plants L and M) used an acetylene process to make chloroprene, which also produces vinyl chloride, a known risk factor for liver cancer (IARC 2008). One of the strengths of these epidemiological studies is that the authors quantitatively estimated historical exposures for individual workers for both chloroprene and, where applicable, vinyl chloride. Mortality follow-up was conducted through 2000, therefore the study benefitted from an extensive follow-up time and ample time for the development of the two cancers of interest, lung and liver cancer. Overall, the study found no evidence of elevated mortality risks from lung, liver, or other cancers.

In contrast, studies conducted in China (Li et al. 1989), Russia (Bulbulyan et al. 1998), and Armenia (Bulbulyan et al. 1999) have not been updated and have serious limitations as described in Acquavella & Leonard (2001), Bukowski (2009), Rice & Boffetta (2001) and Sax et al. (2020). Briefly, these limitations include insufficient statistical power due to small cohort sizes, incomplete exposure assessments, poor control for confounding factors (e.g. smoking and drinking), poor documentation of cohort enumeration, and inappropriate reference rates.

In 2010, USEPA concluded that chloroprene was "likely to be carcinogenic to humans," in part because of its assessment of the epidemiological evidence (USEPA 2010). In their evaluation of this evidence, USEPA designated the evidence presented in the Marsh et al. (2007a, 2007b) studies as supporting a causal association between chloroprene exposures and elevated mortality from liver cancer. As noted in Sax et al. (2020), USEPA misinterpreted the Marsh et al. findings as providing evidence of an exposure-response relationship between chloroprene exposure and liver cancer mortality based on comparisons between exposure groups within the cohorts. In fact, the internal comparisons were misleading due to the very low liver cancer mortality rates among the employees. For example, the standardized mortality ratio (SMR, their mortality rate compared with the general population) for those in the lowest cumulative exposure category in Plant L was 0.40, or 60% lower than expected when compared with the general population in the area surrounding the plant. The SMR for the highest cumulative exposure category was 0.85, or about 15% below the expected rate compared with the general population (Marsh et al. 2007b). When these two rates are compared in the relative risk calculation, the ratio of these two low rates provides a mathematical result that is above 1.0 (specifically, 2.32), and misleadingly implies an excess risk for those in the highest cumulative exposure category. In part because of USEPA's reliance on and misinterpretation of the Marsh et al. (2007a, 2007b) results, Marsh et al. (2021) published analyses of an extended follow-up period for the US occupational cohorts, summarized below.

3.2 Summary of Epidemiological Evidence Published since the USEPA Toxicological Review of Chloroprene

A recent update by Marsh et al. (2021) includes additional follow-up of the US cohorts, from 2001 to 2017. Marsh et al. (2021) conducted an update in order to increase the person-years and total numbers of deaths observed, and thereby provide a more reliable evaluation of cancer mortality patterns in relation to chloroprene exposure in the two large US plants that were included in the 2007 studies (i.e. Plants L and P).

The updated study by Marsh et al. (2021) added 47,299 and 19,942 person-years of observation and 1399 and 214 new deaths from the Plant L and Plant P cohorts, respectively. Using the National Death Index, the authors identified 4,118 deaths and with an underlying cause of death recorded for 97.2% of them (n=4004). Exposure estimates were not updated for the re-analysis but were based on the exposure estimates as described in the earlier publications (Marsh et al.

2007a, 2007b). This is appropriate given the decades-long induction period for solid tumors: any recent exposure data added to the updated analysis would not contribute information to cancer risk calculations, because it would have occurred outside of the time period relevant for the development of cancer. Marsh et al. (2021) used the same statistical analyses reported in Marsh et al. (2007a, 2007b), including both external and internal comparisons. External comparisons included national and local cancer rates, and internal comparisons included comparisons based on exposure levels (i.e. exposure duration in years, exposure concentration in ppm, or cumulative exposure in ppm-yrs), with the lowest exposure group as the referent category.

The external comparisons showed statistically significant deficits at both plants (SMR<1.0) for all types of cancer (combined) using both national and local rates as comparisons. Compared to local cancer mortality rates, there were statistically significant deficits reported for the key outcomes of lung cancers (each plant) and liver cancers (Plant P). There were no statistically significant excess risks in either plant (Tables 1 and 2, below, and Marsh Table 4). As in the earlier reports, (Marsh et al. 2007a, 2007b) the internal analysis showed some elevated relative risks (RR) for some exposure categories at each plant, but these were arithmetical results due to comparisons between pairs of low rates. As discussed above, the internal referent categories had substantially lower mortality rates than both national and county rates, again yielding a comparison between a deficit of deaths in one group and a larger deficit of deaths in another group. Overall, the authors noted that "Although we observed elevated RRs in many exposure categories, we found no compelling evidence of a positive exposure-response relationship in either study plant" (Marsh et al. 2021).

Table 1. Observed Deaths and SMRs for Selected Causes of Death Total Plant L (Louisville, KY) Cohort

Cancers	Observed	US		Local County	
		SMR	95% CI	SMR	95%CI
All cancer	974	0.89**	0.84-0.95	0.75**	0.70-0.80
Biliary Passages & Liver Primary	31	1.06	0.72-1.51	0.95	0.65-1.35
Bronchus, Trachea, Lung	340	1.0	0.89-1.11	0.72**	0.65-0.80

From Marsh et al. (2021, Table 3); Observed deaths between 1960-2017; ** P<0.01

Table 2. Observed Deaths and SMRs for Selected Causes of Death Total Plant P (Pontchartrain, LA) Cohort

Cancers	Observed	US		Local County	
		SMR	95% CI	SMR	95%CI
All cancer	92	0.69**	0.56-0.85	0.64**	0.52-0.78
Biliary Passages & Liver Primary	1	0.2	0.01-1.10	0.16*	0.00-0.88
Bronchus, Trachea, Lung	30	0.71	0.48-1.02	0.62**	0.42-0.89

From Marsh et al. (2021, Table 4); Observed deaths between 1960-2017; * P<0.05 **P<0.01

As with the prior studies (Marsh et al. 2007a, 2007b), this follow-up study has several strengths that are discussed in detail in Bukowski (2009) and Sax et al. (2020). Briefly, they include a large cohort size, long follow-up period, comprehensive case ascertainment, a detailed exposure assessment (including of vinyl chloride) and use of appropriate local and national population

comparisons. The follow-up study adds confidence to the prior findings by the increased statistical power from added person-years and numbers of deaths. The choice to not update work histories and exposure estimates would not affect the results because 97% and 70% of workers from Plant L and Plant P, respectively, left their jobs before 2001 and because the original exposure assessment is more pertinent to the assessment of cancer risk, due to the long latency period for cancers.

Occupational epidemiology data, especially the best quality data from the occupational cohorts described by Marsh et al. (2007a, 2007b) and Marsh et al. (2021), do not support the elevated risk estimates suggested by the results of the NATA assessments.

4. LOUISIANA TUMOR REGISTRY REPORTS

The Louisiana Tumor Registry (LTR) participates in the CDC Surveillance, Epidemiology, and End Results (SEER) program, which records incident cancers in 43 US states and Washington D.C., Guam, Puerto Rico, the U.S. Virgin Islands, and Bermuda[2,3]. As part of the SEER program, LTR is held to specific standards of quality and completeness. It has received awards for meeting or exceeding these standards in every year since 2002 (Maniscalco et al. 2020). The results of a recent audit for St. John the Baptist Parish, specifically for the parts of the parish nearest to the Denka facility, have further demonstrated that the LTR is complete and accurate (Williams et al. 2021)—i.e. all cancers reported by the community members who participated in the audit were found in the LTR data.

The purpose of the LTR, and all cancer registries, is to collect information to identify locations or population subgroups that experience unusual patterns of cancer, such as higher than expected rates of specific cancer types, unusual occurrences of rare forms of cancer, or unexpected numbers of cancers in certain age ranges. This is accomplished by comparing patterns of cancer incidence between regions.[4] Therefore, the LTR periodically issues a report summarizing cancer incidence and mortality rates (all cancers and specific cancers) in Louisiana as a whole, in the seven parishes comprising the Industrial Corridor (IC), and in each individual parish. In the context of identifying cancer risks in the vicinity of the Denka facility, the LTR provides an important means of verifying the risk estimates suggested by NATA. If the NATA risk assessment were accurate, and the area around the Denka facility were at high risk of cancer, the LTR would identify higher cancer incidence rates in St. John the Baptist Parish than elsewhere. In fact, the incidence rates of cancers of concern, i.e. cancers of the lung/bronchus and liver/intrahepatic bile duct, were similar to or statistically significantly lower than the incidence of these cancers in the IC compared with Louisiana as a whole in each of the periods reported in the last three LTR reports, covering the years 2007-2011, 2011-2015, and 2013-2017 (Table 3). Among white men, the incidence of all cancers (combined) was higher in the IC than in Louisiana as a whole during 2007-2011, but rates were similar or lower for all other time intervals. For all time intervals and all other race/gender groups reported (White women, Black men, Black Women)

[2] National Program of Cancer Registries program standards, 2017-2022 (cdc.gov), accessed March 2, 2021 and Scope of Standards | SEER Training (cancer.gov), accessed March 2, 2021
[3] National Interstate Data Exchange Agreement (naaccr.org), accessed March 2, 2021
[4] How Cancer Registries Work | CDC, accessed March 3, 2021; Cancer Registries' Value for You | CDC, accessed March 3, 2021; How Cancer Registries Work | CDC, accessed March 3, 2021;Cancer Registries' Value for You | CDC, accessed March 3, 2021

the incidence was similar to or statistically significantly lower than the incidence rate for Louisiana as a whole.

Statistical comparisons between individual parishes or between parishes and the IC or the state are not included in the published LTR reports. Since 2019, however, parish-level comparisons have been available from the LTR by way of an on-line data visualizer[5]. These data indicate that, for the period 2012-2016, cancer incidence rates in St. John the Baptist parish have been below the state-wide average for all cancers (combined) and for cancers of the lung/bronchus and liver (Figures 1, 2, and 3). Therefore, the premise offered by the estimates modeled by NATA, that this parish has or its constituent census tracts have the highest rates of cancer in the U.S., is incorrect.

In 2018, the LTR began reporting cancer data for individual census tracts, in addition to providing data at the Parish and State levels.[6] These reports provide data aggregated over a 10-year period to protect the privacy of residents and to increase the statistical reliability of the estimates. Specifically, the LTR is legally restricted from reporting data for populations of less than 20,000. Reliable statistics can only be obtained if there is a sufficient number of cases (generally greater than 16 cases or more).

The latest LTR census tract-level report provided for the period from 2008-2017 (Maniscalco et al. 2021). The results from this report were consistent with the findings from the Parish-level analysis. Specifically, for St. John the Baptist Parish, none of the 11 census tracts reported a statistically significantly elevated rate of all cancers (combined) compared to the State-level rates. Similarly, for lung and bronchus cancers, none of the 9 census tracts with reported data showed statistically significant elevations compared to the State rates. There were no census tract-level data reported for St. John the Baptist Parish for liver cancers.

LTR data at neither the Parish nor the census tract level indicate elevated rates of the cancers potentially associated with chloroprene exposure in St. John the Baptist Parish compared to Louisiana.

[5] Louisiana Cancer Data Visualization - Public Health (lsuhsc.edu). Accessed June 2021

[6] Cancer Incidence in Louisiana by Census Tract - 2018 - Public Health (lsuhsc.edu) Accessed June 2021

Table 3. Average annual incidence rates by race and sex in Louisiana (LA), the Industrial Corridor, St. John the Baptist and surrounding parishes, 2007-2011, 2011-2015, and 2013-2017

	All cancer			Lung & Bronchus			Liver and Intrahepatic Bile Duct		
	2013-2017	**2011-2015**	**2007-2011**	**2013-2017**	**2011-2015**	**2007-2011**	**2013-2017**	**2011-2015**	**2007-2011**
White men									
LA state	547.2	544.8	578.1	77.9	82.4	92.3	13.4	12.5	10.8
Industrial corridor‡	559.0	551.3	**595.3**§	**66.6§**	**69.9**§	**78.8**§	11.9	**10.2**§	**7.3§**
St. John the Baptist	539.5	487.5	524.5	75.9	72.2	104.3	NR		
Ascension	573.0	581.1	595.5	81.4	82.4	95.5	NR		
Jefferson	522.4	530.4	555.7	71.0	74.0	83.3	NR		
Lafourche	580.1	569.5	547.2	74.5	78.2	84.8	NR		
Livingston	542.1	562.5	615.9	91.3	111.8	115.7	NR		
St. Charles	503.4	499.2	583.9	42.8	61.6	86.1	NR		
St. James	626.1	642.2	599.3	84.2	70.9	65.7	NR		
St. Tammany	562.4	555.4	589.3	76.3	75.5	82.3	NR		
Tangipahoa	527.8	539.0	600.8	88.0	90.3	110.5	NR		
Black men									
LA state	592.4	605.1	652.1	99.1	105.8	113.8	22.6	21.5	16.0
Industrial corridor‡	599.9	629.2	675.2	**88.0**§	98.0	104.0	25.2	23.6	17.2
St. John the Baptist	597.0	619.8	627.4	89.2	103.0	90.6	^		
Ascension	463.6	562.0	690.0	51.1	104.9	116.4	^		
Jefferson	603.8	601.1	640.5	98.1	99.1	103.5	26.8		
Lafourche	611.8	634.5	593.8	124.0	123.3	103.2	^		
Livingston	573.5	566.9	619.6	^	^	^	^		
St. Charles	524.4	547.0	586.0	75.2	102.2	96.7	^		
St. James	553.9	638.7	813.9	92.6	103.5	132.7	^		
St. Tammany	659.1	614.9	579.5	90.1	111.1	108.7	25.1		
Tangipahoa	613.3	604.4	684.0	112.9	108.8	126.8	^		
White women									
LA state	432.1	420.6	413.1	56.8	57.1	59.1	4.2	3.4	3.2
Industrial corridor‡	**418.1**§	**398.4**§	**397.6**§	**46.4**§	**43.5**§	**52.7**§	3.1	2.5	3.3
St. John the Baptist	439.7	422.8	396.9	47.7	41.5	43.9	NR		
Ascension	421.7	393.1	392.2	56.6	52.3	69.3	NR		

Table 3. Average annual incidence rates by race and sex in Louisiana (LA), the Industrial Corridor, St. John the Baptist and surrounding parishes, 2007-2011, 2011-2015, and 2013-2017

	All cancer			Lung & Bronchus			Liver and Intrahepatic Bile Duct		
	2013-2017	**2011-2015**	**2007-2011**	**2013-2017**	**2011-2015**	**2007-2011**	**2013-2017**	**2011-2015**	**2007-2011**
Jefferson	449.9	442.2	423.5	57.6	60.4	60.6	NR		
Lafourche	434.3	417.2	408.0	52.9	49.6	56.0	NR		
Livingston	417.0	405.0	414.3	62.2	65.1	56.3	NR		
St. Charles	415.7	427.9	399.3	59.9	53.9	63.1	NR		
St. James	395.1	332.4	373.2	^	^	44.8	NR		
St. Tammany	452.3	447.3	434.2	49.5	50.3	59.6	NR		
Tangipahoa	415.7	405.7	405.6	53.8	56.0	55.0	NR		
Black women									
LA state	421.9	415.4	415.4	46.7	49.0	52.7	4.9	4.5	4.4
Industrial corridor‡	422.0	416.3	418.6	**40.5**§	**41.5**§	48.3	5.0	3.9	4.6
St. John the Baptist	351.9	359.5	392.7	31.7	38.2	56.5	NR		
Ascension	370.4	389.8	429.0	30.5	32.6	54.2	NR		
Jefferson	450.4	421.8	429.1	49.1	50.9	62.1	NR		
Lafourche	377.8	352.9	395.4	^	^	70.1	NR		
Livingston	426.9	391.7	458.1	^	^	^	NR		
St. Charles	482.7	418.5	410.7	65.1	67.3	65.1	NR		
St. James	502.8	439.1	355.0	51.5	48.8	^	NR		
St. Tammany	434.8	458.7	461.6	48.5	57.9	56.7	NR		
Tangipahoa	414.2	429.2	430.3	41.8	44.8	70.8	NR		

Figure 1. Cancer Incidence (All Cancers) in Louisiana: 2012-2016

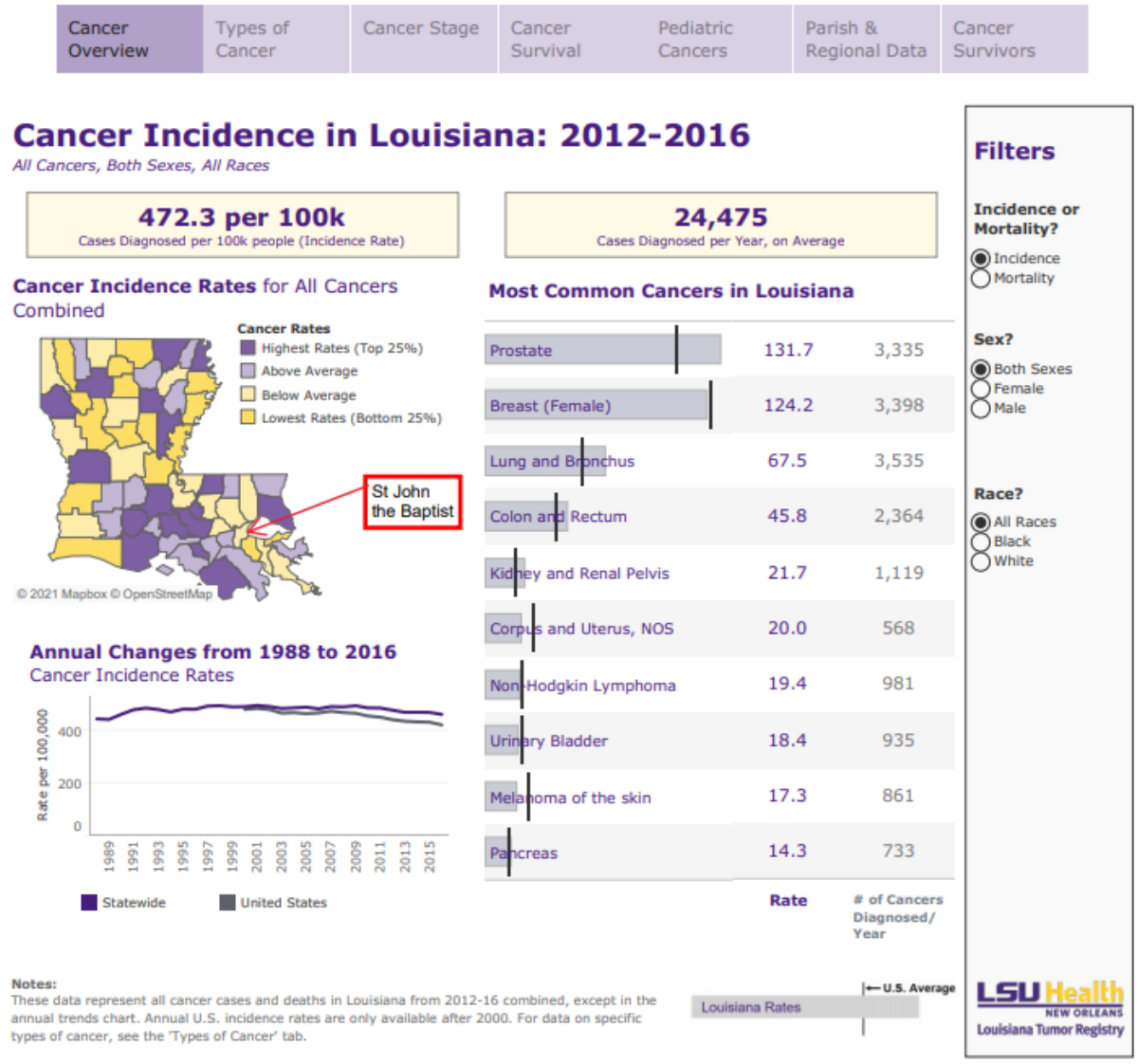
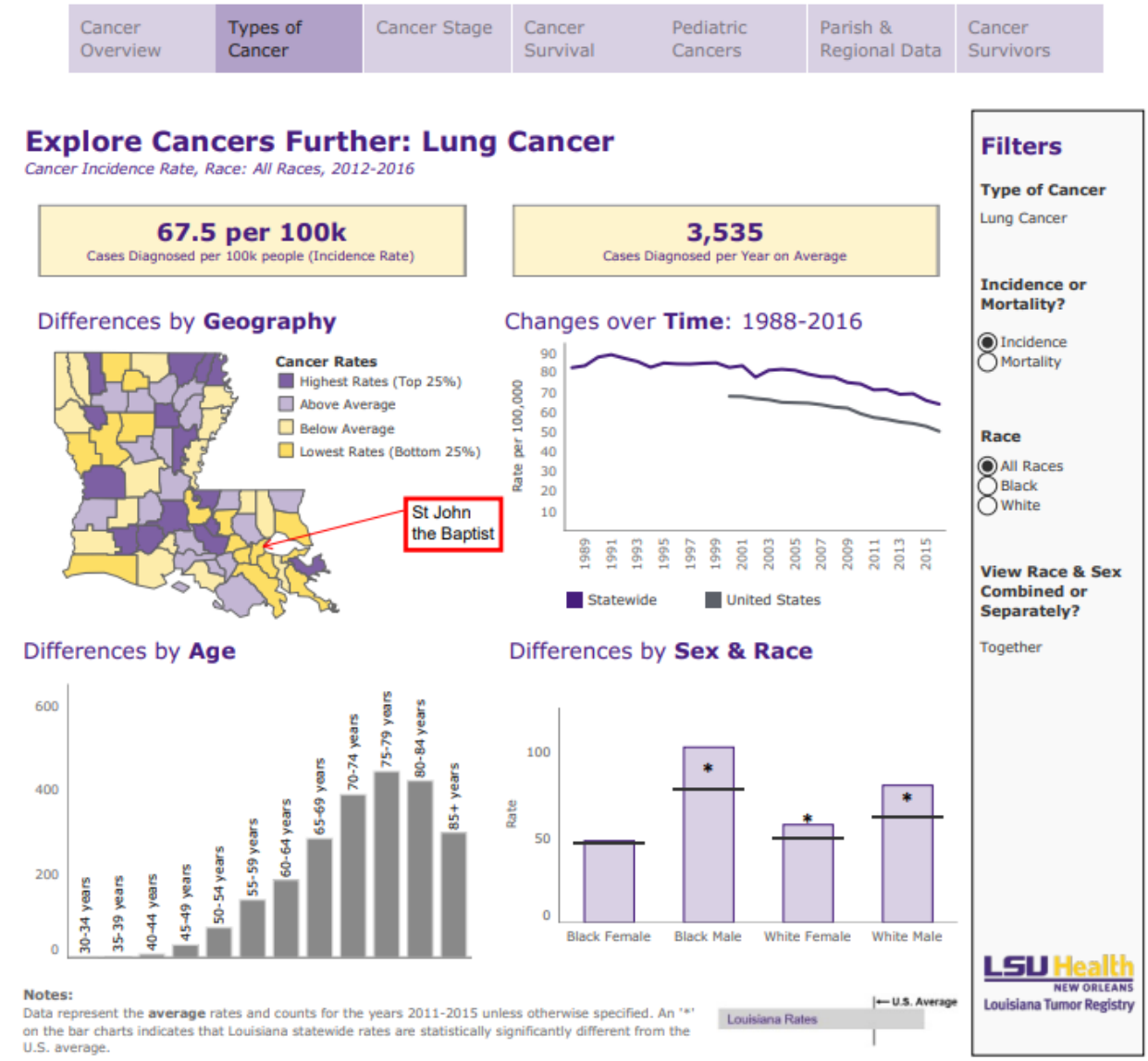
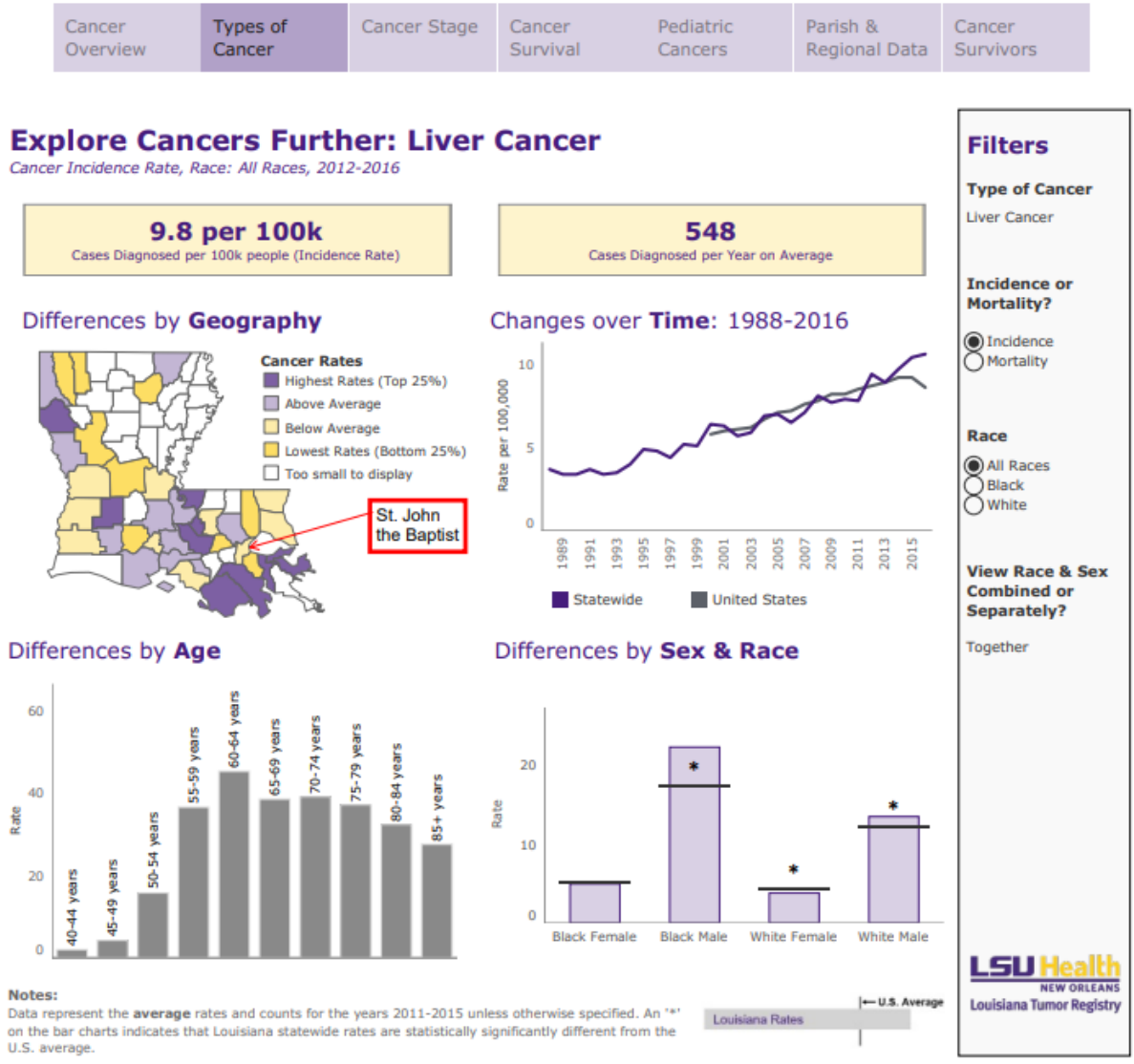


Figure 2. Lung Cancer Incidence in Louisiana: 2012-2016



Source: [Louisiana Cancer Data Visualization - Public Health (lsuhsc.edu)](). Accessed June 2021

Figure 3. Liver Cancer Incidence in Louisiana: 2012-2016



Source: [Louisiana Cancer Data Visualization - Public Health (lsuhsc.edu)](). Accessed June 2021

5. UNIVERSITY NETWORK FOR HUMAN RIGHTS (UNHR) 2019 REPORT AND FOLLOW-UP PUBLICATION

In 2019, the University Network of Human Rights (UNHR) self-published a report describing a community survey conducted in two residential areas surrounding the Denka facility in St. John the Baptist Parish. This report, in slightly revised form, was published in 2021 in the journal Environmental Justice (Nagra et al. 2021). As outlined in a response to the unpublished UNHR report[7], the survey and its analyses used incorrect and non-standard methods that led to an incorrect conclusion that the 23-year period prevalence of all cancer (combined) in the residential area (so-called Zone 1) closest to the Denka facility is elevated due to environmental exposures from the Denka facility. The comments that follow apply to both the original, unpublished UNHR report and to the paper published in 2021; they are collectively referenced here as Nagra et al. (2021).

Nagra et al. (2021) used residential distance from the Denka facility as a surrogate for exposure to chloroprene, without using any measured exposures and assuming that all the residences within each of the zones they identified had the same exposure. We focused our assessment of their methods on Zone 1, where they reported an apparent increase in the 23-year cancer prevalence.

Nagra et al. (2021) relied on data from a subset of households to represent the entire population of interest. This is often done in community health surveys, but properly conducted surveys attempt to corroborate the validity of data collected by interviews, and particularly data collected from proxy respondents. In the Nagra et al. (2021) study, one volunteer per included household answered survey questions, including questions about cancer diagnoses, for all household members. It is impossible to speculate about the validity of these self- and proxy-reports, but, had the authors obtained appropriate Institutional Review Board approval and informed consent from the participants, and had they recorded individually identifying information, they could have verified the reported cancer cases against either medical records or data recorded in the LTR. This was not done.

In properly conducted surveys, the included participants represent the target population. To validly estimate the 23-year cancer prevalence in Zone 1, the study should have been based on a representative sample of current and former residents covering the 23-year time-period of interest. If the population of Zone 1 had been stable over time, data for current residents might have provided a valid estimate of cancer prevalence in the target population. This was not the case, however. Almost all current residents of Zone 1 can be mapped to Block 1 of US Census tract 708, where the US Census American Community Survey (ACS) found a shift in the gender and age distributions with relatively more men and residents aged 70+ years in 2015-19 compared with 2010-14. Because older age and male gender are risk factors for cancer (see, for example, Clegg et al. 2009; Ward et al. 2004; Yin et al. 2010, and data from SEER[8]), the cancer prevalence Nagra et al. (2021) estimated based on the current population does not represent the true cancer prevalence in Zone 1 over the past 23 years, and likely overestimates that value. An analysis conducted according to standard epidemiological practice would have evaluated and

[7] https://edms.deq.louisiana.gov/app/doc/view.aspx?doc=11830771&ob=yes
[8] https://seer.cancer.gov/statfacts/html/all.html

adjusted for such changes in the distribution of cancer risk factors before applying the current data to the target population.

The survey questions used by Nagra et al. (2021, appendix A1) did not clearly indicate if respondents should only provide information for current household members or if former household members should be included; if former household members were to be included, the questions could be interpreted as applying only if the former household members had had cancer. If only those former household members who had had cancer were included, rather than a representative sample of former residents with and without cancer, then the cancer prevalence estimated for Zone 1 would again have been artificially inflated.

It is imperative that epidemiological studies be constructed to avoid bias. In the community survey conducted by Nagra et al. (2021) an unknown proportion of the volunteer participants in the survey are among the community members who are plaintiffs suing Denka and DuPont (the owner of the facility until November 1, 2015) for personal injury and damages related to alleged chloroprene exposure. If plaintiffs in the lawsuit are among the survey participants, there is increased likelihood that they may – consciously or otherwise -- over-report health conditions among themselves and their family members.

The effect of the non-representative study population on the prevalence estimate might have been reduced if Nagra et al. (2021) had excluded cancer cases that must have resulted from causes other than environmental chloroprene exposure instead of analyzing all cancers (combined). For example, Nagra et al. (2021) could have focused on lung and liver cancers, which have been proposed to be potentially associated with chloroprene exposure (USEPA 2010). In addition, under their questionable assumption that residence location is a valid surrogate for environmental exposure, Nagra et al. (2021) should have confirmed that the individuals with cancer included in their prevalence estimate had lived in Zone 1 during a time period relevant to the development of their cancers. This was not done, however.

By restricting the study to a sub-population that had recently undergone a sociodemographic shift, which resulted in an increase in cancer risk factors that were unrelated to any environmental exposures, and by analyzing all cancers (combined), thereby including types of cancer that could not—even theoretically—have been associated with environmental chloroprene exposure, Nagra et al. (2021) likely created an artificial, false association between residential proximity to the Denka plant and cancer. This major shortcoming would have been exacerbated if they included former household members only if they had had cancer and by failing to assess or account for the likely participation of plaintiffs suing Denka among the study population.

Overall, Nagra et al. (2021) incorrectly analyzed the data they collected, ignored relevant, available data, and conducted an analysis that was fundamentally flawed to reach the incorrect conclusion that there was an increase in cancer prevalence attributable to environmental exposures in the surveyed population living closest to the Denka facility.

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