Table 1: Screening Assessment of the 61 Studies

The studies are set out in the Table in the order in which they were listed as exhibits from the 2023-12-08 - Revised - Affidavit of Beatrice Olivastri (Friends of the Earth)

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
E1	Mao Q, et al. "The Ramazzini Institute 13-week pilot study on glyphosate and Roundup administered at human-equivalent dose to Sprague Dawley rats: effects on the microbiome" Environ Health. 2018 May 29;17(1):50. https://ehjournal.biomedcentral.com/articles/10.1186/s12940-018-0394-x.	Health effects: Microbiome	Incomplete test material characterization. A single dose level was tested. Substance intake was not measured, therefore actual exposure levels to animals were unknown. No general toxicity was reported in the study. Any claimed effects of glyphosate on gut microbiome were also not linked to adverse outcomes in the host animal. Further, study authors noted "given the differences in taxonomic composition of the microbiomes of rats and humans, the extent to which the results of this analysis can be relevant to humans is not clear". For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E2	Leino L. et al. "Classification of the glyphosate target enzyme (5-enolpyruvylshikimate-3-phosphate synthase) for assessing sensitivity of organisms to the herbicide" J. Hazard. Mater. 2020;408:124556. doi: 10.1016/j.jhazmat.2020.124556.	Health effects: Microbiome / Herbicidal MOA	This study utilizes a bioinformatic / in silico research design that does not account for the complexities of whole-animal integrated metabolism and microbe-host interactions. The study authors acknowledge that the findings of this study should be considered with the context of empirical studies. Robust empirical in vivo studies, such as the Danish[1] EPA study, do not show adverse effects on whole organism mediated via microbiome linkages. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E3	Motta E.V. et al. "Glyphosate perturbs the gut microbiota of honey bees". Proc. Natl. Acad. Sci. USA. 2018;115:10305–10310. doi: 10.1073/pnas.1803880115.	Environment: Effects on bees	The study reports changes in the microbiome and increased mortality with co-exposure to glyphosate and the pathogen. However, the laboratory setting has challenges, notably that this does not allow for the consideration of the complex dynamics of the microbial community of a whole colony. In the lab, the artificial diet does not include pollen, which contains amino acids known to impact the microbiome. The relevance of the *Serratia* infection dose is also unknown.

[1] Nielsen, L. N., Roager, H. M., Casas, M. E., et al. (Ministry of Environment of Denmark – The Danish Environmental Protection Agency). Effects of glyphosate on the intestinal microbiota. (2021). https://www2.mst.dk/Udgiv/publications/2021/03/978-87-7038-284-7.pdf

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			As such, the translation of the observed effects in the laboratory to a natural setting are unclear. In addition, there are a number of uncertainties with the study design that limit its reliability as a stand-alone endpoint in the risk assessment (for instance, environmental relevance of the high dose is not explained, no measurements of actual consumed doses, small sample sizes). Other higher-tiered field studies (Thompson et al. 2014; Odemer et al. 2020) reported no effects at the colony level, though effects on brood development were observed by Odemer et al. (2020). For these reasons, the study is not expected to change the existing risk assessment of glyphosate. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E4	Ruuskanen S. et al. "Glyphosate-Based herbicides influence antioxidants, reproductive hormones and gut microbiome but not reproduction: A long-term experiment in an avian model" Environ. Pollut. 2020; 266:115108.	Environment: Effects on birds	While the study is of acceptable quality, certain limitations were noted as follows: The tested concentration in feed of 160 mg/kg feed is reported to be 1/2 of that calculated in grains available to granivorous birds, and the corresponding dietary concentration corresponds to a dietary dose of 12-20 mg glyphosate/kg bw/d. However, feed consumption was not reported in the study, and as such, confirmation of this dietary dose cannot be confirmed explicitly using measured raw data. Only one test concentration was studied. A range of test concentrations within a toxicity study is needed to statistically verify appropriate effect levels (e.g., EC_{10}, LC_{50}). As such, effects noted at one test concentration offer limited understanding of the toxicological impacts of an active ingredient within the test. Further, the study reports effects that are not considered to be apical in nature (testosterone measurement, measures of oxidative stress, and relative gut microbiome). There is no evidence suggested in this study that these effects would impact overall populations of birds in the field. Effects on testosterone levels did not translate into notable effects on overall reproductive maturity in male birds or reproductive success in mating pairs. As such, although this effect may warrant further research, it does not provide an endpoint that is considered within the scope of the risk assessment framework. For these reasons, the study is not expected to change the existing risk assessment of glyphosate. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E5	Aitbali Y.A., et. al. "Glyphosate based- herbicide exposure affects gut microbiota, anxiety and depression-like behaviors in mice" Neurotoxicol.	Health effects: Microbiome / Neurotoxicity	Incomplete test material characterization. No general toxicity was reported in the study.

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	Teratol. 2018;67:44–49. doi: 10.1016/j.ntt.2018.04.002.		Current PMRA toxicology reference values provide adequate margins to the dose level of 250 mg/kg bw/day, which was the lowest dose tested in this study. For example, the current Canadian glyphosate ADI of 0.3 mg/kg bw/day provides a margin of greater than 800 to the 250 mg/kg bw/day dose and is therefore protective of the findings. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E6	Mesnage, R., Teixeira, M., Mandrioli, D. et al. Use of Shotgun Metagenomics and Metabolomics to Evaluate the Impact of Glyphosate or Roundup MON 52276 on the Gut Microbiota and Serum Metabolome of Sprague-Dawley Rats. Environmental Health Perspectives 129(1). (2021). https://doi.org/10.1289/EHP6990.	Health effects: Microbiome	Microbiome assessment was done at a single time point in the study, which was at the end of the study. No general toxicity was reported in the study. Reported changes in the microbiome profiles were not linked to any adverse health effects in the host. The metabolites affected in cecum were seemingly not altered in serum. The authors concluded that further methodological developments are needed to quantify shikimic acid levels in serum. The study authors acknowledged the exploratory nature of their work and suggested that further research is needed to understand the health implications of glyphosate inhibition of the shikimate pathway. The study authors further acknowledged that the findings of this study could be used to develop biomarkers for epidemiologic studies. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E7	Blot N., et. al. “Glyphosate, but not its metabolite AMPA, alters the honeybee gut microbiota” PLoS ONE. 2019;14: e0215466.	Environment: Effects on bees	The study observed altered gut microbiota in honeybees from exposure to glyphosate, but this change did not translate to any effect on mortality. Therefore, the significance of microbiome change is unknown. With the lack of a link between the observed sublethal effect (gut changes) to an adverse outcome for honeybees (changes in mortality, growth or reproduction), this study would not change the assessment regarding toxicity of glyphosate to bees/insect pollinators. The study also has other limitations common to the Motta et al. (2018) (E3) study (including a potentially unrealistic exposure dose and small sample size) which raise uncertainties regarding the environmental relevance of the study. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E8	Mesnage R., Antoniou M.N. “Computational modelling provides insight into the effects of	Health effects: Microbiome	This study utilizes a bioinformatic / in silico research design that does not account for the complexities of whole-animal integrated metabolism and microbe-host interactions. Robust

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	glyphosate on the shikimate pathway in the human gut microbiome" Curr. Res. Toxicol. 2020;1:25–33.		empirical in vivo studies, such as the Danish EPA study[2], do not show adverse effects on whole organism mediated via microbiome linkages.
E9	Puigbò P, et. al. "Does Glyphosate Affect the Human Microbiota? Life" (Basel). 2022 May 9;12(5):707. doi: 10.3390/life12050707.	Health effects: Microbiome	This study utilizes a bioinformatic / in silico research design that does not account for the complexities of whole-animal integrated metabolism and microbe-host interactions. The study authors acknowledged the limitations of this current study and recommended further experimental and epidemiological studies to explore impacts of glyphosate on gut microbiome and linkage to human health. Robust empirical in vivo studies, such as the Danish EPA study[3], do not show adverse effects on whole organism mediated via microbiome linkages. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E10	Hu J., et. al. "Low-Dose exposure of glyphosate-based herbicides disrupt the urine metabolome and its interaction with gut microbiota" Sci. Rep. 2021;11:3265. doi: 10.1038/s41598-021- 82552-2.	Health effects: Microbiome	Incomplete test material characterization. A single dose level was tested. Substance intake was not measured; therefore, actual animal test substance exposure levels were unknown. No general toxicity was reported in the study. The proposed correlation between glyphosate exposure and changes to urine metabolites and the microbiome were not causally linked and were also not causally linked to an adverse outcome in the host. Study authors acknowledged that study limitations included small sample size and single time-point urinalysis and recommended further studies with larger sample sizes. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E11	Suppa, A., et al. "Roundup causes embryonic development failure and alters metabolic pathways and gut microbiota functionality in non-target species" Microbiome 8, 170 (2020). https://doi.org/10.1186/s40168-020- 00943-5.	Environment: Effects on the aquatic environment	Suppa et al. (2020) provide insights into sublethal effects of glyphosate and Roundup on the gut microbiota of *Daphnia magna*. However, the reported microbiome shifts are not currently relevant as standalone endpoints in ecological risk assessment of pesticides. These changes lack dose–response data and have uncertain relevance to population-level outcomes such as survival, growth, or reproduction, which are not explained. The high natural variability of microbiome

[2] Nielsen, L. N., Roager, H. M., Casas, M. E., et al. (Ministry of Environment of Denmark – The Danish Environmental Protection Agency). Effects of glyphosate on the intestinal microbiota. (2021). https://www2.mst.dk/Udgiv/publications/2021/03/978-87-7038-284-7.pdf

[3] Nielsen, L. N., Roager, H. M., Casas, M. E., et al. (Ministry of Environment of Denmark – The Danish Environmental Protection Agency). Effects of glyphosate on the intestinal microbiota. (2021). https://www2.mst.dk/Udgiv/publications/2021/03/978-87-7038-284-7.pdf

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			communities and the absence of established thresholds or adverse outcome pathways for microbial disruption further limit their interpretability in a risk assessment context. In addition, the aquatic invertebrate risk assessment in RVD2017-01 used a species sensitivity distribution, which incorporated more sensitive apical endpoints, and thus is more protective of aquatic invertebrates than the threshold concentration (1 mg/L) used in this study. Thus, while these findings contribute to the broader understanding of potential mechanisms of glyphosate toxicity, they are not expected to impact the conclusions of RVD2017-01. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E12	Benchimol EI, Bernstein CN, Bitton A, Carroll MW, Singh H, Otley AR, Vutcovici M, El-Matary W, Nguyen GC, Griffiths AM, Mack DR, Jacobson K, Mojaverian N, Tanyingoh D, Cui Y, Nugent ZJ, Coulombe J, Targownik LE, Jones JL, Leddin D, Murthy SK, Kaplan GG. Trends in Epidemiology of Pediatric Inflammatory Bowel Disease in Canada: Distributed Network Analysis of Multiple Population-Based Provincial Health Administrative Databases. Am J Gastroenterol. 2017.	Health effects: Epidemiology / Microbiome	This study is related to recurring scientific themes, i.e. microbiome, however it makes no mention of glyphosate and therefore does not contribute to the evidence base for this pesticide. As such, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate.
E13	Dylan E. O'Sullivan, Robert J. Hilsden, Yibing Ruan, Nauzer Forbes, Steven J. Heitman, Darren R. Brenner, The incidence of young-onset colorectal cancer in Canada continues to increase,Cancer Epidemiology,Volume 69, 2020.	Health effects: Epidemiology / Carcinogenicity	This study is related to recurring scientific themes, i.e. microbiome, however it makes no mention of glyphosate and therefore does not contribute to the evidence base for this pesticide. As such, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate.
E14	Portier, C.J. A comprehensive analysis of the animal carcinogenicity data for glyphosate from chronic exposure rodent carcinogenicity studies. Environ Health 19, 18 (2020).	Health effects: Carcinogenicity	This reference is a scientific review article. The review report itself does not offer original data. Instead, study authors conducted a pooled analysis across all primary sources of data – all of which were previously considered during Health Canada's re-evaluation (RVD2017-01). The author of this review article contributed to the IARC review of glyphosate. This review article has also been extensively considered by major international regulatory authorities. For example, see here: European Food Safety Authority. Report of Pesticide Peer Review TC 80 - Glyphosate. (2022). https://www.efsa.europa.eu/sites/default/files/2023-01/glyphosate-peer-review-minutes-nov-dec-2022.pdf For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.

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E15	Zhang, L., et. al. Exposure to glyphosate-based herbicides and risk for non-Hodgkin lymphoma: A meta-analysis and supporting evidence. Mutation Research, (2019) 781, 181–206.	Health effects: Epidemiology / Cancer	This reference is a scientific review article. A limited number of epidemiologic studies (6) were included as part of the meta-analysis. These studies were previously considered as part of re-evaluation (REV2017-01). This review report itself does not offer original data. A declaration of interest section of this review indicates that the lead authors served as the science review board members of the USEPA SAP meeting that evaluated glyphosate in December 2016. A critical analysis by other well-known researchers in the area identified limitations in this review around exposure characterization and the choice of latency period that would impact the conclusions of meta-analysis. See reference: Kabat, G. C., Price, W. J., & Tarone, R. E. On recent meta-analyses of exposure to glyphosate and risk of non-Hodgkin's lymphoma in humans. Cancer causes & control: CCC, 32(4), 409–414 (2021). https://doi.org/10.1007/s10552-020-01387-w The authors of this critical analysis further concluded that "formal quantification of risk in meta-analyses combining the AHS with case-control studies is unwise. All such meta-analyses, including our own, should be interpreted with great caution." Notably, Dr. Tarone, the lead author of this critical analysis and expert in the field, led the design of the AHS and coauthored several of the first studies using AHS data. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E16	Dennis D. Weisenburger, "A Review and Update with Perspective of Evidence that the Herbicide Glyphosate (Roundup) is a Cause of Non-Hodgkin Lymphoma," Clinical Lymphoma Myeloma and Leukemia, 21(9) (2021) https://doi.org/10.1016/j.clml.2021.04.009.	Health effects: Epidemiology / Cancer	This reference is a scientific review article. The review report itself does not offer original data. Instead, study authors conducted a pooled analysis across all primary sources of data – all of the epidemiologic studies were previously considered during Health Canada's re-evaluation (RVD2017-01). This review paper was critically reviewed by another well-known researcher in the area who noted several limitations. Reference: Response to "A Review and Update with Perspective of Evidence that the Herbicide Glyphosate (Roundup) is a Cause of Non-Hodgkin Lymphoma" - Clinical Lymphoma, Myeloma and Leukemia Notably, Dr. Tarone, the author of this critical analysis, and expert in the field, led the design of AHS and coauthored several of the first studies using AHS data. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E17	Deepika Kubsad, et al. "Assessment of Glyphosate Induced Epigenetic Transgenerational Inheritance of Pathologies and Sperm Epimutations: Generational Toxicology, Nature, 23 (2019).	Health effects: Reproduction	Incomplete test material characterization. A single dose level was tested. Study authors followed a 14-hour light:10-hour dark cycle of animal husbandry, which is different than the 12-hour light/dark cycle recommended by OECD test guidelines and can introduce confounders related to circadian disruption, hormone modulation and behavioural change. Tissue assessment and sperm epigenetic analysis were done at a single time point in the study, which was at 12 months

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			of age. Proposed linkages between reported histopathological findings and changes in sperm DMRs were not causally linked. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E18	Duforestel M, Nadaradjane A, Bougras-Cartron G, Briand J, Olivier C, Frenel JS, Vallette FM, Lelièvre SA, Cartron PF. Glyphosate Primes Mammary Cells for Tumorigenesis by Reprogramming the Epigenome in a TET3- Dependent Manner. Front Genet. 2019 Sep 27.	Health effects: Carcinogenicity	Incomplete test material characterization. The study used a mix of in vitro and in vivo design. A low number of animals were used in the in vivo component of the study. The study authors acknowledged that the findings of the study need to be further investigated. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E19	Armen Nerseyan et al. "Evaluation of the scientific quality of studies concerning genotoxic properties of glyphosate" https://s3.amazonaws.com/s3.sumofus.org/images/Evaluation_scientific_quality_studies_genotoxic_glyphosate.pdf.	Health effects: Genotoxicity / Cancer	This reference is a scientific review article. This review report itself does not offer original data. Instead, it refers to primary sources of genotoxicity data previously considered during Health Canada's re-evaluation (RVD2017-01). For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E20	Defarge N, et al "Co-Formulants in Glyphosate-Based Herbicides Disrupt Aromatase Activity in Human Cells below Toxic Levels" Int J Environ Res Public Health. (2016) Feb 26;13(3):264. doi: 10.3390/ijerph13030264.	Health effects: Formulant	As this was an in vitro study, the absence of systemic metabolism limits the ability to fully assess the biotransformation that may occur in vivo, which could impact the relevance of the results. This study was previously considered during Health Canada's re-evaluation (see p85 of RVD2017-01). For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E21	Mesnage R, Antoniou MN. "Ignoring Adjuvant Toxicity Falsifies the Safety Profile of Commercial Pesticides" Front Public Health. 2018 Jan 22; 5:361. doi: 10.3389/fpubh.2017.00361.	Health effects: Formulant	This reference is a scientific review paper. This review report itself does not offer original data. Instead, it refers to primary sources of data. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. More recently in 2023, Barbara Casassus referred to Dr. Mesnage, an expert in the area, endorsing the registration of glyphosate in the EU, noting that "there are too many conflicting studies on the product, some of poor quality" and "he does not

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			think that it poses a risk to consumers". See here: Casassus, B. EU allows use of controversial weedkiller glyphosate for 10 more years. Nature. (2023). https://doi.org/10.1038/d41586-023-03589-z The glyphosate re-evaluation revisited and addressed any issues related to the toxicity of the formulant (e.g. POEA) used in end-use products of glyphosate. Additional related info is available in PRVD2015-01 and/or RVD2017-01. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E22	Robin Mesnage, et al, "Insight into the confusion over surfactant co-formulants in glyphosate-based herbicides," Food and Chemical Toxicology, 128, (2019) 137-145 https://doi.org/10.1016/j.fct.2019.03.053.	Health effects: Formulant	This reference is a scientific review paper. This review report itself does not offer original data. Instead, it refers to primary sources of data. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. More recently in 2023, Barbara Casassus referred to Dr. Mesnage, an expert in the area, endorsing the registration of glyphosate in the EU, noting that "there are too many conflicting studies on the product, some of poor quality" and "he does not think that it poses a risk to consumers". See here: Casassus, B. EU allows use of controversial weedkiller glyphosate for 10 more years. Nature. (2023). https://doi.org/10.1038/d41586-023-03589-z The glyphosate re-evaluation revisited and addressed any issues related to the toxicity of the main formulant (e.g. POEA) used in formulated products of glyphosate. Additional related info is available in PRVD2015-01 and/or RVD2017-01. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E23	Sheldon Krimsky "glyphosate-based herbicides and public health: making sense of the science" Journal of Agricultural and Environmental Ethics (2022) 35(3) https://doi.org/10.1007/s10806-021-09874-z.	Health effects: Cancer / IARC	This reference is a scientific review paper. This review report itself does not offer original data. Instead, it refers to primary sources of data. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. The glyphosate re-evaluation revisited and addressed any

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			issues related to the toxicity of the main formulant (e.g. POEA) used in the formulated products of glyphosate. Additional related info is available in PRVD2015-01 and/or RVD2017-01. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E24	Defarge, N. et al. "Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides. Toxicology Reports, (2018) 5, 156–163,	Health effects: Formulant	This reference is a scientific review paper. This review report itself does not offer original data. Instead, it refers to primary sources of data. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. One area of focus of the glyphosate re-evaluation was to specifically revisit and address any issues related to the toxicity of the main formulant (e.g. POEA) used in the formulated products of glyphosate. Additional info related is available in PRVD2015-01 and/or RVD2017-01. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E25	Hao, Y. W., et al.. "Adjuvant contributes Roundup's unexpected effects on A549 cells" Environmental Research, 184(109306), 1–8 (2020).	Health effects: Formulant	Incomplete test material characterization. As this was an in vitro study, the absence of systemic metabolism limits the ability to fully assess the biotransformation that may occur in vivo, which could impact the relevance of the results. The study authors recommended further investigations of toxicity mechanisms of formulants. One area of focus of the glyphosate re-evaluation was to specifically revisit and address any issues related to the toxicity of the main formulant (e.g. POEA) used in the formulated products of glyphosate. Additional info related is available in PRVD2015-01 and/or RVD2017-01. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E26	Mesnage, R., Clair, E., & Séralini, G.-E. "Roundup® in genetically modified plants: Regulation and toxicity in mammals" In B. Breckling & R. Verhoeven (Eds.), Implications of GM-crop cultivation at large spatial scales. Theorie in der Ökologie16. Frankfort	Health effects: Formulant	This reference is an abstract written in the style of a scientific review paper. As such, it does not offer original data. Instead, it refers to primary sources of data. The glyphosate re-evaluation addressed issues related to the toxicity of the main formulant (e.g. POEA) used in the formulated products of glyphosate. Additional related info is available in PRVD2015-01 and/or RVD2017-01. More recently in 2023, Barbara Casassus referred to Dr. Mesnage, an expert in the area, endorsing the registration of glyphosate in the EU, noting that "there are too many

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			conflicting studies on the product, some of poor quality" and "he does not think that it poses a risk to consumers. See here: Casassus, B. EU allows use of controversial weedkiller glyphosate for 10 more years. Nature. (2023). https://doi.org/10.1038/d41586-023-03589-z For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate.
E27	Nagy et al. Systematic review of comparative studies assessing the toxicity of pesticide active ingredients and their product formulations. Environmental Research, (2020) 181, 108926.	Environment: Effects of glyphosate formulations Health effects: Formulant	**Environment**: The environmental effects of glyphosate formulations were considered in PRVD2015-01 and RVD2017-01, where studies on the effects of glyphosate formulated with (or without) POEA were included for the assessment of non-target aquatic and terrestrial organisms. For additional context, the information presented in the study appears limited in comparison to the information considered in PRVD2015-01. For the ecotoxicological portion of the re-evaluation, PRVD2015-01 considered 99 studies from the open literature where more than 530 terrestrial and aquatic endpoints tested with POEA and other glyphosate formulation were selected and added to the 116 registrant studies in order to build a species sensitivity distribution (SSD) analysis for each organism group. Results of these SSDs were used in the environmental risk assessment (see monograph, PMRA# 2746503). For the preceding reasons, the results presented in the study are not expected to impact the existing risk assessment. The study has been retained for further consideration during the next PMRA science review of glyphosate. **Health effects:** This reference is a scientific review article summarizing primary literature on some herbicides, fungicides and insecticides, including products containing glyphosate. The sections on glyphosate itself do not offer original data. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. Indeed, study authors noted several limitations for interpretations, including heterogeneity and the relatively limited number of studies evaluated, and "advise that equi-effective concentrations should be taken into account when designing the studies in order to have a more accurate conclusion on the relative toxicity of active ingredients and commercial formulations". For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E28	Benbrook, C. M. "How did the US EPA and IARC reach diametrically opposed conclusions on the	Health effects: Carcinogenicity	This reference is a scientific review paper. The review report itself does not offer original data. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
	genotoxicity of glyphosate-based herbicides?" Environmental Sciences Europe, (2019) 31(2), 1–16.		potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. The study authors noted that "more research is needed on real-world exposures to the chemicals within formulated GBHs and the biological fate and consequences of such exposures". The key issue of differences in various scientific organization's genotoxicity conclusions have been addressed in several other reviews and research plans, including the more recent US national toxicology program's (NTP's) research on glyphosate and formulated products of glyphosate. The NTP's research findings demonstrated that the other components in formulated products containing glyphosate were responsible for genotoxicity in instances of positive findings. Reference: National Toxicology Program U.S. Department of Health and Human Services. Glyphosate and Glyphosate Formulations. (2023). https://ntp.niehs.nih.gov/whatwestudy/topics/glyphosate For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E29	EPA "Glyphosate" (Oct 6 2022) https://www.epa.gov/ingredients-used-pesticide-products/glyphosate "EPA's underlying scientific findings regarding glyphosate, including its finding that glyphosate is not likely to be carcinogenic to humans, remain the same. In accordance with the court's decision, the Agency intends to revisit and better explain its evaluation of the carcinogenic potential of glyphosate and to consider whether to do so for other aspects of its human health analysis.	Health effects: Carcinogenicity	Health Canada is aware of the US court decision to vacate the US EPA human health portion of the assessment that supports the US EPA's registration review decision. While the US EPA has determined that withdrawal of the glyphosate interim decision is appropriate in consideration of the Ninth Circuit's June 17, 2022 decision, the US EPA also note that their underlying scientific findings, including the finding that glyphosate is not likely carcinogenic to humans, remain the same but that they intend to better explain and communicate their evaluation of carcinogenic potential of glyphosate in accordance with the court's decision. (PMRA# 3717842; United States Environmental Protection Agency. Memorandum - Withdrawal of the Glyphosate Interim Registration Review Decision. (2022). DACO: 12.5 https://www.regulations.gov/document/EPA-HQ-OPP-2009-0361-14447) For these reasons, this communication is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate.
E30	Gabriella Andreotti, "Glyphosate Use and Cancer Incidence in the Agricultural Health Study" JNCI: Journal of the National Cancer Institute, 110(5) (2018) 509–516, https://doi.org/10.1093/jnci/djx233.	Health effects: Epidemiology / Cancer	This epidemiologic study examined glyphosate exposure and cancer incidence using the AHS data / prospective cohort design. The authors stated there was no apparent association between use of products containing glyphosate and any solid tumours or lymphoid malignancies overall, including NHL and its subtypes – consistent with the conclusions of the existing PMRA assessment of glyphosate. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E31	Winstone, J.K., Pathak, K.V., Winslow, W. et al. "Glyphosate infiltrates the brain and increases pro-inflammatory cytokine TNFα: implications for neurodegenerative disorders" J Neuroinflammation 19, 193 (2022). https://doi.org/10.1186/s12974-022-02544-5.	Health effects: Neurotoxicity	No general toxicity was reported in the study. Small number of mice (6 per dose) examined for brain tissue. The study authors reported an accumulation of amyloid-beta peptides in primary cortical neurons cultured in vitro and concluded that exposure at the levels detected in the brain in vivo are sufficient to increase Aβ40-42 levels in a dose-dependent manner and reduce cell viability when tested in vitro. The study authors reported that increased test material levels in brain correlated positively with both peripheral blood plasma and brain Tumour Necrosis Factor alpha (TNFα) levels. Study authors noted future work to uncover "the molecular overlap between glyphosate exposure and AD pathology". Current PMRA toxicology reference values provide adequate margins to the dose level of 125 mg/kg bw/day, which was the lowest dose tested in this study. For example, the current Canadian glyphosate ADI of 0.3 mg/kg bw/day provides a margin of greater than 400 to the lowest dose tested of 125 mg/kg bw/day dose and is therefore considered protective of the findings. The study authors also acknowledged that the dose levels used for testing were above the NOAEL benchmarks established by the US EPA. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate, especially regarding additional scientific information relevant to its metabolism and distribution profile, such as evidence of detection in brain tissues, and potential for neuro-immune disfunction.
E32	Marino M, Mele E, et al. "Pleiotropic Outcomes of Glyphosate Exposure: From Organ Damage to Effects on Inflammation, Cancer, Reproduction and Development" Int J Mol Sci. 2021 Nov 22; 22(22):12606.	Health effects: Carcinogenicity	This reference is a scientific review article. This review report itself does not offer original data. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E33	Torretta, V et al. "Critical Review of the Effects of Glyphosate Exposure to the Environment and Humans through the Food Supply Chain" Sustainability 2018, 10, 950.	Environment: Other exhibits Health effects: Cancer	**Environment**: The study cannot be used directly in the environmental risk assessment of glyphosate because it does not report original data, especially new environmental hazard endpoints, for consideration in the risk assessment. For these reasons, the study is not expected to impact the conclusions of RVD2017-01.

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			In the study, the authors stated that the "application of glyphosate in large quantities can also cause effects on insects, such as bees, and on birds, for which the herbicide is toxic". The statement is based on the study of Herbert et al. (2014). Herbert et al. (2014) did report sublethal effects related to sensory sensitivity and learning, but it did not find negative effects related to foraging, motor skills, or measurements such as survival, food uptake and locomotive activity of bees. That study also did not discuss bird toxicity related to glyphosate. **Health effects:** This reference is a scientific review article. This review report itself does not offer original data. The study authors concluded that "it is not possible to attribute a clear and unambiguous definition to glyphosate, especially regarding its potentially harmful effects on humans". Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E34	Najm Alsadat Madani et al "Effects of glyphosate and glyphosate-based herbicides like Roundup™ on the mammalian nervous system: A review," Environmental Research, 214 (4) (2022). https://doi.org/10.1016/j.envres.2022.113933.	Health effects: Neurotoxicity	This reference is a scientific review article. This review report itself does not offer original data. Instead, it refers to primary sources of data. Study authors noted that "most of the studies on nervous systems effects described above use concentrations of GBHs or glyphosate that are much higher than ones to which most humans are likely to be exposed." Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. Study authors noted that "whether current concentrations in foods and drinks pose a hazard to the mammalian nervous system is less clear" and concluded that "more research is necessary to fully answer the question of what the impacts of GBHs and glyphosate on human neurological health". Study authors also declared a competing interest: "Dr. Carpenter has served as an expert witness in Roundup cases with all reimbursement going to support students and staff."

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E35	Jing-Bo Liu et al "Glyphosate damages blood-testis barrier via NOX1-triggered oxidative stress in rats: Long-term exposure as a potential risk for male reproductive health," Environment International, 159 (2022) 107038, https://doi.org/10.1016/j.envint.2021.107038.	Health effects: Reproduction	Incomplete test material characterization. Only 2 dose levels were tested. Low number of animals for BTB assay (n=3 per group) suggests low statistical power or increased risk of errors. Parts of unilateral testis from 2 rats in each replicate (n= 6 per dose) were selected for histopathological observation, and unilateral epididymides of rest 3 rats in each replicate (n=9) were used for determination of sperm parameters. It is unclear if the samples were pooled. The majority of data was reported graphically, without numerical values. The study authors reported treatment-related effects on sperm quality and quantity, blood-testis barrier measures, and the testicular transcriptome profile at all dose levels. However, these findings did not always show a dose-dependent pattern despite a significant 25x dose spread and the report lacked historical control data to contextualize sperm effects. Sperm effects were observed at much higher doses in definitive studies considered during the re-evaluation, including in the 90-day rat (F344; LOAEL = 811 mg/kg bw/day; NOAEL = 410 mg/kg bw/day)) and 24-month rat (SD; LOAEL = 362 mg/kg bw/day; NOAEL = 89 mg/kg bw/day), with clear NOAELs at dose levels higher than those in the Liu (2022) study. While assessed in a 2-generation repro study in rats (Wistar), no effects were observed up to almost the limit dose. With increased number of animals per dose group, and increased number of dose groups, these studies are expected to have increased power to detect treatment-related changes from controls. For these reasons, this study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E36	Mendez F, et. al. "Effects of Glyphosate Exposure on Reproductive Health: A Systematic Review of Human, Animal and In-Vitro Studies" Exposure and Health. 2021.	Health effects: Reproduction	This reference is a scientific review article. This review report itself does not offer original data. Instead, it refers to primary sources of data. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. Study authors noted that "the lack of epidemiological studies using biomarkers and the heterogeneity in the methods that characterize exposure may explain the differences in the results of human research and could be considered a limitation in the scope of this review".

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E37	Liu JB, et. al. “Glyphosate-induced gut microbiota dysbiosis facilitates male reproductive toxicity in rats” Sci Total Environ. 2021 Sep 16.	Health effects: Microbiome / Reproduction	Incomplete test material characterization. The study authors reported treatment-related effects on sperm quality, blood-testis barrier measures, and the microbiome profile at all dose levels. However, these findings did not always show a consistent dose-dependent pattern, and the report lacked historical control data to contextualize sperm effects. The majority of data was reported graphically, without numerical values. Also, the results of this study were slightly inconsistent with the other study with the similar design from the same researchers (E35; Liu, J. et al, 2022) including inconsistency on reporting impacts on sperm quantity / concentration levels. It is noteworthy that several control values for sperm parameters from this study are comparable to the low dose results from the E35 study (suggesting those effects may be within margins attributable to normal variability and not treatment-related). Sperm effects were observed at much higher doses in definitive studies considered during the re-evaluation, including in the 90-day rat (F344; LOAEL = 811 mg/kg bw/day; NOAEL = 410 mg/kg bw/day) and 24-month rat (SD; LOAEL = 362 mg/kg bw/day; NOAEL = 89 mg/kg bw/day). While assessed in a 2-generation repro study in rats (Wistar), no effects were observed up to almost the limit dose. With increased number of animals per dose group, and increased number of dose groups, these studies are expected to have increased power to detect treatment-related changes from controls. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E38	Parvez, S., Gerona, R.R., Proctor, C. et al. Glyphosate exposure in pregnancy and shortened gestational length: a prospective Indiana birth cohort study. Environ Health 17, 23 (2018). https://doi.org/10.1186/s12940-018-0367-0.	Health effects: Reproduction	This is an epidemiologic study with biomonitoring aspects included in its design. No general toxicity was reported in the study. The authors suggest a weak correlation between urine glyphosate levels and shortened gestational length. Impact from the confounding factors, and other limitations, such as low sample size (e.g. samples from 71 women) on the positive association were not completely addressed. The study investigators also acknowledged the need for studies with much larger sample size and detailed assessment of exposure-response relationship including AMPA measurements. The proposed linkages between urine glyphosate levels and shortened gestational length cannot be causally linked. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E39	Juan P. Muñoz, et al "Glyphosate and the key characteristics of an endocrine disruptor: A review" Chemosphere, 270 (2021). https://doi.org/10.1016/j.chemosphere.2020.128619.	Environment: Effects on non-target mammals Health effects: Reproduction / Endocrine	**Environment**: The article is a literature review that does not report original experimental data directly related to environmental endpoints at the organism or population level. For the reasons given below, this review article is also not expected to have an impact on human health toxicology reference values which may be considered in the environmental non-target mammalian risk assessment. However, the review provides informative mechanistic insights that contribute contextual information on the effects of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate. **Health effects:** This reference is a scientific review paper. This review report itself does not offer original data. Instead, it refers to primary sources of data. The study author noted that “prospective cohort studies are still needed to elucidate the real effects in the human endocrine system”. Attributing the noted effects in the review to a specific test substance or a defined group of test substances poses a challenge. This difficulty arises from the review's examination of numerous potential combinations of formulated products containing glyphosate across multiple studies. Additionally, the lack of full characterization of the test substance further complicates the ability to pinpoint a singular cause for the noted effects. The heterogeneity of studies further poses a challenge to synthesize findings and draw firm conclusions. For these reasons, the study is not expected to have an impact on the relevant outcomes and conclusions, including the toxicology reference values, of the existing PMRA human health risk assessment of glyphosate. The study is retained for further consideration during the next PMRA science review of glyphosate.
E40	CDC “National Health and Nutrition Examination Survey – Glyphosate” (June 2022). https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/SSGLYP_H.htm.	Health exposure: Biomonitoring	No biomonitoring or exposure related data were included in the paper. For this reason, this study is not relevant as it contains no usable data that could be used in the exposure assessment.
E41	Environmental Defence, 2018. What is in Your Lunch. From Farm to Table.ind https://environmentaldefence.ca/wp-content/uploads/2018/09/Whats-In-Your-Lunch-Glyphosate-Report-Sept-2018.pdf.	Environment: Other exhibits Health exposure: Food residues	**Environment**: This document is not relevant to the environmental risk assessment of glyphosate. It does not provide any original scientific data relevant for conducting an exposure or hazard assessment. Risk assessment decisions are informed by the original research reports. For these reasons, the information in the report is not expected to impact the existing risk assessment. **Exposure**: For the CFIA data, results were only reported as a percentage of samples with detectable level, rather than the measured detectable residue level. As residue levels were not

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			reported, they could not be incorporated into PMRA's existing dietary exposure assessment. For the independent lab data, measured levels of glyphosate and AMPA residues in food products were reported. As residues were reported for entire food products, not raw commodities, the study results cannot be directly used in the dietary exposure assessment. For these reasons, this study is not relevant for PMRA's existing dietary exposure assessments.
E42	Grau, D., et al. "Quantifiable urine glyphosate levels detected in 99% of the French population, with higher values in men, in younger people, and in farmers" Environ Sci Pollut Res 29, 32882–32893 (2022). https://doi.org/10.1007/s11356-021-18110-0.	Health exposure: Biomonitoring	Biomonitoring data conducted in other countries has limited utility for the Canadian exposure assessment, as the products registered, use pattern, consumption patterns, cultural practice, occupational exposure, etc. may be different between Canada and the study jurisdiction and can impact exposure in the population. For this reason, this study is not relevant for the exposure assessment conducted for the Canadian use pattern.
E43	Gillezeau, C., et al. "The evidence of human exposure to glyphosate: a review" Environ Health 18, 2 (2019). https://doi.org/10.1186/s12940-018-0435-5.	Health exposure: Biomonitoring	Most of the data in this study was related to biomonitoring data conducted in other countries. As noted above for exhibit E42, biomonitoring data conducted in other countries has limited utility. For this reason, this aspect of the study is not relevant for the exposure assessment conducted for the Canadian use pattern. There is one part of the study that touches on Canadian blood serum levels for a limited sample of non-pregnant women (39 women). While detected, the presence of a chemical does not mean that there are risks of concern. In order to interpret biomonitoring data in a human health risk context, models developed using pharmacokinetic data are required. Currently methods to interpret glyphosate blood serum levels have not been developed, so these serum levels could not be used in the exposure assessment. However, methods to interpret levels of glyphosate in urine have been developed. As levels of glyphosate in urine are related to blood serum levels, urine is typically used to monitor for glyphosate exposure in biomonitoring studies. Given the larger sample sizes (1800-2300) and national sampling methodology, the available Canadian urinary biomonitoring data were considered to address the detectable blood levels in the limited samples of non-pregnant women mentioned in this paper. For these reasons, this aspect of the study is considered to be relevant but does not provide additional information that would change PMRA's existing glyphosate exposure assessment.
E44	Álvarez Bayona MA, Maturana Córdoba A, Gallardo Amaya RJ and Muñoz Acevedo A, "Occurrence of glyphosate in surface and drinking water sources in Cúcuta, Norte de Santander, and its removal using membrane technology" Frontiers in Environmental Science 10 2022.	Environment: Other exhibits	As the monitoring data are from outside of Canada (and the United States), the study is not representative of the Canadian exposure assessment. Therefore, the data presented in the study cannot be used directly to inform the environmental risk assessment of glyphosate.

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
	https://www.frontiersin.org/articles/10.3389/fenvs.2022.941836.		
E45	Maren KrusePlaß et al. "Pesticides and pesticide related products in ambient air in Germany" Environ Sci Eur (2021) 33:114. https://doi.org/10.1186/s12302021005534.	Environment: Other exhibits Health exposure: air concentrations	**Environment**: This study is not representative of the Canadian exposure assessment. Air monitoring data from other countries has limited utility in informing the environmental exposure assessment in Canada. The presence of glyphosate in the air is influenced by spray drift or wind erosion, which is mainly related to use pattern, cultural practices and climate, all of which may be different in other jurisdictions. Therefore, the study would not impact the existing risk assessment. **Exposure**: Air monitoring data conducted in other countries has limited utility for the Canadian exposure assessment due to potential differences between the Canadian context and the study jurisdiction. Air levels can vary depending on the registered products, use pattern, cultural practices, climate, etc. For this reason, this study is not relevant for the exposure assessment conducted for the Canadian use pattern.
E46	Helander M, Lehtonen TK, Saikkonen K, et al. “Field-realistic acute exposure to glyphosate-based herbicide impairs fine-color discrimination in bumblebees” Sci Total Enviro. 2023; 857:159298. doi: 10.1016/j.scitotenv.2022.159298.	Environment: Effects on bees	The study observed that glyphosate impaired bees fine color discrimination. However, the biological importance of the change in color vision was not determined. No effects on foraging were evaluated. With the lack of a link between the observed sublethal effect (fine color discrimination changes) and an adverse outcome for bees (such as reduced foraging or foraging success, which can be linked to potential effects on mortality, growth or reproduction), this study is not expected to change the conclusions regarding toxicity to bees/insect pollinators. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E47	Thompson LJ, et al. “Bumblebees can be Exposed to the Herbicide Glyphosate when Foraging” Environ Toxicol Chem. 2022 Oct;41(10):2603-2612. doi: 10.1002/etc.5442. Epub 2022 Aug 29. PMID: 35866464.	Environment: Effects on bees	This study demonstrated that bees do not avoid glyphosate-treated plants. This study is not expected to change the risk assessment conclusions because the PMRA risk assessment framework does not assume avoidance. The pollinator risk assessment estimates exposure using the maximum single application rate of the pesticide. Additionally, the study design did not link the exposure to any adverse outcomes in bees (such as effects on mortality, growth or reproduction), and as such does not provide any new information beyond that already considered in RVD2017-01. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E48	Anja Weidenmuller et al “glyphosate impairs collective thermoregulation in bumblebees” Science	Environment: Effects on bees	Increased mortality was determined when nest temperatures were lower, and in a separate experiment glyphosate was found to inhibit thermoregulation (during resource limitation only).

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
	(2022) 376:6597; James Crall, "Glyphosate impairs bee thermoregulation," Science, 376, 6597, (1051-1052), (2022). /doi/10.1126/science. abq5554.		However, a direct link of glyphosate exposure leading to increased mortality due to impaired thermoregulation was not established. There was no single experiment that measured mortality after exposure to glyphosate during reduced food availability while recording nest temperature (i.e. the observed sublethal effect was not directly linked to increased mortality). It is also uncertain if the effects would translate to nature, where additional sources of forage and stored reserves are available. Additionally, the split colony design adds an uncertainty to the study, as this may impact the colony and potentially contribute to the observed effects. As such, for the above reasons due to the study design, this study is not expected to impact the current risk assessment of glyphosate. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E49	James Crall, "Glyphosate impairs bee thermoregulation," Science, 376, 6597, (1051- 1052), (2022)./doi/10.1126/science.abq5554.	Environment: Effects on bees	This document does not report any original data. As such, it does not contain information that would change the risk conclusions for bees. Regulatory decisions are informed by the original research reports. This article mainly details the Weidenmuller et al. 2022 study on bee thermoregulation, which was cited as E48 and discussed there. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E50	IUCN "Migratory monarch butterfly now Endangered - IUCN Red List" (2022) https://iucn.org/press-release/202207/migratory-monarch-butterfly-now-endangered-iucn-red-list.	Environment: Other exhibits	This document does not discuss glyphosate specifically and does not provide original scientific data relevant for conducting an environmental risk assessment of glyphosate. As such, the information in this report would not impact the conclusions of RVD2017-01. As noted in the response to public comments on RVD2017-01, monarch butterflies rely completely on plants in the milkweed family, especially the common milkweed (*Asclepias syriaca*), for both reproduction and larval food. Glyphosate is not intended to affect monarch habitats beyond the boundaries of agricultural fields. To protect these habitats, spray buffer zones are established along agricultural fields adjacent to hedgerows and other terrestrial and aquatic environments. These spray buffer zones are crucial for mitigating the potential effects of herbicide drift on non-target organisms in both terrestrial and aquatic ecosystems. Various pressures, such as in-field herbicide use, agricultural intensity, and climate events, may contribute to reduced milkweed habitat across North America.
E51	Barbosa da Costa et al. 2021 "Resistance, resilience, and functional redundancy of freshwater bacterioplankton facing agricultural stress" by in Molecular Ecology DOI: doi: 10.1111/mec.16100.	Environment: Effects on the aquatic environment	Freshwater bacterioplankton density exposed to glyphosate (GPS) and nutrient phosphorus enrichment was not negatively impacted at the highest tested concentration of 15 mg a.e./L which is 50 times higher than the normal daily concentrations found in reservoirs and 375 times higher than the detection value obtained from the Canadian surface water monitoring survey, respectively (see Environmental Assessment Directorate monograph, PMRA# 2746503). As mentioned by the study authors, results indicate that, despite increasing over time across ponds,

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			bacterioplankton densities also slightly increased in response to nutrient and glyphosate addition. No negative effects on bacterioplankton were observed except for community structure where glyphosate appeared to show a time-independent effect on community diversity and composition. The study also has scientific limitations which raise uncertainties as to the reliability of the results. These include: 1) The complete dataset not being available for review, the publication figures including endpoint identifications that are difficult to read and to determine, 2) the presence of the surfactant POEA, which is known to affect glyphosate toxicity, was not indicated, and 3) the mesocosm study shows limited seasonality, short-term duration (43 days), and does not capture long-term impacts of full seasonal dynamics and potential turnover. For the above reasons, the outcomes of the study are not expected to impact the existing risk assessment of glyphosate. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E52	MP Hébert et al "Widespread agrochemicals differentially affect zooplankton biomass and community structure" Ecological Applications. DOI: 10.1002/eap.2423.	Environment: Effects on the aquatic environment	As also seen in E51, freshwater zooplankton biomass exposed to glyphosate (GPS) alone was not negatively impacted (complete recovery) at the highest tested concentration of 15 mg a.e./L after 30 days following a first application (pulse), although a decline was observed at day 8 (0.3 mg glyphosate/L) followed by a recovery and then by a positive effect on the biomass at end. A shift was also observed on community richness, especially in rotifers. The lowest observed endpoint for aquatic organisms at the time of the re-evaluation was 0.2 mg glyphosate/L and concerned freshwater invertebrates; this suggests a higher sensitivity than that of zooplankton (observed at 0.3 mg glyphosate/L at day 8 followed by a total recovery at day 30) as indicated in the E52 study. For these reasons, the study is not expected to impact the existing risk assessment of glyphosate. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E53	Fugère V et al. "Community rescue in experimental phytoplankton communities facing severe herbicide pollution" Nature Ecology & Evolution. DOI: https://doi.org/10.1038/s41559-020-1134-5.	Environment: Effects on the aquatic environment	Phytoplankton biomass exposed to a first pulse of glyphosate concentrations varying between 0 and 15 mg/L showed reduction after 8 days following applications, but most affected communities recovered quickly and effects of glyphosate on phytoplankton biomass were no longer evident by day 15 even at the highest tested glyphosate concentrations. A negative effect was seen at > 3.0 mg glyphosate/L before day 15 followed by a recovery and then a positive effect at dose > 4.0 mg glyphosate/L after day 15. As mentioned by the study authors, this recovery occurred even though the glyphosate concentration remained constant during this period and also following a second pulse where the effect was found to be positive. Despite

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			glyphosate concentration exceeding 30 mg/L in some ponds, this second (unintentionally more severe) dose did not have a negative effect on biomass. As indicated earlier (E52), the lowest observed endpoint for aquatic organisms at the time of the re-evaluation was 0.2 mg glyphosate/L and concerned freshwater invertebrates. This suggests a higher sensitivity than that of phytoplankton as presented in the current E53 study. Raw data availability was implied but not explicitly detailed in publication. Figures used in the publication are difficult to interpret and critical endpoint values difficult to determine. Scientific shortcomings observed in the current study are similar to what was observed in E51 and E52. For these reasons, the study is not expected to impact the existing risk assessment of glyphosate. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E54	Hébert, Marie-Pier, et al. "The overlooked impact of rising glyphosate use on phosphorus loading in agricultural watersheds" Front Ecol Environ 17(1) 1540-9295 (2018) https://doi.org/10.1002/fee.1985.	Environment: Other exhibits	The potential impacts of nutrient (N, P, K) releases are not part of the standard risk assessment framework described in Health Canada's Approach to Environmental Risk Assessment. However, the mobility of phosphorus and its accumulation in Canadian soils was discussed in the ENVIRONMENT monograph for glyphosate (PMRA# 2746503) along with adsorption (binding) and desorption (removal) mechanisms. The contribution of phosphorus by glyphosate to soils was determined to be minor in comparison to the supply by fertilizers and farm manure, which is in agreement with study E54. Overall, the study does not bring new insight into the environmental toxicity of glyphosate. For these reasons, the study is not expected to impact the existing risk assessment of glyphosate. The study has been retained for further consideration during the next PMRA science review of glyphosate.
E55	CBC "grooming forests could be making fires worse, researchers warn" (Nov 2019) https://www.cbc.ca/news/canada/british-columbia/forest-fires-glyphosate-1.5366185.	Environment: Effects on forest systems	This document discusses forest management in relation to wildfires, which is not in the scope of the environmental risk assessment framework described in Health Canada's Approach to Environmental Risk Assessment. In addition, the document does not present novel scientific data relevant to the environmental risk assessment of glyphosate. For these reasons, the study is not expected to impact the existing risk assessment of glyphosate.
E56	Daniels, L.D., R.W. Gray and P.J. Burton. (2020). "2017 Megafires in British Columbia - Urgent need to adapt and improve resilience to wildfire". In: Hood, Sharon M Drury, Stacy; Steelman, Toddi; and	Environment: Effects on forest systems	This document concerns forestry management in relation to wildfires which is not in the scope of the environmental risk assessment framework described in Health Canada's Approach to Environmental Risk Assessment. The document does not mention glyphosate or present novel scientific data relevant to the environmental risk assessment of glyphosate.

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
	Steffens, Ron, eds. The fire continuum—preparing for the future of wildland fire: Proceedings of the Fire Continuum Conference. 21-24 May 2018, Missoula, MT. Proc. RMRS-P-78. Fort Collins, CO: U.S. Department of Agriculture, Forest Service, Rocky Mountain Research Station. 358 p. Published in U.S. Forest Service RMRS P-78. 2020.		For these reasons, the study is not expected to impact the existing risk assessment of glyphosate.
E57	Lisa J. Wood. 2019 "The presence of glyphosate in forest plants with different life strategies one year after application" Canadian Journal of Forest Research. 49(6): 586-594. https://doi.org/10.1139/cjfr-2018-0331.	Environment: Effects on forest systems	The study did not include apical terrestrial plant endpoints (e.g. ER_{25}, ER_{50}, NOER, etc.) and therefore does not provide information that is directly relevant to the environmental risk assessment of glyphosate. In addition, no information was provided regarding the potential content of the surfactant polyethoxylated tallow amine (POEA) in the studied end-use product. POEA is known to increase the toxicity to terrestrial plants and also to aquatic organisms in comparison to glyphosate alone (see ENVIRONMENT monograph, PMRA# 2746503). For these reasons, the report is not expected to impact the existing risk assessment. The study has been retained for consideration during the next PMRA science review of glyphosate.
E58	Timms, K., Wood, LJ. "Sub-lethal glyphosate disrupts photosynthetic efficiency and leaf morphology in fruit-producing plants, red raspberry (*Rubus idaeus*) and highbush cranberry (*Viburnum edule*)" Global Ecology and Conservation (2020) https://doi.org/10.1016/j.gecco.2020.e01319 2351-9894.	Environment: Effects on forest systems	The study is scientifically sound; however, it cannot be used directly within the environmental risk assessment framework because no clear effect metrics (e.g. EC_{25} or EC_{50}) were determined for raspberry and cranberry plants based on dose response treatments, although there is clear effect of raspberry leaf morphology post-treatment at low rate. Health Canada is aware of new research into the potential impacts of glyphosate on the boreal forest, especially shrubs that may serve as forage for mammals. At the time of the re-evaluation, a study by Roy et al. (1989) indicated glyphosate was short lived-in raspberry tissues (half-life of less than 13 days, with only 6% remaining after 33 days). At odds with these conclusions are recent studies by Wood (2019, E57) and Timms and Wood (2020, E58), which found that glyphosate can persist in plant tissues (raspberries and cranberries) for more than a year when applied at low rates in forest cut-block openings. Their results showed that low glyphosate application rates resulted in effects on plant shape, size, flavonoid contents (e.g. antioxidant) and photosynthetic performance. Typical application rates employed in forestry to remove shrubs that compete with conifer seedlings once every 50-70 years are much higher. These recent studies may be helpful in determining the potential impact of drift from the area of application (cut block) to understory plants in non-harvested forest areas nearby. The potential impact of this drift needs to be better understood before mitigation measures can be recommended. In a recent review article, Rolando *et al*. (2017) examined 146 scientific studies related to use of glyphosate in planted forests, concluding that glyphosate-based herbicides do

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
			not pose a significant risk to humans or cause significant adverse effects to terrestrial and aquatic fauna. For the above reasons, the study is not expected to directly impact the conclusion and the existing risk assessment of glyphosate. The study has been retained for consideration during the next PMRA science review of glyphosate.
E59	Golt, AR, Wood LJ. “Glyphosate-based herbicides alter the reproductive morphology of Rosa acicularis (prickly rose)” Frontiers in Plant Science – Functional Plant Ecology. Manuscript Accepted, May 24, 2021. Manuscript ID #698202.	Environment: Effects on forest systems	The study, although scientifically sound, cannot be used directly within the environmental risk assessment framework because no clear effect metrics (e.g. EC_{25} or EC_{50}) were determined. Glyphosate application is expected to occur only in the first years (0-3) following wood harvest after site preparation and new tree planting and as such is not expected to be used in the following 50-70 years until next harvest, therefore reducing its exposure to new understory shrubs such as prickly rose or raspberries. The study’s authors note that further research is required to fully understand the effects of glyphosate-based herbicides on forest understory plant reproduction and how these differ from the existing literature based on agricultural systems. For the above reasons, the study is not expected to directly impact the conclusion and the existing risk assessment of glyphosate. The study has been retained for consideration during the next PMRA science review of glyphosate.
E60	Botten, N. Wood LJ. “Glyphosate remains in forest plant tissues for a decade or more” Forest Ecology and Management 493 (1). doi.org/10.1016/j.foreco.2021.119259.	Environment: Effects on forest systems Health Exposure: Food residues	**Environment**: The study reports on the persistence of glyphosate residues in forest ecosystems beyond previously documented durations, suggesting that current assumptions regarding environmental persistence may be underestimated. However, the authors note that the quantities of glyphosate contained in plant tissues after 3–12 years are extremely low. The study also highlights the importance of considering climate and ecological differences (such as plant species and tissue types) in glyphosate regulatory evaluations. However, the study does not provide new standard plant effects metrics (e.g. EC_{25} or EC_{50}) and therefore is not expected to directly impact the conclusion and the existing risk assessment of glyphosate. The study has been retained for consideration during the next PMRA science review of glyphosate. **Exposure**: The detectable residue levels reported for berries in the study are less than or similar to the residue level used for berry crop group 13 (includes blueberries and raspberries) in PMRA’s existing dietary exposure assessment. For this reason, this study is relevant for the Canadian use pattern but does not provide additional information that would change PMRA’s existing exposure assessment conducted for glyphosate.

Exhibit E #	Reference	Risk Assessment Theme	Screening Findings and Conclusions
E61	Briere, B., Wood, LJ., Kirby, B., Botten, N. "Sensitivity of non-target annual plants to glyphosate-based herbicide, according to growth form" (2020) Canadian Journal of Pesticides and Pesticide Management. doi: 10.34195/can.j.ppm.2020.02.002.	Environment: Effects on forest systems	The study provides information on plant survival following exposure to glyphosate in the forest environment. Dose-response treatments would have been needed in order to compare to other sensitive plant endpoints in PRVD2015-01. As the study does not provide new standard plant effects endpoints (e.g. ER_{25}, ER_{50}, NOER, etc.), it is not expected to directly impact the existing risk assessment In addition, no information was provided regarding the potential content of the surfactant polyethoxylated tallow amine (POEA) in the end-use product of VisionMax Sylviculture herbicide™. This is an uncertainty with the study as POEA is known to increase the toxicity in terrestrial plants in comparison to glyphosate alone (see ENVIRONMENT monograph, PMRA# 2746503). The study has been retained for consideration during the next PMRA science review of glyphosate.