

EXHIBIT 3

TCAS

Toxicology Consultants & Assessment Specialists, LLC

6450 Pine Avenue, Sanibel, FL 33957

29 Fennell Street, Skaneateles, NY 13152

(239) 472-2436 [FL] (315) 685-2345 [NY] (800) 308-0080 U.S./CA

E-mail: drsawyer@experttoxicologist.com & Website: experttoxicologist.com

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January 22, 2021

Ken Moll, Esq.

Moll Law Group, PC

22 W. Washington St, 15th Floor

Chicago, IL 60602

Re: Estate of Robert Karman v. Monsanto

Dear Attorney Moll:

Per your request with regard to this matter, I have reviewed the complete list of pertinent documents as compiled in Appendix A. Based upon the information provided and the application of generally-accepted toxicological methodology and referenced sources as cited herein, I have stated my opinions in this matter to reasonable toxicological certainty.

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The POEM methodology has been peer-reviewed, generally-accepted, used internationally, and tested with a known rate of error as published within the seven studies footnoted below.²

Hence, this toxicological assessment has four fundamental objectives: (1) to arrive at a scientifically-reliable exposure dose estimation for Mr. Karman (*in units of 8-hour time-weighted exposure days*) based upon the available objective evidence, (2) to assess the potential of toxicological confounding risk factors contributing to his NHL onset, (3) to provide a general causation assessment of personal protective gear (PPE), product formulation, toxicological factors such as absorption, distribution, metabolism and excretion (ADME) and mechanism of action of Roundup® and (4) to render a scientifically-supported and reliable opinion as to whether Mr. Karman's Roundup® exposures (dose) were sufficiently above the thresholds within the peer-reviewed studies to substantially contribute to the development of his NHL.

2. Plaintiff Background Summary

Introduction

Robert Karman was born [REDACTED] in Chicago, Illinois, and died December 15, 2015 at the age of 77 from non-Hodgkin lymphoma (DLBCL).³ He is survived by his wife, Christine Stanley Karman who is the administrator of his estate, and their five children.

Mr. Karman began using Roundup® in 1980 at [REDACTED], [REDACTED], where he lived with his family. In 1989, he and his wife moved to [REDACTED]

² Abukari, Wumbi, "Pesticides Applicator Exposure Assessment: A Comparison between Modeling and Actual Measurement," 2015, Journal of Environment and Earth Science ISSN 2224-3216 (Paper) ISSN 2225-0948 (Online) Vol.5, No.11.

U.K. Health and Safety Executive, HSE, "Operator Exposure," 2016, Data requirements handbook, Retrieved from: <http://www.hse.gov.uk/pesticides/topics/pesticide-approvals/pesticides-registration/data-requirements-handbook/operator-exposure.htm>

"Operator exposure assessment for MON 2139 UK – Case" MONGLY06509236

"UK POEM calculations in preparation of meeting Spanish competent authorities." MONGLY01275627

Lawson, A., et al., "Three Methods to Assess Levels of Farmers' Exposure to Pesticides in the Urban and Peri-urban Areas of Northern Benin," 2017, Tunisian Plant Protection Journal, Vol.12, pp. 91–108.

Ilyassou, K., et al., "Risk Assessment for Small Farmers Exposed to Plant Protection Products in the Niger River Valley," 2017, Comm. Appl. Biol. Sci.

EPA, "Risk Assessment Methodology for Hazardous Substances: How to assess the risk, cost and benefit of new hazardous substances for use in New Zealand," 2018, Environmental Protection Authority.

³ Death certificate stated "lymphoma" as cause of death.

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██████████, and he lived there until his death. He applied Roundup® Weed and Grass Killer from 1989 to 2015 on this property.

Mr. Karman's wife (who testified in deposition following his passing) recalled that applications may have initiated as early as 1980 at their prior home. Mr. Karman used a hand-held sprayer to apply liquid Roundup®. He also maintained powdered (dry, granulated) Roundup® in his garage.⁴

Mr. Karman did not wear any personal protective equipment (PPE) in the course of his Roundup® applications. According to the Plaintiff's Fact Sheet, he applied Roundup® once per week during 40 weeks of the year.⁵

NHL Diagnosis and Pathology

Mr. Karman was diagnosed with diffuse large B-cell lymphoma (DLBCL) in July 2015. A left axillary lymph node biopsy performed on July 27, 2015, revealed findings consistent with diffuse large B-cell lymphoma. The anatomic pathology report states, "*The diffuse cellular infiltrate consists of sheets of large, atypical cells intermixed with scattered smaller lymphocytes and a few eosinophils. The large, atypical cells are large in size and have prominent nucleoli. Immunohistochemically, the large, atypical cells are positive for LCA and CD20 and negative for AE1/AE3, CD3, CD5, CD10, S100, CD30, CD15, Bcl-2 and CD138; rare cells are weakly positive for cyclin D1.*"⁶

Mr. Karman was not deposed as he had passed away on December 15, 2015, prior to the start of litigation. Mrs. Karman brought Mr. Karman's diary along to her deposition which revealed the following: Mr. Karman had a regular six month visit on June 22, 2015, with his primary care physician, Dr. Myrda. Due to a lump in his left groin, he underwent CT scans on July 1st. On July 9th, he saw Dr. Myrda again who referred him to Dr. Aron for a biopsy of concerning lymph nodes. The biopsy was carried out July 23rd. On July 27th, the lymphoma was confirmed. He had a bone marrow test on August 3rd. His first chemo treatment was on August 20, 2015.

⁴ Deposition of Christine Karman, November 13, 2019, p. 294.

⁵ Plaintiff Fact Sheet completed by Christine Karman, p. 21 of 28.

⁶ Sherman Hospital Oncological Medical Records, p. 41 of 36.

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The available medical records state that Mr. Karman's enlarged lymph nodes became more pronounced in the latter part of the summer as noted by his oncologist.⁷ The records reveal on-going pathology highly consistent with diffuse large B-cell lymphoma.

Medical History

Mr. Karman had been diagnosed with hypertension in 2003 and chronic obstructive pulmonary disease (COPD) in 2010. He had a surgical hemorrhoidectomy in 1970.⁸ He displayed tardive dyskinesia⁹ on July 12, 2007. He was "allergic" to codeine.¹⁰ It was noted on July 23, 2015, that he had a history of transfusion.¹¹ His body mass index (BMI) on July 9, 2015, was 31.20.¹² His medications at the time of his NHL diagnosis were Proair inhaler, losartan potassium, labetalol and naproxen.¹³

Table 1
Summary of Mr. Karman's Medical History

Date	Procedure	Results/Diagnosis	Reference
9/3/14	Office visit for chest discomfort and shortness of breath	Height: 66.75 inches; weight: 193 lbs. Current Medications: Proair inhaler, Z-pak, losartan potassium, ¹⁴ labetalol, ¹⁵ naproxen	p. 15-17
9/3/14	Chest x-ray for cough/chest pain	Small left effusion with mild increase left lower lobe subsegmental atelectasis compared to 5/22/2012	p. 21
9/18/14	Follow-up	Had pneumonia; evidence of chronic bronchitis. Weight 199 lbs. Start Dulera inhaler. ¹⁶	p. 12/81
2/2/15	Chest CT	Ground-glass infiltrates in right lobes, a few mildly enlarged mediastinal lymph nodes and atherosclerosis including coronary arteries. Indeterminate liver hypodensities.	p. 28-29/81

⁷ Fox Valley Hematology Oncology, August 3, 2015, p. 1 of 4.

⁸ Sherman Hospital Oncological medical records, p. 37 of 360. Winters Family Practice medical records, p. 62 of 81.

⁹ Tardive dyskinesia includes obvious uncontrolled, involuntary movement often associated with certain disease states or pharmaceutical adverse toxicological effects.

¹⁰ Sherman Hospital Oncological Medical Records, p. 47 of 360.

¹¹ Id., p. 37 of 360.

¹² Winters Family Practice medical records, p. 4 of 81. (Note: His BMI was less than 30 throughout most of his NHL pre-diagnostic years).

¹³ Id., p. 8 of 81.

¹⁴ For hypertension.

¹⁵ For hypertension.

¹⁶ Corticosteroid.

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Table 1
Summary of Mr. Karman's Medical History

Date	Procedure	Results/Diagnosis	Reference
6/15/15	Clinical laboratory results	Creatinine 1.3, ALT 7, hemoglobin 12.0 g/dL, hematocrit 38.7%, monocytes 19%	p. 34/81
6/22/15	Routine follow-up	Presented with 2.5 cm lump in left groin. Remains unchanged over a few months. CT of chest <i>"showed some lymphadenopathy but nothing terribly significant."</i> 3 beers per day; 15 cigarettes per day.	p. 6/81
7/1/15	CT chest, abdomen and pelvis. Follow-up for abnormal chest CT of 2/2/15.	Multiple masses/lymphadenopathy in the chest, abdomen and pelvis. Lungs demonstrate no gross masses or effusion, but multiple scattered ground glass opacities are noted.	p. 26/81
7/27/15	Excisional biopsy of deep left axillary lymph node	Diffuse large B-cell lymphoma. Cells are positive for LCA & CD20; rare cells are weakly positive for cyclin D1. Fifty % lymphocytes are positive for Ki-67. Dr. Aron	p. 40/81
8/20/2015	Chemotherapy start date	Dr. Nabrinsky – oncologist	
9/2015	Admitted to St. Joseph's Hospital	Pneumonia treated with antibiotics (No medical records)	p. 176/360
10/26/15 to 10/30/15	ED visit for shortness of breath; hospitalization	Admitted to hospital for COPD exacerbation which improved with steroids, bronchodilators and antibiotics. He was discharged on 10/30/15.	p. 163
10/26/15	CT pulmonary angiogram	Emphysematous changes present throughout the lungs. Prominent bilateral nodular-appearing infiltrates. Likely related to an acute infectious process.	p. 24-25
11/16/15	Admitted to St. Joseph's Hospital	No medical records	Per attorney summary
11/25/15	PET scan	Lymphoma progression as evidenced by development of 2.5 x 3.0 x 2.5 cm paratracheal mass with increased metabolic activity.	p. 348
12/7/15	Admitted to Presence St. Joseph	Decided on hospice. No medical records	Per attorney summary
12/15/15		Mr. Karman passed away at home.	

Family Medical History

According to his medical records, Mr. Karman's mother suffered from a myocardial infarction and his father had kidney disease. Mr. Karman had no siblings, and all of his

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children are healthy with no occurrences of cancer per Mrs. Karman during our interview of January 11, 2021.

History of Tobacco, Alcohol and Drug Use

Mr. Karman began smoking in 1954 and quit briefly (for 4 weeks) in 2015¹⁷ but resumed smoking in late October 2015 just prior to his death.¹⁸ His medical records dated May 8, 2003, reported him smoking approximately 1.5 packs per day; records dated September 18, 2014, reported 16 cigarettes per day.¹⁹ According to his wife, Mr. Karman had smoked from about 1954²⁰ to 2015, stopping once for about five years and on two or three other occasions for up to six months at a time. He rolled his own cigarettes and smoked about one pack per day.²¹ Thus, he had over a 50 pack-year history.

At an office visit at Winters Family Practice on September 3, 2014, Mr. Karman reported that he drank 4+ beers per day.²² On May 8, 2003, he was drinking 30 beers weekly (4.2 beers per day).²³ Mrs. Karman testified that he drank two or three beers every day.²⁴ No illicit drug use or history was reported in any of the available medical records.

Employment History

Mr. Karman served in the U.S. Armed Forces.²⁵ He worked as a jet mechanic but never served overseas or in battle.²⁶ He served in the Marine Corps Reserve for five years from 1958 to 1963.

Mr. Karman worked for Automatic Electric in Northlake, Illinois, as a draftsman for a couple of years in the early 1960s. He then obtained a draftsman job with Motorola and was promoted to a circuit board designer during his eight year tenure there. He then worked as a circuit board designer at three different companies before working as a carpenter for about six months in the early 1980s.

¹⁷ Winters Family Practice medical records, p. 56 of 81.

¹⁸ Sherman Hospital Oncological medical records, p. 178 of 360.

¹⁹ Winters Family Practice medical records, pp. 7, 12 of 81.

²⁰ They met in 1958.

²¹ Telephone interview of Christine Karman, January 11, 2021.

²² Winters Family Practice medical records, p. 9 of 81.

²³ Winters Family Practice medical records, p. 71 of 81.

²⁴ Deposition of Christine Karman, November 13, 2019, p. 228.

²⁵ Certificate of death.

²⁶ Deposition of Christine Karman, November 13, 2019, pp. 181-182.

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In approximately 1990, he started his own business, Associated Design Services, in which he designed circuit boards as a contractor for Motorola. He retired in 2003.²⁷ Mr. Karman never applied Roundup® occupationally in any manner.

Deposition of Christine Karman, November 13, 2019

Christine Karman was married to Robert Karman for 54 years from September 23, 1961, until his death in 2015.²⁸ They have four daughters, Nancy, Ann, Roberta and Catherine and one son, Michael. Christine has smoked a pack of cigarettes per day for 60 years.²⁹ She had bladder cancer 11 years ago that resolved without special treatment.

She recalled that in July 2015, her husband's oncologist, Stanley Nabrinsky, told them³⁰ that Mr. Karman had lymphoma and that lymphoma is caused primarily by pesticides.³¹ Their daughter Nancy had asked if it was caused by cigarette smoking.³²

In an email written on August 3, 2015, by daughter Nancy from notes she had prepared at the physician's office, Nancy wrote that the physician stated that the lymphoma was caused by exposure to "fertilizer, pesticides and asbestos."

Mr. Karman assisted his carpenter son (Michael) to build their new home on [REDACTED] in 1989 - a 2,500 square foot house on a 0.75-acre lot.^{33,34} Mrs. Karman testified that her husband helped carry lumber, hired plumbers, talked with inspectors, swept and burned the garbage. He did not do any work with the painters. No toxic exposures were reported.

Prior to the [REDACTED] residence, Mr. & Mrs. Karman lived at [REDACTED] for 24 years.

²⁷ Plaintiff Fact Sheet, p. 3 of 28; Deposition of Christine Karman, p. 140.

²⁸ Deposition of Christine Karman, November 13, 2019, p. 164.

²⁹ Id., p. 18.

³⁰ Christine, Robert and Nancy.

³¹ Deposition of Christine Karman, November 13, 2019, p. 30.

³² Id., p. 33.

³³ Id., p. 103.

³⁴ Id., pp. 46 and 61.

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Mrs. Karman recalled that her husband used fertilizers, mainly Scott's.³⁵ She believes she purchased Scott's fertilizer for him to use at the 1500 Spruce Avenue residence where they lived prior to 1989.³⁶ Mr. Karman fertilized the lawn with a spreader.³⁷

Roundup® Applications

Mrs. Karman recalled that she and her husband both used Roundup® to spot-treat weeds in the yard of their [REDACTED] residence from 1991/1992 to about 2013.³⁸ She would purchase Spectracide³⁹ if it was on sale, but her husband purchased and used Roundup® because he believed that it *"worked better."*⁴⁰

When using Roundup® in their yard, Mr. Karman typically wore jeans, shoes with socks and a short-sleeved, cotton shirt and/or a flannel, long-sleeved shirt.⁴¹ He did not wear gloves and only wore a mask if he had a cold.⁴² He sprayed Roundup® for 3-4 minutes per discrete area, twice a month for eight months of the year, per deposition as noted:⁴³

Q. And when he would treat the areas that we marked in Exhibit 3, would that be, you know, a 10- to 15-minute thing or would it be longer?

A. When he was treating them?

Q. Yeah.

A. Shorter.

Q. How long would it take him to treat those areas each time on Exhibit 3?

A. Three, four minutes.

Mrs. Karman testified that her husband used a direct stream to spot-spray weeds in the lawn and always sprayed as close to the ground as possible to avoid killing surrounding grass. He did not spray the Roundup® up in the air or on his face, and she never saw him

³⁵ Id., p. 54.

³⁶ Id., p. 57.

³⁷ Id., p. 181.

³⁸ Id., pp. 92-93.

³⁹ Contains diquat dibromide rather than glyphosate as an active ingredient.

⁴⁰ Deposition of Christine Karman, November 13, 2019, pp. 87 and 92.

⁴¹ Id., p. 89.

⁴² Id., p. 90.

⁴³ Id., pp. 95-96.

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spill it on himself.⁴⁴ It was always pre-mixed Roundup[®]⁴⁵ and she recalled that the Roundup[®] container was a 1 gallon spray bottle with a hose and a 10 inch wand.⁴⁶

Significantly, Mrs. Karman testified that Mr. Karman sprayed Roundup[®] "...completely around the whole house at given times wherever there was a weed." She testified that they had a real problem with weeds; "They were all over."⁴⁷

Mr. Karman also used Roundup[®] on the gravel driveway for six years, from the garage to the street. He held the sprayer "...at arm's length until he got close to the side grass along the driveway."⁴⁸ He sprayed only where there were weeds. He wore the same clothing and sprayed during the same eight months as previously described. She could not estimate how long it took him to spray the driveway each time, but it took longer than it did to spray the patches.⁴⁹

He sprayed around the culverts on Sherwood and where the street turns into [REDACTED]. "That was, is still, a constant menace."⁵⁰ He also sprayed around the shed at the back of the house and in the patches of assorted weeds that grew all over the property.⁵¹

Mrs. Karman testified that her husband would sit on the back porch and relax after doing the yard work; he didn't shower immediately after spraying Roundup[®].⁵² She laundered his dirty clothes.⁵³

Mrs. Karman estimated that until her husband retired in 2003, she used Roundup[®] more frequently than he did.⁵⁴

According to Mrs. Karman, her husband did not suffer from other malignancies, rheumatoid arthritis, ulcers, diabetes, obesity, Epstein-Barr virus, lupus, Hepatitis B or C

⁴⁴ Deposition of Christine Karman, November 13, 2019, pp. 88-89; pp. 96-97.

⁴⁵ Id., p. 211.

⁴⁶ Id., pp. 80-81.

⁴⁷ Id., p. 186.

⁴⁸ Id., p. 143.

⁴⁹ Id., p. 144.

⁵⁰ Id., pp. 186-187.

⁵¹ Id., p. 187.

⁵² Id., p. 202.

⁵³ Id., p. 202.

⁵⁴ Id., p. 207.

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or any immunologic disorder.⁵⁵ Additionally, Mrs. Karman testified that the only symptom her husband initially experienced was the lump (noticed in May 2015). He experienced no fevers, night sweats or other pre-diagnostic symptomatic conditions.⁵⁶

Note: Mrs. Karman advised during deposition that some of the medical information in Mr. Karman's PFS (as originally completed by herself) required updating.

Residential Properties

The following images were provided by Mrs. Karman showing some of the areas at their [REDACTED] residence where she and Mr. Karman regularly applied Roundup®.



Figure 1: Google image of the Karman property where Mr. Karman regularly sprayed Roundup® from 1989 to 2015.

⁵⁵ Deposition of Christine Karman, November 13, 2019, pp. 226-227

⁵⁶ Id. pp. 231-232

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Figure 2: Photo of Karman property where Roundup® was regularly sprayed.



Figure 3: Photo of Karman property where Roundup® was regularly sprayed. The arrows point to the pen lines drawn by Mrs. Karman during deposition marking where she saw Mr. Karman spray Roundup.

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Figure 4: Photo of Karman property where Roundup® was regularly sprayed.

Telephone Interview with Christine Karman, January 11, 2021

I interviewed Mrs. Christine Karman by telephone and questioned her on specific aspects of her husband's medical history, exposure to other chemicals and Roundup® use.

Regarding Mr. Karman's family history, Mrs. Karman reported that he was an only child and neither of his parents ever developed any malignancies. None of their children has ever been diagnosed with cancer.

Mrs. Karman stated that of all her family members, she has the most knowledge of Mr. Karman's Roundup® use. He began using Roundup® in 1980 at their home property at [REDACTED]. This was, at most, a ¼ acre property. They lived there until June 1989 when their newly built home on [REDACTED] was ready. She estimated that for eight months of the year, Mr. Karman sprayed Roundup® at the Spruce Avenue property once per week for about 30 minutes, primarily along the curb and driveway.

The Karmans moved into their new home at [REDACTED], in June 1989. The yard of their 1 acre property had only been rough-graded when they moved in so she recalled that Mr. Karman began using Roundup® in the spring of 1990. The driveway to their home was gravel for about 6 years before it was paved.

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Mrs. Karman reported that she used Roundup® in her flower bed and only occasionally in other areas of the lawn. (She used Spectracide when she could buy it on sale.) Her husband only used Roundup® and he did all the spraying on the rest of the property which included the driveway, in the gully, along the street, around the shed, between the bushes and in the weedy patches throughout the lawn. She estimated that it took him between one hour and one and a half hours to spray all areas on the property. He sprayed about every two weeks on weekends during eight months of the year. He continued spraying Roundup® until the time of his NHL diagnosis in the summer of 2015.

Figure 3 above is a copy of Exhibit 3 from Mrs. Karman's deposition. The arrows point to the blue pen lines that she drew during deposition which mark brown weed patches in the grass where Mr. Karman typically sprayed Roundup®. During this interview, I questioned her about her deposition testimony wherein she stated that it took "three, four minutes" for her husband to spray the areas marked in Exhibit 3. Mrs. Karman clarified that it took about three or four minutes to spray just the areas marked with pen.⁵⁷ She explained that the roots from a nearby tree were very close to the surface here and would brown out the grass, enabling weeds to grow. She testified that it took about three or four minutes for her husband to spray just this one particular spot.

Mrs. Karman stated that her husband used a handheld wand sprayer as well as a trigger-type sprayer to spray premixed Roundup®. She does not recall if he ever used concentrated Roundup® mixed with water in the handheld sprayer. She recalled that on a couple of occasions, he was wet from the mist during his spraying as revealed by his clothing. She reported that his spray routine was generally to spray for a while and then take a break (for example, sitting on the porch and talking with her) before going back to spraying. He would then typically sit and relax after he had finished spraying. If the weather was particularly humid, he would shower when he finished spraying.

Mrs. Karman reported that their daughter, Roberta, remembers seeing a box of powdered or granulated Roundup® on a shelf in their garage. She does not have any recollection of seeing her father applying the granulated product.

Mr. Karman began smoking cigarettes in 1954. Mrs. Karman reported that since 1958 when they met, Mr. Karman, with some exceptions, smoked about one pack of hand-made cigarettes per day until his death in 2015. He stopped smoking for a period of about five years at one time and on two or three occasions had stopped smoking for up to six

⁵⁷ Mrs. Karman explained during her interview that such weed patches were over the entire property, not just confined to the Exhibit 3 location.

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months at a time. She reported that he drank about two or three Miller Lite beers every day. She explained that he would drink socially; typically, when their son or work associates dropped by their house.

Summary of Exposure Factors

Mr. Karman sustained regular episodic Roundup[®] exposures through direct application of both liquid and possibly powder/granulated Roundup[®] for personal use from 1980 to approximately 2015 (35 years).

Personal Protective Equipment (PPE)

Mr. Karman did not use PPE. As previously noted, Mr. Karman typically wore jeans, shoes with socks and a short-sleeved, cotton shirt and/or a flannel, long-sleeved shirt.⁵⁸ He did not wear gloves and only wore a mask if he had a cold.⁵⁹ He had no pragmatic reason to believe that it was necessary to wear protective equipment and thus, he did not do so.

Potential Confounding Exposures

Defendant's attorneys speculated during Mrs. Karman's deposition that Mr. Karman may have been exposed to joint compound containing asbestos while helping his son build their home in 1989. However, there is no evidence to support this speculation.⁶⁰ Additionally, asbestos was no longer available in consumer products at that time.⁶¹ Even if it had been used, wet joint compound is not a matrix capable of producing friable asbestos dust during application.

The construction work on the new home took approximately 6 months. Mr. Karman assisted on weekends⁶² as a helper. Mrs. Karman recalled that one of his tasks was to sweep the floor, probably once a week. She believes he wore a dust mask but doesn't recall specifically.⁶³ Mrs. Karman has possession of the purchase orders of the products used in the building of their home.⁶⁴

⁵⁸ Deposition of Christine Karman, November 13, 2019, p. 89.

⁵⁹ Id., p. 90.

⁶⁰ Id., p. 46.

⁶¹ In 1977, the Consumer Product Safety Commission banned the use of asbestos in joint compound.

⁶² Deposition of Christine Karman, November 13, 2019, p. 61.

⁶³ Id., p. 62.

⁶⁴ Id., p. 51.

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Mrs. Karman testified that her husband changed the oil in their cars, changed brake pads and performed other normal and expected vehicle maintenance.

Table 2 summarizes responses to questions presented to Mrs. Karman in interview and/or deposition regarding her husband's activities that might have included potentially confounding exposures.

Table 2
Additional Interview Questions Presented to Mrs. Karman

Potential Causative Factors	Comments
Family medical history	No
Alcohol consumption history	Consumed 2-3 beers daily
Smoking history and pack-year calculations	Approximately 50 pack-years Not significantly associated with DLBCL
Drugs-of-abuse	No
Any history of obesity?	Moderate obesity: BMI 31
Prior pharmacological regimens	Anti-hypertensive medication – no known carcinogenic risks
Any history of prior hematopoietic malignancies or other cancers?	No
Ever been prescribed long-term immunosuppressive pharmaceuticals such as prednisone?	No
Ever prescribed cyclophosphamide or any other drugs to treat cancer prior to NHL treatment?	No
History of organ transplant?	No
Ever been diagnosed with HIV, AIDS?	No
Ever been diagnosed with Hepatitis B or C?	No
Ever been diagnosed with Crohn's disease?	No
Ever been diagnosed with rheumatoid arthritis?	No
Ever been diagnosed with ulcerative colitis?	No
Significant radiological exposures or CT scans prior to NHL treatment?	No
Ever lived near or adjacent to a Superfund site?	No
Paint and/or paint solvent exposure?	Seldom used latex paint
Exposure to benzene?	No
Exposure to petroleum products?	No
Any unusual or chronic gasoline exposures?	No

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Table 2
Additional Interview Questions Presented to Mrs. Karman

Potential Causative Factors	Comments
Use of solder for pipe welding?	No; minor soldering
Ever welded pipes?	No
Ever used plumbing PVC glue?	Rarely
Use of a wasp killer or other insecticide/pesticide?	No
Use of Ortho Weed B Gon or herbicide other than Roundup?	No
Ever used 2,4-D?	No
Ever used Weed & Feed?	No
Ever used Snake-A-Way?	No
Ever used Sevin?	No
Use of any other home gardening/landscape chemicals?	No
Ever farmed or been exposed to livestock?	No
Other underlying chemical exposures?	No

Exposure Frequencies and Durations

As Mr. Karman was not deposed prior to his death, all calculations are based upon Mrs. Karman's deposition testimony and responses to questions posed during my telephone interview. The following objective facts are extant in the present matter:

- As noted in the residential photos, the Karman property contained multiple areas containing various types of shrubs and decorative foliage. Elimination of weeds was an ongoing project requiring diligence and exactitude. There were also areas devoid of grass in which weeds regularly appeared; these were also sprayed.
- At the [REDACTED] property, Mr. Karman applied Roundup® once per week for about 30 minutes for eight months (30 weeks) of the year.
- At his [REDACTED] property, Mr. Karman sprayed Roundup® from 1990 until mid-2015 (25 years). Per Mrs. Karman's deposition testimony, Mr. Karman sprayed Roundup® for 3-4 minutes per discrete area twice a month for eight months of the year. This included "patches of assorted weeds all over the property," gravel driveway

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(during the first six years), culvert, between bushes and around the shed's perimeter. Mrs. Karman estimated that 60 to 90 minutes were required per application event.

- Mr. Karman continued to apply Roundup® half-way through 2015, the year of his diagnosis. Hence, the total exposure interval is **35 years**. **Table 3** compiles evidential factors and calculates the resulting scope of exposures as expressed in *exposure-days*.

Scope of Exposures and Exposure-Day Calculations

This section assesses Mr. Karman's exposure history to arrive at a reasonably accurate number of *8-hour time-weighted exposure-days*. **Table 3** presents a conservative compilation of Mr. Karman's episodic Roundup® exposures as obtained from Mrs. Karman's deposition record and my telephone interview with Mrs. Karman. She recalled critical details during interview based on direct observation and demonstrated reasonable recall of past dates and events.

Note: These calculations exclude exposures for which no specific exposure intervals can be quantifiably assigned for toxicological assessment. Consequently, the results shown are minimal and therefore, conservative.

Table 3

Mr. Karman's 8-Hour Time-Weighted Roundup® Exposure-Days

Date	Years	Events Per Year	Hours Per Event	Total Hours			Exposure Days (8 hours/day)		
				Min	Mid	Max	Min	Mid	Max
1980 - 1989	9	30	0.5		135			16.9	
1990 - 2015	25	16	1.0 - 1.5	400	500	600	50	62.5	75
Totals:				535	635	735	67	79	92

The information compiled in **Table 3** reveals that Mr. Karman sustained a minimum of **67** exposure-days [$535 \div 8 \text{ hrs./day}$], a maximum of **92** exposure-days [$735 \div 8 \text{ hrs./day}$], and a midpoint of **79** exposure-days [$635 \div 8 \text{ hrs./day}$].

NHL Latency Interval

Based on his first confirmed exposure to Roundup®, Mr. Karman's latency interval to date of diagnosis was approximately **35 years** (1980-2015).

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Glyphosate Human NHL Studies

My toxicological opinions with respect to dose are based, in part, on six (6) primary epidemiological studies that provide objective data with respect to several prongs of the Bradford Hill criteria. My toxicological opinion is grounded in animal experimental evidence, *in vitro* human studies and human epidemiological studies as summarized within this report and previously provided by Dr. Portier, et al., in the Federal Daubert motion proceedings. Specifically, I have assessed dose response, temporality, latency period, biological plausibility (toxicological mechanisms), coherence (demonstrated by molecular-based studies) and animal studies as well as the strength of association and consistency with the toxicological mechanisms of Roundup® formulation ingredients. I have used the six primary epidemiological studies which include Eriksson, et al., 2008,⁶⁵ McDuffie, et al., 2001,⁶⁶ Andreotti, et al., 2018,⁶⁷ Leon, et al., 2019,⁶⁸ Zhang, et al., 2019⁶⁹ and Pahwa, et al., 2019,⁷⁰ primarily with respect to dose assessment.

My toxicological focus on these studies is on study design, statistical power, and exposure thresholds at different odds ratios, etc. I am using these study results in my toxicological assessment in conjunction with generally-accepted, peer-reviewed studies on genotoxicity (including direct human studies) mechanisms of action (promotion, etc.) absorption, distribution, metabolism, and excretion (ADME), etc. In general, I have relied on studies that have documented the various aspects of the Bradford Hill criteria at or in excess of the 95% confidence threshold. However, I am deferring to the epidemiologist with respect to the internal statistical designs and meta-analysis bio-statistical methodologies employed within each study. Summaries of these six studies are provided below:

⁶⁵ Eriksson, M., et al., "Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis," 2008, International Journal Cancer, Vol.123, pp. 1657 – 1663.

⁶⁶ McDuffie H., et al., "Non-Hodgkin's lymphoma and specific pesticide exposures in men: Cross-Canada study of pesticides and health," 2001, Cancer Epidemiology, Biomarkers & Prevention, Vol.10, pp. 1155 – 1163.

⁶⁷ Andreotti, G., et al., "Glyphosate Use and Cancer Incidence in the Agricultural Health Study," 2018, JNCI J Natl Cancer Inst., Vol.110 (5), doi: 10.1093/jnci/djx233.

⁶⁸ Leon, Maria, et al., "Pesticide use and risk of non-Hodgkin lymphoid malignancies in agricultural cohorts from France, Norway and the USA," 2019, International Journal of Epidemiology, pp. 1–17.

⁶⁹ Zhang, L., et al., "Exposure to Glyphosate Based Herbicides and Risk for Non-Hodgkin Lymphoma: A Meta-Analysis and Supporting Evidence," July-September 2019, Mutation Research/Reviews in Mutation Research, Volume 781, pp. 186-206. <https://doi.org/10.1016/j.mrrev.2019.02.001>

⁷⁰ Pahwa, M. et al., "Glyphosate use and associations with non-Hodgkin lymphoma major histological sub-types: findings from the North American Pooled Project," 2019 Jun 27, Scand J Work Environ Health. pii: 3830. doi:10.5271/sjweh.3830

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1. **Eriksson, M., et al., 2008 study:**⁷¹ This is a peer-reviewed, case-control study of exposure to pesticides as a risk factor for non-Hodgkin's lymphoma (NHL) in cases in Sweden between 1999 and 2002. Different exposure levels were classified according to days of exposure.

In this study, the association of glyphosate exposure with non-Hodgkin's lymphoma followed a dose response pattern with an odds ratio (OR) of 1.69 for 10 days of exposure or less, and 2.36 for greater than 10 days of exposure.

The human epidemiological studies have demonstrated statistically significant increased rates of NHL associated with glyphosate exposure. These studies include several different "exposure day" thresholds: "ever/never," greater than one day and <10 days and greater than 10 days.

2. **McDuffie, H., et al., 2001:**⁷² This is a Canadian case-control study which investigated the association of specific pesticides and non-Hodgkin's lymphoma that created dose-response levels based on days/year of personally mixing or applying herbicides. The study revealed that glyphosate exposures between >0 and ≤ 2 days per year had an NHL odds ratio (OR) of 1.0 while exposures greater than 2 days of exposure per year had an NHL odds ratio of 2.12.

The published McDuffie, et al., study presented "Table 6" in which glyphosate exposure was stratified according to "unexposed," ">0 and ≤2 days," and ">2 days" of per year exposure. The study documented statistically significant dose-responses: an odds ratio of **2.12** (1.20–3.73) for the ">2 days" per year group which was statistically significant.

3. **Andreotti, G., et al., 2018:**⁷³ The "Agricultural Health Study" (AHS) is an ongoing cohort study which includes 54,251 licensed pesticide applicators from Iowa and North Carolina with 82.8% reporting use of glyphosate. The study is funded by the National Cancer Institute and the National Institute of Environmental Health.⁷⁴ An updated

⁷¹ Eriksson, M., et al., "Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis," 2008, *International Journal Cancer*, Vol.123, pp. 1657 – 1663.

⁷² McDuffie H., et al., "Non-Hodgkin's lymphoma and specific pesticide exposures in men: Cross-Canada study of pesticides and health," 2001, *Cancer Epidemiology, Biomarkers & Prevention*, Vol.10, pp. 1155 – 1163.

⁷³ Andreotti, G., et al., "Glyphosate Use and Cancer Incidence in the Agricultural Health Study," 2018, *JNCI J Natl Cancer Inst.*, Vol.110 (5), doi: 10.1093/jnci/djx233.

⁷⁴ *Id.*

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evaluation of glyphosate and cancer risk was conducted in the AHS⁷⁵ and included cancer incidences through 2012 in North Carolina and 2013 in Iowa. The reported lifetime days' frequency of pesticide application is shown in **Table 4**.

Table 4
Demographics of "Agricultural Health Study"⁷⁶ Cohort (Applicators n = 54,251)

Lifetime days of glyphosate use (Quartiles)	Lifetime days of glyphosate use (Tertiles)
1 – 13.74	1 – 19.9
13.75 – 38.74	20 – 61.9
38.75 – 108.4	≥ 62.0
≥ 108.5	

Exposure days can be compared to **Table 4** with the corresponding quartiles or tertiles of the Agricultural Health Study to determine if his exposure was consistent with that of these applicators. The Agricultural Health Study did not find a statistically elevated risk of NHL; however, the study is useful with respect to comparison of other epidemiological studies.

4. **Leon, et al., 2019:**⁷⁷ In this analysis combining data from >300,000 farmers or agricultural workers from France, Norway and the USA and accruing more than 3.5 million person-years under risk, the possible association between pesticide use and the risk of lymphoid malignancies was investigated. Specifically, the authors investigated the relationship of the "ever use" of 14 selected pesticide chemical groups and 33 individual active chemical ingredients with non-Hodgkin's lymphoid malignancies (NHL). Pesticide use was derived from self-reported history of crops cultivated combined with crop-exposure matrices (France and Norway) or self-reported lifetime use of active ingredients (USA). Cox regression models were used to estimate cohort specific hazard ratios (HRs) and 95% confidence intervals (CIs) which were combined using random effects meta-analysis to calculate meta-hrs.

During follow-up, 2,430 NHL cases were diagnosed in 316,270 farmers accruing 3,574,815 person-years under risk. Moderately elevated meta-HRs were seen for NHL overall or certain subtypes with use of specific pesticides compared with "never" use

⁷⁵ Id.

⁷⁶ Id.

⁷⁷ Leon, Maria, et al., "Pesticide use and risk of non-Hodgkin lymphoid malignancies in agricultural cohorts from France, Norway and the USA," 2019, International Journal of Epidemiology, pp. 1–17.

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of the same pesticides. In particular, elevated hazard ratios of diffuse large B-cell lymphoma (DLBCL) were seen with glyphosate use (1.36, CI: 1.00–1.85). It is noteworthy that although this study found no association between risk of *all types of NHL overall* and ever use of glyphosate, there was a statistically-elevated risk of borderline significance for DLBCL (the most common type of NHL).

5. **Zhang, L., et al., (2019):**⁷⁸ The Zhang, et al., study is a meta-analysis design that included the most recent update of the Agricultural Health Study (AHS) cohort published in 2018 along with five case-control studies. The study reported that glyphosate-based herbicide (GBH) exposure is associated with increased risk of NHL in humans. Using the highest exposure groups when available in each study, they further reported that the overall meta-relative risk (meta-RR) of NHL in glyphosate-based herbicide exposed individuals was increased by 41% (meta-RR = 1.41, 95% CI, confidence interval: 1.13–1.75). For comparison, a secondary meta-analysis using high-exposure groups with the earlier AHS (2005) determined a meta-RR for NHL of 1.45 (95% CI: 1.11–1.91) which was higher than the meta-RRs reported previously.
6. **Pahwa, M. et al., (2019):**⁷⁹ In a 2019 study, the associations between glyphosate use and NHL incidence, overall, and by histological sub-type, were evaluated in a pooled analysis of case-control studies. NHL cases were recruited from cancer registries and hospitals in four states between 1991 and 1994, as well as six Canadian provinces. This analysis included 5,131 controls and 1,690 cases of NHL; 647 diffuse large B-cell lymphoma, 468 follicular lymphoma, 171 small lymphocytic lymphoma and 404 other sub-types. The authors found that subjects who had ever used glyphosate had an excess of NHL overall (OR 1.43, 95% CI 1.11–1.83). After adjustment for other pesticides, the OR for NHL overall with "ever use" was 1.13 (95% CI 0.84–1.51) with a statistically-significant association for handling glyphosate more than two days per year (OR 1.73, 95% CI 1.02–2.94, P-trend=0.2). In pesticide-adjusted NHL sub-type analyses, the ordinal measure of lifetime-days was statistically significant (P=0.03) for small lymphocytic lymphoma (SLL) and associations were elevated, but not statistically significant, for "ever years" or "days/year" of use. The authors also showed

⁷⁸ Zhang, L., et al., "Exposure to Glyphosate Based Herbicides and Risk for Non-Hodgkin Lymphoma: A Meta-Analysis and Supporting Evidence," July-September 2019, Mutation Research/Reviews in Mutation Research, Volume 781, pp. 186–206. <https://doi.org/10.1016/j.mrrev.2019.02.001>.

⁷⁹ Pahwa, M. et al., "Glyphosate use and associations with non-Hodgkin lymphoma major histological sub-types: findings from the North American Pooled Project," 2019 Jun 27, Scand J Work Environ Health. pii: 3830. doi:10.5271/sjweh.3830

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that subjects handling glyphosate more than two days per year had an excess of DLBCL (OR 2.14, 95% CI 1.07-4.28).

These findings (as summarized in **Table 5**) are consistent with results reported from prior meta-analyses but show higher risk for NHL due to the focus on the highest exposure groups. The authors caution on the interpretation of the numerical risk estimates because of the heterogeneity between the studies.

Nevertheless, all of the evidence from these studies of glyphosate-exposed mice support this association in humans and mechanistic studies of glyphosate-induced immunosuppression/inflammation, endocrine disruption, genetic alterations, and oxidative stress suggest clinically-plausible links between GBH exposure and NHL development. The authors conclude “*The overall evidence from human, animal and mechanistic studies presented here supports a compelling link between exposures to GBHs⁸⁰ and increased risk for NHL.*”

⁸⁰ Glyphosate-based herbicides.

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Summary of Epidemiological Studies

Table 5 shows the various exposure parameters and assessment metrics for the six (6) epidemiological studies noted herein.

Table 5
Exposure Parameters for Six Referenced Epidemiological Studies⁸¹

Study	Type of study	Exposure Parameters	
		Metrics (dose intervals)	Cut-off between Cases and Controls
McDuffie, H. et al., 2001	Case-control study of men in six Canadian provinces.	Unexposed >0 days and ≤2 days >2 days/year	Cases were diagnosed with STS, HD, NHL, or MM between 9/1/1991 and 12/31/1994. Controls did not have NHL diagnoses.
Eriksson, M., et al., 2008	Case-control study of men and women in Sweden	≥1 day and ≤ 10 days >10 days	Cases were newly diagnosed NHL patients aged 18-74 years. Controls were randomly selected from the population registry.
Andreotti, G., et al., 2018	Prospective cohort study of pesticide applicators	Never use Quartiles ranging from 1 day to ≥ 108.5 days Tertiles ranging from 1 day to ≥ 62.0 days	Cases reported ever use of glyphosate. Reference subjects may have used any other pesticides.
Leon, et al, 2019	Pooled analysis of three agricultural worker cohorts	Ever use	Cases reported ever use of glyphosate. Reference subjects may have used any other pesticides.
Zhang, et al., 2019	Meta-analysis	Ever use	6 studies included in primary analysis: one cohort and five case-control.
Pahwa, M. et al., 2019	Case-control study	2 days/year	Subjects handling glyphosate more than two days/year had an excess of DLBCL (OR 2.14, 95% CI 1.07-4.28.

⁸¹ All studies in the table revealed statistically significant increased rates of some type of NHL except Andreotti, et al., 2018. Leon, et al., reported a borderline statistic of 1.36, CI: 1.00–1.85.

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Comparisons of Exposure Days to Human Epidemiological Studies

The results of the “exposure-day” calculations (based on validated, reported exposure intervals in the above tables) indicate that Mr. Karman’s cumulative exposures were above all of the exposure threshold metric cut-offs. That is, he exceeded the “*ever use*” threshold, the “*>0 and ≤ 2 days*” threshold, the “*>2 days per year*” threshold, the “*≥1 day ≤ 10 days*” total threshold, and the “*>10 days*” total exposure threshold.

Putting this into a dose-metric context, Mr. Karman’s **minimum of 67 exposure-days** exceeds the highest tertile of exposure as defined in the Agricultural Health Study of “*≥62 days*” and lies within the third highest quartile of exposure defined as “*≥38.75 and ≤108.4days*.” (Note that no statistically-significant finding of NHL was reported in the Agricultural Health Study). Thus, Mr. Karman approached the maximum exposure metrics of the cited human epidemiological studies documenting the fact that he was within range of human studies revealing *statistically significant increased NHL cases among glyphosate applicators*.

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Summary of Objective Toxicological Factors

The generally-accepted, peer-reviewed toxicological literature is not based on unsubstantiated, subjective opinions, but rather statistically significant data at the 95% level of confidence. The various 8 prongs of the well-established Bradford Hill criteria have been evaluated in my assessment by considering the strength of various associations within genotoxicity and other mechanistic studies, the specificity of the adverse effect(s) as well as their consistencies among different studies.

Additionally, dose-responsiveness has been evaluated among the various genotoxicity and other mechanistic studies as referenced within this report (in some cases using human equivalent dosing (HED methodology). Also, coherence of studies among different study designs has been considered along with latency (temporality) and experimental studies in which animal dose equivalency comparisons to human dosage were assessed.

Expert opinions must always be based on objective, reliable evidence without deviation from the generally accepted methodology. Using the weight-of-evidence methodology of significant findings within the human epidemiological studies that employ dose-metrics, coupled with a scientific understanding of the genotoxic mechanisms, bone distribution/ADME and the mechanisms in which the Roundup® mixtures are absorbed, distributed to bone marrow and other locations, retention time in such tissues prior to metabolism and excretion, reliable toxicological opinions are provided.

The evidence of glyphosate potency when applied as a chemical mixture has also been evaluated from both mechanistic findings and dose-response evidence. Mr. Karman's exposure histories have been compared to the dose-metrics in human epidemiological studies with respect to determining whether 8-hour time-weighted exposure day thresholds were exceeded.

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Evidential Considerations

The following evidential factors are useful in formulating an objective toxicological assessment of Mr. Karman with regard to his Roundup® exposures and subsequent NHL diagnosis:

- **Diagnosis:** Mr. Karman's pathology records reveal a diagnosis of diffuse large B-cell lymphoma (DLBCL) in July 2015. His disease was aggressive and he passed away from the disease only five months later on December 15, 2015. The medical records reveal an on-going pathology consistent with diffuse large B-cell lymphoma.
- **Prolonged Acute Exposure and Absorption:** Mr. Karman's belief that Roundup® was not harmful to him resulted in him not using any form of personal protective equipment (PPE). Mr. Karman typically wore jeans, shoes with socks, and a short-sleeved, cotton shirt and/or a flannel, long-sleeved shirt.³⁸⁵ He did not wear gloves, and only wore a mask if he had a cold.³⁸⁶ He had no pragmatic reason to believe that it was necessary to wear protective equipment and thus, he did not do so.
- **Chronic Glyphosate Exposure:** Per Mrs. Karman's deposition testimony, Mr. Karman sprayed Roundup® initially weekly, then twice a month for 8 months of the year for a total of approximately 35 years of applications. Pursuant to Mrs. Karman's deposition testimony, this pattern repeated without variance for the duration of the two exposure interval scenarios. Additional Roundup® exposures, spills, accidents, etc. may have occurred and are not included in this total.
- **Dermal Absorption Rates Higher than Presented by Monsanto:** As previously discussed in great detail, the correct dermal absorption rate for glyphosate ranges between 3% and greater (as opposed to the defective values recently issued by Monsanto's contractor, DTL Laboratory). Additionally, numerous other factors are known to increase skin absorption of glyphosate including (but not limited to) elevated temperatures, continuing to wear herbicide-soaked clothing and gloves, sweating (which contributes to increased skin absorption) and cracked skin as well as the various surfactants formulated in the actual Roundup® products (as most of the dermal absorption studies were performed on pure glyphosate without the additives).

³⁸⁵ Deposition of Christine Karman, November 13, 2019, p. 89.

³⁸⁶ Id., p. 90.

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Lack of Personal Protective Equipment (PPE): Mr. Karman was not instructed via the product label to wear personal protective equipment such as impermeable pants, boots, mask, long sleeve shirt, face shield, *chemically-resistant* gloves, etc. He believed Roundup® was “safe” to use for many reasons and proceeded accordingly. Notably, Monsanto employees (in the previously referenced study) were protected with PPE on all exposed body areas during their own dermal exposure testing procedures, but consumers are not protected because the product label provides no such instructions.³⁸⁷ (Even though the Monsanto research study and report recommended multiple warnings with respect to PPE.)

- **Mechanism of Carcinogenicity:** Mr. Karman’s exposures are to Roundup® product, not to glyphosate alone. Roundup® and glyphosate have been demonstrated in several studies to repeatedly cause DNA damage with promotion by Roundup® being more damaging than glyphosate alone. Genotoxicity is the first stage in cancer formation. Wozniak, et al.,³⁸⁸ and other studies as referenced in this report further demonstrated that Roundup®, at a higher dose, was even able to impede the natural repair of damaged DNA.

The George, et al., study³⁸⁹ documented cancer promotion at relatively low dermal exposure doses in mice. The dose levels, when converted to human doses, are reasonably similar to that sustained by applicators (when applying the HED factor and dermal absorption rate of 3%). More importantly, the test model employed DMBA (as found in cigarette smoke/tar). This primary carcinogen was dermally applied at low doses on the shaved skin of mice with no tumors produced unless glyphosate was also applied to the skin in which case 40% of the animals developed tumors (2.8 tumors per animal). The mechanism of glyphosate carcinogenesis is important with respect to tumor promotion among smokers prior to the onset of NHL. The George study reveals substantial promotion (40% of the mice with tumors) with realistic concentrations of glyphosate as compared to that of applicators using HED methodology.

³⁸⁷ Some later labels included recommendation of gloves during mixing.

³⁸⁸ Wozniak, E., et al., “The mechanism of DNA damage induced by Roundup® 360 PLUS, glyphosate and AMPA in human peripheral blood mononuclear cells – genotoxic risk assessment,” 2018, Food and Chemical Toxicology, doi: 10.1016/j.fct.2018.07.035

³⁸⁹ George, J., et al., “Studies on glyphosate-induced carcinogenicity in mouse skin: A proteomic approach,” 2010, Journal of Proteomics, Vol. 73, pp. 951 – 964.

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- **Latency of non-Hodgkin's Lymphoma:** The compilation of peer-reviewed latency estimates presented herein (see **Table 20**) demonstrates latency intervals within a typical range of 2 to 25 years. Based upon the study findings, the weight of available evidence indicates that a minimum latency interval of 2 to 25 years is required and is scientifically reliable. Mr. Karman's clinical NHL diagnosis and latency of **35 years** meets the minimal latency requirement. It is noteworthy that studies by Eriksson, et al., (2008) found an increased effect estimate for subjects with more than 10 years of glyphosate exposure prior to NHL diagnosis, thus favoring a longer latency interval.
- **Scope of Exposure in Comparison to Epidemiological Studies:** Mr. Karman's exposure doses in units of duration and frequency were compared to the reference doses in six epidemiological studies. The studies included Eriksson, et al.³⁹⁰, McDuffie, et al.³⁹¹, Leon, et al., 2019,³⁹² (study combining data from >300,000 farmers or agricultural workers from France, Norway and the USA), the Agricultural Health Study (AHS), Pahwa, M. et al., 2019³⁹³ and Zhang, L., et al., (2019).³⁹⁴

The Zhang, et al., study is a meta-analysis design that included the most recent update of the Agricultural Health Study cohort published in 2018 along with five case-control studies. Mr. Karman's calculated 8-hour, time-weighted midpoint exposure dose (**79 exposure-days**) was consistently in excess of the threshold exposure doses reported within all of the studies revealing statistically significant increased rates of NHL.³⁹⁵

³⁹⁰ Eriksson, M., et al., "Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis," 2008, International Journal Cancer, Vol.123, pp. 1657 – 1663.

³⁹¹ McDuffie H., et al., "Non-Hodgkin's Lymphoma and Specific Pesticide Exposures in Men: Cross-Canada Study of Pesticides and Health," 2001, Cancer Epidemiology, Biomarkers & Prevention, Vol.10, pp. 1155 – 1163.

³⁹² Leon, Maria, et al., "Pesticide use and risk of non-Hodgkin lymphoid malignancies in agricultural cohorts from France, Norway and the USA," 2019, International Journal of Epidemiology, pp. 1–17.

³⁹³ Pahwa, M. et al., "Glyphosate use and associations with non-Hodgkin lymphoma major histological sub-types: findings from the North American Pooled Project, 2019 Jun 27. Scand J Work Environ Health. pii: 3830. doi:10.5271/sjweh.3830

³⁹⁴ Zhang et al., "Exposure to Glyphosate-Based Herbicides and Risk for Non-Hodgkin Lymphoma: A Meta- Analysis and Supporting Evidence," 2019, Mutation Research-Reviews in Mutation Research <https://doi.org/10.1016/j.mrrev.2019.02.001>

³⁹⁵ The Leon study was of borderline statistical significance (@ 95% confidence interval, but not exceeding it).

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Summary and Conclusions

My toxicological assessment of the current matter includes assessment of the human epidemiological studies discussed above, the dose/response (biological gradient), strength of association, consistency and coherence of the six primary studies and the studies of various chemical formulants and additives found in the Roundup® product as well as experimental evidence including absorption, distribution (*i.e.*, measurement in bone marrow), metabolism and excretion (ADME) and the various mechanisms of carcinogenesis (including genotoxicity, impairment of DNA repair mechanisms and promotion). Additionally, I have focused on dermal absorption, the manner and degree to which Roundup® penetrates the skin, the lack of adequate PPE and additive toxicological effects of POEA and POEA derivatives used in the product.

I have carefully examined Mr. Karman's history for any potential confounding toxicological factors and have found slight to moderate obesity in his later years (BMI 31) and a 50 pack-year history of smoking. However, DLBCL has not been shown to be significantly causally associated with smoking.³⁹⁶

Based on the findings of applicable studies as noted herein and on the basis of sufficient exposure, dose, duration and episodic exposures to Roundup® consistent with the human exposure durations in the epidemiological studies, it is my opinion, to reasonable toxicological certainty, that Mr. Karman's exposure to Roundup® was a substantial contributing factor to his development and subsequent diagnosis of diffuse large B-cell lymphoma.



William R. Sawyer, Ph.D.

Chief Toxicologist

³⁹⁶ See the above section on "Smoking as Potential NHL Risk Factor."