Neoplastic outcomes were of the type common in mice of this age and strain. Of the tumour types observed, bronchiolar-alveoli tumours of the lungs, hepatocellular neoplasms and tumours of the lymphoreticular system, none were dose related and all were seen in all treatment groups (Table 19). Lymphoreticular tumours were more frequently observed in female mice, but the incidences were low and did not approach statistical significance (nonsignificant trend and pair wise comparison). With the possible exception of kidney tumours (renal tubular adenomas) in males, all tumour types were considered spurious and unrelated to treatment (see Table 19).

Table 19. Neoplasia in male and female mice treated with glyphosate for 24 months

	Incidence per dietary concentration of glyphosate							
	Males				**Females**			
Site / Neoplasia	**0 ppm** [a]	**1 000 ppm**	**5 000 ppm**	**30 000 ppm**	**0 ppm** [a]	**1 000 ppm**	**5 000 ppm**	**30 000 ppm**
Lung								
Bronchiolar alveolar adenoma	5/48	9/50	9/50	9/50	10/49	9/50	10/49	1/50
Bronchiolar alveolar adenocarcinoma	4/48	3/50	2/50	1/50	1/49	3/50	4/49	4/50
Lymphoblastic lymphosarcoma with leukaemic manifestations	1/48	4/50	3/50	1/50	–	–	–	–
Liver								
Hepatocellular adenocarcinoma	5/49	6/50	6/50	4/50	1/49	2/50	1/49	0/49
Hepatocellular carcinoma	0/49	0/50	0/50	2/50	2/49	1/50	0/49	4/49
Lymph node (mediastinal)								
Lymphoblastic lymphosarcoma with leukaemic manifestations	1/45	2/49	1/41	2/49	–	–	–	–
Kidney								
Renal tubular adenoma	0/49	0/49	1/50	3/50	–	–	–	–
Lymphoblastic lymphosarcoma with leukaemic manifestations	1/49	3/49	2/50	2/50	–	–	–	–
Total lymphoreticular neoplasms (sum of lymphoblastic lymphosarcoma, composite lymphosarcoma and histiocytic sarcoma)	2/48	6/49	4/50	2/49	5/50	6/48	6/49	10/49

ppm: parts per million; PWG: Pathology Working Group

Results presented as number of neoplasm-bearing animals / number of animals examined.

[a] Incidence of effect in controls from the study report prior to PWG re-evaluation.

Source: (Knezevich and Hogan, 1983)

At the request of the USEPA, the Pathology Working Group (PWG) examined all sections of the kidneys from this study as well as additional renal sections. The PWG evaluation included a renal tubule adenoma in one control male mouse that was identified during a re-evaluation of the original renal section. The PWG noted that because differentiation between tubular-cell adenoma and tubular-cell carcinoma is not always clearly apparent and because both lesions are derived from the same cell type, it appropriate to combine the incidences for statistical analysis. Statistical analyses performed by the PWG are presented in Table 20. The PWG concluded that these lesions are not treatment-related based on the following considerations: 1) renal tubular-cell tumours are spontaneous lesions for which there is a paucity of historical control data for this mouse stock; 2) there was no statistical significance

Table 25. Malignant lymphoma in glyphosate-treated mice

			Measure per dietary concentration of glyphosate							
			Males				Females			
	M	F	0 ppm	100 ppm	1 000 ppm	10 000 ppm	0 ppm	100 ppm	1 000 ppm	10 000 ppm
Dead and moribund mice										
No. examined	75	77	22	20	22	27	16	16	20	20
No. affected	20	49	9	12	13	13	9	10	13	12
Incidence (%) [a]	26.7	63.6	41.0	60.0*	59.0*	48.0	56.0	63.0	65.0	60.0
Terminated mice										
No. examined	175	173	28	30	28	23	34	34	30	30
No. affected	26	50	1	3	3	6*	9	10	6	13
Incidence (%) [a]	14.9	28.9	3.6	10.0	10.7	26.1*	26.5	29.4	20.0	43.3*
Mean percentage	14.9	28.8	–	–	–	–	–	–	–	–
Range of percentage	8–24	2–43	–	–	–	–	–	–	–	–
All fates										
No. examined	250	250	50	50	50	50	50	50	50	50
No. affected	46	99	10	15	16	19*	18	20	19	25
Incidence (%) [a]	18.4	39.6	20.0	30.0	32.0	38.0*	36.0	40.0	38.0	50.0*
Mean percentage	18.4	41.6	–	–	–	–	–	–	–	–
Range percentage	6–30	14–58	–	–	–	–	–	–	–	–

F: females; M: males; –: not examined/not determined; *: significant increase compared with historical controls (no *P* value provided)

[a] Incidence expressed as number of animals affected as a percentage of the number examined.

Source: Kumar (2001)

The increased incidences of kidney tumours at high doses (0/50, 0/50, 1/50 and 2/50 at 0, 100, 1000 and 10 000 ppm, respectively) were statistically significant in the trend test but not in a pairwise comparison. No historical control data were available.

The NOAEL for systemic toxicity in the 18-month carcinogenicity study in mice was 1000 ppm (equal to 149.7 mg/kg bw per day) for increased mortality at 10 000 ppm. Glyphosate was not carcinogenic in mice at doses up to 10 000 ppm, the highest dose tested (Kumar, 2001).

In a carcinogenicity study, glyphosate (purity 95.7%) was fed in the diet to groups of 51 male and 51 female CD-1 mice per dose at concentrations of 0, 500, 1500 and 5000 ppm (equal to 0, 71.4, 234.2 and 810 mg/kg bw per day for males and 0, 97.9, 299.5 and 1081.2 mg/kg bw per day for females) for 79 weeks. An additional 12 mice per sex, designated as veterinary controls, were housed and maintained alongside the treated animals. Ten animals per sex from each group were set aside for an interim termination (toxicity assessment) at week 39. Stability, homogeneity and dietary concentrations were evaluated periodically. Cage-side and detailed clinical observations were conducted, and body weight and feed intake monitored throughout the study. Water consumption was observed daily. Blood smear samples were collected after 12 months and at termination from all animals and from mice terminated in extremis. Differential white blood cell counts were performed on all control and high-dose animals and on the animals terminated in extremis. Gross pathological examinations were conducted at termination and on moribund and pre-terminally dead mice. Selected

synthesis in isolated rat hepatocytes. Studies of chromosome aberrations and gene mutation in mammalian cells using the acetylated metabolites were negative.

(a) In vitro studies

Bacteria

Glyphosate or Roundup was used in approximately 40 studies of mutagenicity in bacteria. Most were conducted with and without metabolic activation (using S9, 9000 × *g* supernatant fraction from induced male rat liver homogenate). The actual number of tests performed was well over 150 as multiple tester strains with and without S9 were used in most studies. Glyphosate or Roundup was found to be negative for genotoxic effects in almost all of these; weak positive results were reported in only one or two studies. Glyphosate was also reported to be negative in three assays measuring DNA repair (rec) in *Bacillus subtilis* and positive in one SOS-chromotest assay in *Escherichia coli*. Several studies reported that glyphosate could enhance DNA strand breaks or interfere with DNA strand break repair in cyanobacteria following exposure to ultraviolet-B radiation.

In the case of AMPA or the acetylated metabolites, no increases in mutation in bacteria were seen in the in vitro studies (Table 33).

Table 33. Summary of in vitro genotoxicity studies with glyphosate, glyphosate formulations, AMPA or their metabolites in bacteria

End-point	Test object	Concentration	Purity	GLP (Yes/ No)	Results		Reference
					−S9	+S9	
Point mutations	*Salmonella typhimurium* TA98, 100, 1535, 1537	0.1–1 000 µg/plate	Glyphosate (98.4%)	No	Negative	Negative	Kier (1978)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537, 1538	0.005–50 µL/plate	Glyphosate trimesium SC-0224 (19.2%)	Yes	Negative	Negative	Majeska (1982)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537, 1538; *E. coli* WP2 uvrA	10– 5 000 µg/plate	Glyphosate (98%)	No	Negative	Negative	Li & Long (1988)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537, 1538; *E. coli* WP2 uvrA	1.6–5 000 µg/plate	Glyphosate trimesium ICIA 0224	Yes	Negative	Negative	Callander (1988a)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	313–5 000 µg/plate	AK-01 Technical (glyphosate acid) (96.4%)	Yes	Negative	Negative	Yanagimoto (1991)
Point mutations	*S. typhimurium* TA98, 100, 1535 and 1537	160–5000 µg/plate	Glyphosate (98.6%)	Yes	Negative	Negative	Jensen (1991a)
Point mutations	*S. typhimurium* TA97, 98, 100, 1535	33–10 000 µg/plate	Glyphosate (98.6%)	No	Negative	Negative	Chan & Mahler (1992)
Point mutations	*S. typhimurium* strains TA98, 100, 1535, 1537	50–5 000 µg/plate	Rodeo (40% glyphosate)	Yes	Negative	Negative	Kier et al. (1992)

End-point	Test object	Concentration	Purity	GLP (Yes/ No)	Results		Reference
					–S9	+S9	
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537, 1538; *E. coli* WP2, WP2 uvrA	100–5 000 µg/plate	Glyphosate trimesium TMSC (95%)	Yes	Negative	Negative	Callander (1993)
Point mutations	*S. typhimurium* TA98, TA100	180–1 440 µg/plate	Roundup	No	Weak positive / equivocal	Weak positive / equivocal	Rank et al. (1993)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537	156–5 000 µg/plate	HR-001 (95.7%)	Yes	Negative	Negative	Akanuma (1995a)
Point mutations	*S. typhimurium* strains TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	50–5 000 µg/plate	Glyphosate (95.3%)	Yes	Negative	Negative	Thompson (1996)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2,WP2 uvrA	100–5 000 µg/plate	Glyphosate (95.6%)	Yes	Negative	Negative	Callander (1996)
Point mutations	*S. typhimurium* TA97a, 98, 100, 1535	1–5 000 µg/plate	Glifos (360 g/L glyphosate)	No	Negative	Negative	Vargas (1996)
Point mutations	*S. typhimurium* TA97a, 98, 100, 102	0.025–0.3 µg/plate	Glyphosate formulation Perzocyd 10, soluble liquid concentrate	No	Negative	Negative	Chruscielska et al. (2000b)
Point mutations	*S. typhimurium* TA98, 100, 102, 1535, 1537	10–5000 µg/plate	Glyphosate technical (97%)	Yes	Negative	Negative	Schreib (2012)
Point mutations	*S. typhimurium* TA98, 100, 102, 1535, 1537	648–5000 µg/plate	Glyphosate technical Helm (98%)	Yes	Negative	Negative	Riberri do Val (2007)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	3–5000 µg/plate	Glyphosate (95.1%)	Yes	Negative	Negative	Sokolowski (2007a)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	3–5000 µg/plate	Glyphosate (97.7%)	Yes	Negative	Negative	Sokolowski (2007b)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	3–5000 µg/plate	Glyphosate (95%)	Yes	Negative	Negative	Sokolowski (2007c)
Point mutations	*S. typhimurium* TA97a, 98, 100, 102, 1535	1–1000 µg/plate	Glyphosate TC (98%)	Yes	Negative	Negative	Miyaji (2008)
Point mutations	*S. typhimurium* TA98, 100, 102, 1535, 1537	31.6–3160 µg/plate	Glyphosate TC (97.5%)	Yes	Negative	Negative	Flügge (2009a)

End-point	Test object	Concentration	Purity	GLP (Yes/ No)	Results		Reference
					−S9	+S9	
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2, WP2 uvrA	3–5000 µg/plate	Glyphosate (96.3%)	Yes	Negative	Negative	Sokolowski (2009)
Point mutations	*S. typhimurium* TA98, 100, 102, 1535, 1537	31.6–5000 µg/plate	Glyphosate (> 96%)	Yes	Negative	Negative	Donath (2010)
Point mutations	*S. typhimurium* TA98, 100, 102, 1535, 1537	31.6–3160 µg/plate	Glyphosate TC (95.2%)	Yes	Negative	Negative	Flügge (2010)
Point mutations	*S. typhimurium* A98, 100, 1535, 1537; *E. coli* WP2 uvrA	31.6–5000 µg/plate	Glyphosate (96%)	Yes	Negative	Negative	Schreib (2010)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	3–5000 µg/plate	Glyphosate (> 95%) spiked with glyphosine (0.63%)	Yes	Negative	Negative	Sokolowski (2010)
Point mutations	*S. typhimurium* TA98, 100, 102, 1535, 1537	31.6–5000 µg/plate	Glyphosate (> 95.8%)	Yes	Negative	Negative	Wallner (2010)
Point mutations	*S. typhimurium* TA98, 100, 102, 1535, 1537	10–2000 µg/plate	Glyphosate (> 95.4%)	Yes	Negative	Negative	Donath (2011a)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	10–5000 µg/plate	Glyphosate (98.8%)	Yes	Negative	Negative	Donath (2011b)
Point mutations	*S. typhimurium* TA98, 100, 1535 1537; *E. coli* WP2 uvrA	10–5000 µg/plate	Glyphosate (97.8%)	Yes	Negative	Negative	Donath (2011c)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	1.5–5000 µg/plate	Glyphosate (85.8%)	Yes	Negative	Negative	Thompson (2014)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	10–5000 µg/plate	Glyphosate technical (94.1%)	Yes	Negative	Negative	Schreib (2015)
DNA damage	*B. subtilis* Rec assay H17 and M45	20–2 000 µg/disk	Glyphosate (98%)	No	Negative	Negative	Li & Long (1988)
DNA damage	*B. subtilis* Rec assay H17 and M45	15–240 µg/disc	AK-01 Technical (glyphosate acid) (96.4%)	Yes	Negative	Negative	Yanagimoto (1992b)
DNA damage	*B. subtilis* Rec assay H17 and M45	7.5–240 µg/disk	Glyphosate (95.7%)	Yes	Negative	Negative	Akanuma (1995b)

End-point	Test object	Concentration	Purity	GLP (Yes/ No)	Results		Reference
					−S9	+S9	
DNA damage	*E. coli* SOS chromotest	0.1–0.25 µg	Roundup	No	Positive	N/A	Raipulis et al. (2009)
Enhanced UV-induced DNA strand breaks	Cyanobacteria (*Scytonema javanicum*)	10 µmol/L	Glyphosate	No	Positive	Negative	Wang et al. (2012)
Delayed UV–B-induced DNA strand break repair	Cyanobacteria (*Anabaena* sp.)	10 µmol/L	Glyphosate	No	Positive	N/A	Chen et al. (2012)
Delayed UV-B-induced DNA strand break repair	Cyanobacteria (*Microcystis viridis*)	10 µmol/L	Glyphosate	No	Positive	N/A	Chen et al. (2012)
DNA damage	Acellular prophage superhelical PM2 DNA	75 mmol/L	Glyphosate (98.4%)	No	Negative	N/A	Lueken et al. (2004)
AMPA							
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	200–5 000 µg/plate	AMPA (99.3%)	Yes	Negative	Negative	Akanuma (1996)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537, 1538; *E. coli* WP2 uvrA	1.6–5 000 µg/plate	AMPA (> 99%)	Yes	Negative	Negative	Callander (1988b)
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537	310–5 000 µg/plate	AMPA (99.2%)	Yes	Negative	Negative	Jensen (1993a)
***N*-Acetyl-AMPA**							
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	50–5 000 µg/plate	*N*-acetyl-AMPA (76%; IN-EY252)	Yes	Negative	Negative	Wagner & Klug (2007)
***N*-Acetyl-glyphosate**							
Point mutations	*S. typhimurium* TA98, 100, 1535, 1537; *E. coli* WP2 uvrA	100–5 000 µg/plate	*N*-acetyl-glyphosate sodium salt (84.3%)	Yes	Negative	Negative	Mecchi (2004)

AMPA, aminomethylphosphonic acid; GLP: good laboratory practice; N/A: not applicable; S9: 9000 × *g* supernatant fraction from induced male rat liver homogenate; −S9: without metabolic activation; +S9: with metabolic activation; UV: ultraviolet

Mammalian cells

Glyphosate and its formulation products were tested for various types of genetic damage in mammalian cells in vitro (Table 34). The results are summarized as follows. Of the four in vitro studies of gene mutation in mammalian cells induced by glyphosate or its formulation products, no increases were reported. In contrast, nine of 10 studies investigating DNA strand breaks induced by glyphosate or Roundup in mammalian cells reported positive results, 4 of 11 studies of chromosome aberrations reported positive results. For two of these (Lioi et al., 1998a,b), the effects were seen at much lower concentrations than the other studies reporting negative results. Two studies reported

Publication bias

A formal analysis of publication bias was not undertaken because the number of studies (risk estimates from non-overlapping study populations) available were few and funnel plot tests for asymmetry should be used only where there are at least 10 studies because otherwise statistical power is insufficient to distinguish true asymmetry from chance (Higgins & Green, 2011; Sterne et al., 2011). Other formal objective statistical tests require an even larger number of studies, typically at least 30, to achieve sufficient statistical power (Lau et al., 2006). As a result, publication bias cannot be fully excluded. However, given the very considerable resources invested in these types of (large, difficult exposure assessment) studies, it is unlikely that results would go unpublished.

Summary of evidence for an association between glyphosate and NHL

This evaluation considered several aspects of each study and of all the studies combined, including factors which decrease the level of confidence in the body of evidence, including risk of bias, unexplained inconsistency, and imprecision, and factors which increase the level of confidence, including large magnitude of effect, a dose–response relationship, residual confounding and consistency (Guyatt et al., 2008; Morgan et al., 2016).

The risk estimates findings for each study are summarized in Table 52, and findings for non-quantitative exposure assessment (predominantly ever- vs never-use) are shown in the forest plot below.

Table 52. Results of Tier 1 evaluation and summary of publications by glyphosate/cancer site

Study/ Location	Glyphosate / NHL	Reference
Meta-analysis	Qualitative exposure only – ever-/never-use of glyphosate Meta risk ratio: 1.5 (95% CI: 1.1–2.0) Meta-analysis includes McDuffie et al. (2001); Hardell et al. (2002); De Roos et al. (2003, 2005a); Eriksson et al. (2008); and Orsi et al. (2009). *N*s for each meta-analysis not presented	Schinasi & Leon (2014)
Agricultural Health Study	Quantitative exposure (cumulative exposure days; intensity-weighted cumulative exposure days [years of use × days/year × estimated intensity level]: in tertiles) Risk estimates – aRR (95% CI) Ever-use 1.1 (0.7–1.9) LED 1–20.0 1.0 (ref.) LED 21–56 0.7 (0.4–1.4) LED 57–2678 0.9 (0.5–1.6) *P* for trend 0.73 IW-LED 0.1–79.5 1.0 (ref.) IW-LED 79.6–337.1 0.6 (0.3–1.1) IW-LED 337.2–18241 0.8 (0.5–1.4) *P* for trend = 0.99 Total *N* = 54 315 (49 211/36 823, depending on the analysis), with 92 incident NHL cases (for ever-use; and 61 for analysis based on tertiles of exposure)	De Roos et al. (2005)
United States Midwest case–control studies	The study population overlaps with that of De Roos et al. (2003). See comment below Qualitative – ever/never (analysis stratified by asthmatics vs non asthmatics) Risk estimates – aRR (95% CI) Non-asthmatics: 1.4 (0.98–2.1) Asthmatics: 1.2 (0.4–3.3) Total *N* = 3208 (872 NHL cases, 2336 controls). *N* = 53/91 glyphosate-exposed NHL cases/controls for non-asthmatics and 6/12 glyphosate-exposed NHL cases/controls for asthmatics	Lee et al. (2004)

Study/ Location	Glyphosate / NHL	Reference
	The study population overlaps with Lee et al. (2004) and total *N* is smaller, but as an exception this study was not excluded in the assessment of consistency of risk estimates as it provides overall risk estimates which are comparable with other studies, while Lee et al. (2004) only provides risk estimates stratified by asthma diagnosis Qualitative (ever/never) Risk estimates – aOR (95% CI) From a logistic regression model: Exposed 2.1 (1.1–4.0) From the hierarchical regression model: Exposed 1.6 (0.9–2.8) Both adjusted for other pesticides Total *N* =2 583 (650 NHL cases, 1 933 controls). *N* = 36 exposed cases; *N* = 61 controls	De Roos et al. (2003)
	Excluded – as this study is pooled in De Roos et al. (2003) and Lee et al. (2004) Qualitative exposure only – ever-/never-use of glyphosate Risk estimates – OR (95% CI) Ever-use = 1.1 (0.7–1.9) Total *N* = 1867 (622 cases, 1245 controls) *N* = 26 exposed cases	Cantor et al. (1992)
Cross-Canada Study of Pesticides and Health	Quantitative exposure – days of use per year (3 categories – cutpoints are given). Risk estimates – OR (95% CI) Ever-use: 1.2 (0.83–1.74) Unexposed 1.0 (ref.) >0–<=2 days/year 1.0 (0.63–1.57) > 2 days/year 2.12 (1.20–3.73) *P* trend = NR Total *N* = 2 023 517 cases, 1 506 controls (overall) *N* = 51 exposed cases, 133 exposed controls	McDuffie et al. (2001)
Sweden – note that there is some overlap between Eriksson et al. (2008), Hardell et al. (2002) and Hardell & Eriksson (1999)	Quantitative exposure – days of use per year (2 categories – cutpoints are given). Risk estimates – aOR (95% CI) Ever-use: 2.02 (1.10–3.71) Risk estimates – aOR (95% CI) Non-farmers: 1.0 (ref.) ≤ 10 days/year: 1.69 (0.7–4.07) > 10 days/year: 2.36 (1.04–5.37) *P* trend = NR Total N = 1926 (910 cases, 1016 controls) *N* = 29 exposed cases; *N* = 18 exposed controls	Eriksson et al. (2008)
	Qualitative exposure only – ever-/never-use of glyphosate. A pooled analysis of Nordström et al. (1998) (NHL subtype only, not evaluated separately here) and Hardell & Eriksson (1999) Risk estimates – aOR (95% CI) Ever-use: 1.85 (0.55–6.20) Total *N* = 1 656 (515 cases, 1 141 controls) *N* = 8 exposed cases; *N* = 8 exposed controls.	Hardell et al. (2002)
	Exclude as this study is pooled in Hardell et al. (2002). Qualitative exposure only – ever-/never-use of glyphosate	Hardell & Eriksson (1999)

Study/ Location	Glyphosate / NHL	Reference
France	Qualitative – ever-/never-use of glyphosate Risk estimates – aOR (95% CI) Ever-use: 1.0 (0.5–2.2) *N* = 12 exposed cases; *N* = 24 exposed controls (The researchers report evaluating quantitative duration with respect to median duration of exposure among exposed controls as never exposed; duration < median; duration > median, but neither the median cutpoint nor ORs/test for trend results are presented in the paper, so this study cannot contribute any information for quantitative risk assessment.)	Orsi et al. (2009)

aOR: adjusted odds ratio; aRR: adjusted risk ratio; CI: confidence interval; IW-LED: intensity-weighted lifetime exposure days, defined as number of years of use × number of days used per year × personal protective equipment use reduction factor × intensity level score (a unit-less score which reflects a combination of self-reported pesticide exposure modifiers, e.g. pesticide mixing status, application method, equipment repair activities); LED: lifetime exposure days, defined as number of years of use × number of days used per year; NHL: non-Hodgkin lymphoma; *N*: sample size; NR: not reported; OR: odds ratio; ref.: reference

The maximally adjusted risk estimates were extracted.

The Glyphosate / NHL evaluation included seven studies (McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003; Lee et al., 2004; De Roos et al., 2005; Eriksson et al., 2008; Orsi et al., 2009) and one meta-analysis (Schinasi & Leon, 2014). Three studies used quantitative exposure metrics, although, the units differed: lifetime exposure days and intensity-weighted lifetime exposure days (De Roos et al., 2005) and days of use per year (McDuffie et al., 2001; Eriksson et al., 2008). The AHS found no evidence of elevated risk of NHL or exposure–response associated with glyphosate exposure (De Roos et al., 2005). Elevated risks were reported in various case–control studies. De Roos et al. (2003) reported significant elevated risk of NHL associated with ever- versus never-use of glyphosate (OR: 2.1 [1.1–4.0] and a borderline nonsignificant OR (1.6 [0.9–2.8]) with an alternative Bayesian hierarchical model) from the United States Midwest pooled case–control studies. There was no evidence of effect modification by asthma diagnosis in the United States Midwest pooled case–control studies (Lee et al., 2004). Ever-use of glyphosate was not associated with risk of NHL in the Cross-Canada Case–control Study of Pesticides and Health, but using glyphosate for longer than 2 days per year was associated with a significant elevated risk (OR: 2.12; 95% CI: 1.20–3.73), although there was no indication of an exposure–response relationship across exposure categories (McDuffie et al., 2001). Eriksson et al. (2008) reported significant elevated risk of NHL associated with ever-use (OR: 2.02 [1.10–3.71]) and use of glyphosate for longer than 10 days per year (OR: 2.36 [1.04–5.37]) and indicate an exposure–response relationship. A pooled study of two Swedish case–control studies reported a nonsignificant elevated risk of NHL for ever-use of (OR: 1.85 [0.55–6.2]); however, with only eight exposed cases, this study had limited power to detect associations (Hardell et al., 2002). Orsi et al. (2009) found no evidence of association. Schinasi & Leon (2014) reported a meta risk ratio of 1.5 (95% CI: 1.1–2.0) for ever- versus never-use of glyphosate. The meta-analysis included the AHS (De Roos et al., 2005) and five out of the six case–control studies included in this evaluation (McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003; Eriksson et al., 2008; Orsi et al., 2009).