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November 7, 2023

Honourable Mark Holland
Minister of Health
Health Canada
Ottawa, Ontario K1A 0K9
Sent via email to hcminister.ministresc@hc-sc.gc.ca

Pest Management Regulatory Agency – Special Reviews
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Dear Minister Holland:

Re: Request for Special Review of Mancozeb Under the *Pest Control Products Act*

This request is sent on behalf of, the Canadian Association of Physicians for the Environment, the David Suzuki Foundation, Ecojustice, Environmental Defence, Friends of the Earth, Prevent Cancer Now, and Safe Food Matters. These organizations are described in Appendix I.

We request that the Minister undertake a special review under section 17 of the *Pest Control Products Act* (PCPA) of the registration of all registered pest control products containing the active ingredient mancozeb. This request should be treated as a formal request under section 17(4) of the PCPA. The request relies on grounds in sections 17(1) and 17(2) of the PCPA.

The below submissions also give rise to a reasonable scientific uncertainty about whether harm may occur to the environment or human health as a result of current registered uses of mancozeb. We note that there are currently 27 products registered, several of which are coming up for renewal this year. It is our position that the Minister does not have jurisdiction to renew these products in light of the reasonable scientific uncertainty raised by the below submissions and we request confirmation that the products will not be renewed by the PMRA until the PMRA can confirm, utilizing current science, that there is reasonable certainty that no harm will occur.

Additionally, we note that the PMRA lacks jurisdiction to renew products unless the labels have been amended in accordance with the 2020 re-evaluation decision since it has found that the previous label conditions presented unacceptable risks. Any labels must be immediately amended, and where the label amendment conditions of the 2020 re-evaluation have not been complied with the PMRA should immediately cancel the registrations under section 25 of the Act.

Section 17(2) of the PCPA imposes a statutory duty on the Minister of Health to initiate a special review of the registration of pest control products containing active ingredients banned by a member nation of the Organization for Economic Co-operation and Development (OECD) because of health or environmental concerns. Specifically, the PCPA provides that the Minister shall initiate a special review of a registered pest control product containing the active ingredient when a member country of the OECD prohibits all uses of an active ingredient for health and environmental reasons. Section 17(1) provides that the Minister **shall** initiate a special review if the Minister has reasonable grounds to believe that the health or environmental risks of a product are unacceptable.

Summary

The requesters seek a special review under section 17(2) of the PCPA on the grounds that all products containing the active ingredient mancozeb and all uses of mancozeb were prohibited in the European Union (EU) in 2021. In December 2022, the European Union gave notification under the Rotterdam Convention. The requesters further seek a special review under section 17(1) of the PCPA.

Background

About mancozeb

Mancozeb (Mn/Zn-ethylene-bis-dithiocarbamate, MNZ) is an organometallic contact fungicide with multi-site mode of action used to control a broad spectrum of plant diseases on a wide variety of food and feed crops, as well as uses in forests and woodlots, outdoor ornamentals and greenhouse food crops. It can be applied as dust, liquid, dispersible granules, or wettable powder. Mancozeb derives from a combination of the two older dithiocarbamate pesticides, maneb and zineb. Mancozeb belongs to the group of fungicides commonly known as ethylene bis

(dithiocarbamates) (EBDCs/DTCs), along with the active ingredients maneb, zineb, metiram and nabam.

Mancozeb's anti-fungal properties involve the release of ethylene-bis-isothiocyanate sulphide, which impairs fungal enzyme functions.[1]

Mancozeb and other EDBC fungicides easily transform into ethylene thiourea (ETU) within all environmental matrices, as well as through enzymatic transformations mediated by aquatic organisms, plants, and mammals. ETU is produced as a contaminant or as degradation product when fungicides are exposed to moisture and oxygen. ETU may form in diluted suspensions of mancozeb prepared for application on crops and as a result may be present immediately after mancozeb application. Additionally, ETU represents the primary metabolite of mancozeb, formed after absorption by living organisms at an approximate ratio of 1:2 (two molecules of ETU form one molecule of mancozeb), and then excreted in urine.[2]

Although EBDCs including mancozeb are characterized by short persistence in the environment, causing mild acute toxicity upon exposure, mancozeb and ETU are known to have additional long-term toxic effects of primary concern, because of their potential to inhibit human enzymes, thereby affecting the implicated biological systems and increasing the risk of endocrine disruption, cancer transformation, and neuronal damage.[3]

Human health effects of mancozeb

Current scientific evidence in occupationally and environmentally exposed populations indicates that mancozeb inhibits thyroid hormone (TH) receptor and impairs the hypothalamus–pituitary–thyroid axis. Additionally, the metabolite ETU seems to act by reducing TH incretion through the inhibition of TH peroxidase. The consequent proliferative hyperstimulation due to thyroid-stimulating hormone action may induce thyroid cancer. This mechanism, observed in rodent studies, might suggest a possible carcinogenic effect in exposed humans.[4] The International

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[1] Thind T.S., Hollomon D.W. Thiocarbamate Fungicides: Reliable Tools in Resistance Management and Future Outlook. Pest Manag. Sci. 2018;74:1547–1551. doi: 10.1002/ps.4844. [PubMed]

[2] Costa C, Teodoro M, Giambò F, Catania S, Vivarelli S, Fenga C. Assessment of Mancozeb Exposure, Absorbed Dose, and Oxidative Damage in Greenhouse Farmers. Int J Environ Res Public Health. 2022 Aug 23;19(17):10486. doi: 10.3390/ijerph191710486. PMID: 36078202; PMCID: PMC9518406. Citing Mandić-Rajčević S., Rubino F.M., Colosio C. Establishing Health-Based Biological Exposure Limits for Pesticides: A Proof of Principle Study Using Mancozeb. Regul. Toxicol. Pharmacol. 2020;115:104689. doi: 10.1016/j.yrtph.2020.104689. [PubMed].

[3] Costa C, Teodoro M, Giambò F, Catania S, Vivarelli S, Fenga C. Assessment of Mancozeb Exposure, Absorbed Dose, and Oxidative Damage in Greenhouse Farmers. Int J Environ Res Public Health. 2022 Aug 23;19(17):10486. doi: 10.3390/ijerph191710486. PMID: 36078202; PMCID: PMC9518406

[4] Costa C, Teodoro M, Giambò F, Catania S, Vivarelli S, Fenga C. Assessment of Mancozeb Exposure, Absorbed Dose, and Oxidative Damage in Greenhouse Farmers. Int J Environ Res Public Health. 2022 Aug 23;19(17):10486. doi: 10.3390/ijerph191710486. PMID: 36078202; PMCID: PMC9518406 citing Axelstad M., Boberg J., Nellemann C., Kiersgaard M., Jacobsen P.R., Christiansen S., Hougaard K.S., Hass U. Exposure to the Widely Used Fungicide Mancozeb Causes Thyroid Hormone Disruption in Rat Dams but No Behavioral Effects in the Offspring. Toxicol. Sci. 2011;120:439–446. doi: 10.1093/toxsci/kfr006. [PubMed]

Agency for Research on Cancer (IARC) classified mancozeb as a Class 3 carcinogen given the limited evidence in humans, although teratogenic and carcinogenic effects have been observed in animal studies.[5] Additionally, EBDC and/or ETU exposure has been associated with neurodevelopmental damage due to the well-known crucial role of thyroid function in brain development.[6] Recent studies suggest possible disrupted neurobehavioral outcomes and neurotoxicity with Parkinson-like neuronal damage upon mancozeb exposure.[7]

ETU is a common transformation product of the EBDC fungicides mancozeb, maneb, metiram, zineb and nabam. ETU is formed, as part of the EBDCs complex, in soil pore water/water bodies from hydrolytic transformation of parent EBDCs following application to soils and/or after reaching water bodies by drift, and/or run-off and in soil pore water. Aging of the complex results in enrichment with the transformation product ethylenethiourea (ETU), and ETU transformation products. ETU may be produced continuously at low concentrations from the slow transformation of the soil/sediment associated bound species via hydrolysis. ETU is very soluble in water and does not bind strongly to soils. It is very mobile in soil and has the potential to leach and reach groundwater.[8]

There is evidence from epidemiology studies, as well as from experimental data, that mancozeb exposure should be considered a risk factor for developmental and reproductive dysfunction in humans.[9] Mancozeb and ETU can cross the placental barrier, directly affecting reproduction at

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[5] Costa ibid. citing Bao J., Zhang Y., Wen R., Zhang L., Wang X. Low Level of Mancozeb Exposure Affects Ovary in Mice. Ecotoxicol. Environ. Saf. 2022;239:113670. doi: 10.1016/j.ecoenv.2022.113670. [PubMed] and International Agency for Research on Cancer Advisory Group Report of the Advisory Group to Recommend Priorities for the IARC Monographs during 2020–2024. [(accessed on 2 July 2022)]. Available online: https://www.iarc.who.int/news-events/report-of-the-advisory-group-to-recommend-priorities-for-the-iarc-monographs-during-2020-2024/ [Ref list]

[6] Costa ibid citing Cocco P. Time for Re-Evaluating the Human Carcinogenicity of Ethylenedithiocarbamate Fungicides? A Systematic Review. Int. J. Environ. Res. Public Health. 2022;19:2632. doi: 10.3390/ijerph19052632. [PMC free article] and Ziech C.C., Rodrigues N.R., Macedo G.E., Gomes K.K., Martins I.K., Franco J.L., Posser T. Pre-Imaginal Exposure to Mancozeb Induces Morphological and Behavioral Deficits and Oxidative Damage in *Drosophila Melanogaster*. Drug Chem. Toxicol. 2022:1–13. doi: 10.1080/01480545.2022.2069802. [PubMed]

[7] Costa et al ibid citing Fuhrimann S., Farnham A., Staudacher P., Atuhaire A., Manfioletti T., Niwagaba C.B., Namirembe S., Mugweri J., Winkler M.S., Portengen L., et al. Exposure to Multiple Pesticides and Neurobehavioral Outcomes among Smallholder Farmers in Uganda. Environ. Int. 2021;152:106477. doi: 10.1016/j.envint.2021.106477. [PubMed]; and Bastías-Candia S., Zolezzi J.M., Inestrosa N.C. Revisiting the Paraquat-Induced Sporadic Parkinson's Disease-Like Model. Mol. Neurobiol. 2019;56:1044–1055. doi: 10.1007/s12035-018-1148-z. [PubMed]

[8] RVD2020-12 p.134.

[9] Costa et al citing Cecconi S., Paro R., Rossi G., Macchiarelli G. The Effects of the Endocrine Disruptors Dithiocarbamates on the Mammalian Ovary with Particular Regard to Mancozeb. Curr. Pharm. Des. 2007;13:2989–3004. doi: 10.2174/138161207782110516. [PubMed]; and Bastías-Candia S., Zolezzi J.M., Inestrosa N.C. Revisiting the Paraquat-Induced Sporadic Parkinson's Disease-Like Model. Mol. Neurobiol. 2019;56:1044–1055. doi: 10.1007/s12035-018-1148-z. [PubMed]; and Saraiva M.A., da Rosa Ávila E., da Silva G.F., Macedo G.E., Rodrigues N.R., de Brum Vieira P., Nascimento M.S., Picoloto R.S., Martins I.K., de Carvalho N.R., et al. Exposure of Drosophila Melanogaster to Mancozeb Induces Oxidative Damage and Modulates Nrf2 and HSP70/83. Oxid. Med. Cell. Longev. 2018;2018:5456928. doi: 10.1155/2018/5456928. [PMC free article]; and Liu Y., Wang Y.-L.,

preconception, pregnancy, and birth stages.[10] A number of *in vitro* (lab) studies report that ETU reactivity is associated with direct DNA damage,[11] nitrosamine formation,[12] apoptosis induction,[13] and the altered expression of genes involved in oxidative stress response,[14] overall causing the gradual accumulation of damage to intracellular macromolecules exerted by reactive oxygen species (ROS).[15] The consequent oxidative stress may be pivotal in the pathogenesis of thyroid, neural, and immune toxicity.[16]

Environmental Risks of mancozeb

Mancozeb is toxic to a wide range of terrestrial and aquatic animals including fish, amphibians, pollinating insects, mammals, and birds. It is noteworthy for its high levels of both chronic (long-term) and acute (short-term) toxicity to fish and has been associated with numerous fish kills.

Uses of mancozeb in Canada

Mancozeb is a contact fungicide used to control a broad spectrum of fungus on a wide variety of food and feed crops, forests and woodlots, outdoor ornamentals, and greenhouse food crops. Mancozeb is applied as a foliar spray to apples, carrots, celery, field cucumbers, ginseng, onions,

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He S., Chen M.-H., Zhang Z., Fu X.-P., Fu B.-B., Liao B.-Q., Lin Y.-H., Qi Z.-Q., et al. Protective Effects of Resveratrol against Mancozeb Induced Apoptosis Damage in Mouse Oocytes. Oncotarget. 2017;8:6233–6245. doi: 10.18632/oncotarget.14056. [PMC free article]

[10] Runkle J., Flocks J., Economos J., Dunlop A.L. A Systematic Review of Mancozeb as a Reproductive and Developmental Hazard. Environ. Int. 2017;99:29–42. doi: 10.1016/j.envint.2016.11.006. [PubMed]

[11] Costa et al. citing Chhabra R. Comparative Carcinogenicity of Ethylene Thiourea with or without Perinatal Exposure in Rats and Mice. Fundam. Appl. Toxicol. 1992;18:405–417. doi: 10.1016/0272-0590(92)90139-9. [PubMed]; Calviello G., Piccioni E., Boninsegna A., Tedesco B., Maggiano N., Serini S., Wolf F., Palozza P. DNA Damage and Apoptosis Induction by the Pesticide Mancozeb in Rat Cells: Involvement of the Oxidative Mechanism. Toxicol. Appl. Pharmacol. 2006;211:87–96. doi: 10.1016/j.taap.2005.06.001. [PubMed]; Costa C., Miozzi E., Teodoro M., Fenga C. Influence of Genetic Polymorphism on Pesticide-Induced Oxidative Stress. Curr. Opin. Toxicol. 2019;13:1–7. doi: 10.1016/j.cotox.2018.12.008.

[12] Costa et al citing Lijinsky W. Induction of Tumors of the Nasal Cavity in Rats by Concurrent Feeding of Thiram and Sodium Nitrite. J. Toxicol. Environ. Health. 1984;13:609–614. doi: 10.1080/15287398409530525. [PubMed]

[13] Costa et al citing Kumar K., Sabarwal A., Singh R.P. Mancozeb Selectively Induces Mitochondrial-Mediated Apoptosis in Human Gastric Carcinoma Cells through ROS Generation. Mitochondrion. 2019;48:1–10. doi: 10.1016/j.mito.2018.06.003. [PubMed]

[14] Santos P.M., Simões T., Sá-Correia I. Insights into Yeast Adaptive Response to the Agricultural Fungicide Mancozeb: A Toxicoproteomics Approach. Proteomics. 2009;9:657–670. doi: 10.1002/pmic.200800452. [PubMed]; Corsini E., Viviani B., Birindelli S., Gilardi F., Torri A., Codecà I., Lucchi L., Bartesaghi S., Galli C.L., Marinovich M., et al. Molecular Mechanisms Underlying Mancozeb-Induced Inhibition of TNF-Alpha Production. Toxicol. Appl. Pharmacol. 2006;212:89–98. doi: 10.1016/j.taap.2005.07.002. [PubMed]

[15] Singh S.K., Bano F., Mohanty B. Vitamin E Pretreatment Prevents the Immunotoxicity of Dithiocarbamate Pesticide Mancozeb in Vitro: A Comparative Age-Related Assessment in Mice and Chick. Pestic. Biochem. Physiol. 2016;126:76–84. doi: 10.1016/j.pestbp.2015.08.001. [PubMed]; Gök E., Deveci E. Histopathological, Immunohistochemical and Biochemical Alterations in Liver Tissue after Fungicide-Mancozeb Exposures in Wistar Albino Rats. Acta Cir. Bras. 2022;37:e370404. doi: 10.1590/acb370404. [PMC free article]

[16] Corsini E., Birindelli S., Fustinoni S., De Paschale G., Mammone T., Visentin S., Galli C.L., Marinovich M., Colosio C. Immunomodulatory Effects of the Fungicide Mancozeb in Agricultural Workers. Toxicol. Appl. Pharmacol. 2005;208:178–185. doi: 10.1016/j.taap.2005.02.011. [PubMed]

potatoes, greenhouse tomatoes, field tomatoes, sugar beets, wheat, lentils, cantaloupe, pumpkin, squash, melons and watermelons, tobacco, various trees including douglas fir, ash, oak, pine and sycamore, and various ornamentals such as ivy and holly.

Approved application rates vary by use, some are quite high such as dry bulb onions (up to 8.8 kilograms of active ingredient per hectare) and some use patterns permit a large number of applications per season. Details are set out in Appendix III. It can be applied as a spray or by aerial application.

Sales of mancozeb in Canada

The production and market volumes of mancozeb, like other pesticides, have followed an overall increasing trend for several decades. In 2010 for example, between 500,000 and 1 million kilograms of mancozeb were sold, In 2020 closer to two million kilograms were sold.[17] Mancozeb fungicides ranked number eight in the top ten pesticides sold in Canada in 2021 and number two for fungicides.[18] Mancozeb is one of the most popular pesticides in Canada. This is because mancozeb has a broad-spectrum efficacy towards a variety of plant diseases (including scab, rust, late blight, and leaf spot), and quite a low purchase price.[19] On request, we obtained the specific sales data that was available from the PMRA and it is as follows:

Year	Kilograms of active ingredients sold
2011	CBI*
2012	CBI
2013	CBI
2014	1822730
2015	1587778
2016	1477230
2017	1871956
2018	1098309
2019	1522519
2020	1905613

[17] PMRA sales report 2010, Appendix I, indicates that mancozeb sold >500,000 kg with the next reported tier being > 1, 000,000 kg.
[18] PMRA 2021 Sales Data Report.
[19] Costa et al.

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**Note: the years 2011-2013 were not disclosed by the PMRA because the PMRA takes the position that the aggregated sales from several products is confidential business information, but only for those years.*

Monitoring reports regarding mancozeb in Canada

There are virtually no monitoring data sources available to the public regarding mancozeb exposures in the Canadian environment. Mancozeb (expressed in monitoring data as total dithiocarbamate), has been detected in field runoff at 1260 µg/L and in a river with a fish kill at 131 µg/L.[21] It is difficult to monitor for mancozeb in the environment or in foods because current routine chemical analyses cannot discriminate between the various dithiocarbamate or EBDC fungicides.[22] Sometimes ETU is used as a marker for mancozeb exposures, in other cases carbon disulfide (CS_2) is used as a marker as it is a potential breakdown product of mancozeb and other dithiocarbamates.[23] However, this too poses difficulties since carbon disulfide will rapidly evaporate from surface waters, and in the air will break down into simpler substances within days to a few weeks.[24] In contrast, ETU is highly water soluble and moderately mobile and may reach both surface and groundwater under some conditions.[25]

According to the 2020 re-evaluation decision of the PMRA, water monitoring data measured in areas with a known history of high EBDC agricultural fungicide use was used in the cancer risk assessment. The only water monitoring study used by the PMRA was conducted by the EBDC/ETU Task Force (i.e. registrants) and submitted to the PMRA (PMRA# 1766450). Potential drinking water sourced from surface water was monitored for a period of two years from watersheds in Maine, New York, Michigan, Minnesota, and Washington for ETU 20 years

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[20] Email from Robert Martin (PMRA) to Laura Bowman (Ecojustice) dated September 18, 2023. The PMRA stated that it is able to share 7 years of data (2014-2020). PMRA takes the position that data prior to 2014 does not meet the requirements of 3 registrants to comply with release under the *Pest Control Products Act*.

[21] Lyons et al "Effects of formulations of five pesticides on growth of Atlantic salmon during parr-smolt transformation" (2018) https://publications.gc.ca/collections/collection_2018/mpo-dfo/Fs97-6-3265-eng.pdf p.19 citing Ken Doe (retired), Environment and Climate Change (Canada, Moncton, NB). This may be referring to a fish kill incident in New Brunswick in August of 1994 that resulted in the death of 10,000 newly released brook trout and which is described in this report at p.89 https://www3.epa.gov/pesticides/endanger/litstatus/effects/redleg-frog/mancozeb-maneb/determination-doc.pdf

[22] Government of Australia: https://www.waterquality.gov.au/sites/default/files/documents/mancozeb-fresh-dgvs-technical-brief.pdf p.7; https://www.pan-europe.info/sites/pan-europe.info/files/public/resources/briefings/Factsheet%20Mancozeb%20-%20March%202020.pdf https://www.researchgate.net/publication/319672994_Environmental_and_biological_monitoring_for_the_identification_of_main_exposure_determinants_in_vineyard_mancozeb_applicators

[23] CS2 represents the sum of all dithiocarbamate compounds and is reported as "total dithiocarbamates" in most cases.

[24] https://oehha.ca.gov/media/downloads/water/chemicals/nl/palcarbondisulfide_0.pdf

[25] EPA 2005 Risk Assessment for re-registration of mancozeb, p.22 https://www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/red_PC-014504_20-Sep-05.pdf

ago. The sample sites ranged from very small watersheds and reservoirs in Maine to large watersheds draining into the Great Lakes in New York and Michigan. A total of 231 sites were sampled multiple times, resulting in a total of 3,971 samples. Concentrations of ETU in surface water were used in the chronic drinking water assessment because it would be expected that surface water concentrations would be higher than in groundwater. The PMRA noted in the 2020 re-evaluation decision that no chronic concentrations could be calculated because "sampling was infrequent" and that the peak value of 0.57 ug/L was used in PVRD2018-17. However, after the registrants complained, the PMRA used 0.21 ug/L for chronic concentrations without any detailed explanation.[26] There does not appear to be any independent monitoring data considered by the PMRA or readily available from a Canadian context and no frequent sampling was conducted based on the Canadian use pattern in any location to identify peak concentrations of either total dithiocarbamates or ETU. **In preparation of this request for a special review, the task force monitoring was requested but this request is being processed by the PMRA as confidential test data, resulting in delays. We reserve the right to make further submissions on the request for a special review once we have received and reviewed that information.**

Regulatory History of mancozeb in Canada

Mancozeb was first used in Canada starting in 1963.[27] It is not clear from publicly available documents when the re-evaluation of mancozeb began, but it appears to be some time around 2008 or 2009. The PMRA published a proposed re-evaluation decision on mancozeb in 2013 (PVRD2013-01). The 2013 re-evaluation proposed mitigation measures for alfalfa grown for seed, certain food/feed uses including greenhouse tobacco, potatoes, wheat, carrots, cantaloupe cucumbers, celery, ginseng, lentils, head lettuce, melons, onions, pumpkins, sugar beets, squash, field tomatoes, and watermelons. The remaining uses of mancozeb (seed treatment for barley, corn, flax, wheat, and potato seed piece, and application on orchard crops including apples, pear, grapes, and greenhouse tomato) were proposed for phase-out because of human health risks and/or risk to the environment. There was a public comment period. In response to the proposed 2013 decision, comments relevant to the dietary exposure were received primarily from the Mancozeb Task Force (MTF) on behalf of Dow AgroSciences Canada Inc. and United Phosphorus, Inc., the Canadian registrants of mancozeb. Various other stakeholders such as the Canadian Horticultural Council, other grower groups, and provincial agricultural/food departments provided information regarding the alleged importance of mancozeb.

The 2013 proposed re-evaluation decision noted significant human health effects of mancozeb from animal and human studies. For example, the PMRA noted potential reproductive toxicity from a 2001 study but reached no specific conclusion. The 2013 proposed re-evaluation dismissed links with Parkinson's disease found in human studies. The PMRA also identified significant data gaps for both mancozeb and the degradation product/metabolite ETU including

[26] RVD2020-12 p.134-135.
[27] PMRA public registry lists this as the exclusive date for all currently registered products.

for developmental neurotoxicity and immunotoxicity.[28] The PMRA concluded that studies show a relationship between mancozeb exposure and human retinopathy.[29]

A key finding highlighted in the 2013 risk assessment was that the aggregate cancer risk for the general population from ETU was 8 in a million and was unacceptable because the acceptable threshold for cancer risk used by the PMRA is one in a million. The PMRA noted that "[s]ince there is no current evidence supporting a threshold for induction of liver tumours, a cancer unit risk (q1 *) of 0.0601 (mg/kg bw/day)-1 based on liver tumours was generated for the cancer risk assessment of ETU and all EBDCs.[30] The finding that there is no evidence supporting a threshold for liver tumors means that liver tumors can be caused even at low doses. This finding was linked to estimated environmental concentrations (EECs) of mancozeb. Estimated environmental concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil, and air. The EECs are estimated using models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications.[31] Normally the PMRA models these concentrations.[32] In the cancer and chronic assessment, residues in drinking water were based on the modelled drinking water reservoir yearly EEC (2.9 µg a.i./L), whereas in the acute human exposure the residues were based on the daily EEC (16 µg a.i./L). The PMRA calculated that the cancer risk estimation from drinking water alone (not including diet, bystander or occupational exposure) was 4 in a million.[33] However, the EEC values used in the cancer risk assessment were not the highest EEC's that the PMRA modeled in 2013 – some EECs for example apple uses in Nova Scotia in a small water body, were as high as 493 ug/L, or 1289 ug/m for potatoes at 1.8 kg/ha with 7-day intervals. The PMRA appears to have significantly underestimated cancer risks for these uses. The 2013 proposed decision noted that water monitoring data for mancozeb in Canada was limited, and so the PMRA relied on the models.[34]

Due to data deficiencies identified in the course of the re-evaluation, the PMRA requested additional data in section 9.2 of the 2013 proposed decision under section 12 of the *Pest Control Products Act*. This included:

- Developmental neurotoxicity study on ETU, and depending on the outcome a DNT study and/or developmental thyroid assay on mancozeb may be required
- Immunotoxicity study

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[28] PRVD2013-01 p.17-18. Also see PRVD2018-17 p.7-11.
[29] PVRD2013-01 p.17.
[30] PVRD2013-01 p.20. also see PRVD2018-17 p.12.
[31] PRVD2013-01 p.45.
[32] Reliance on modelling, particularly where there is no adequate water monitoring, is emphasized in numerous PMRA science policy documents such as Science Policy Note SPN2003-04 entitled "General principles for performing aggregate exposure and risk assessments." and SPN2004-01 "Estimating the water component of a dietary exposure assessment." Utilizing inadequate monitoring instead of modelling is non-compliant with these policies.
[33] PVRD2013-01 p.41.
[34] PRVD2013-01 p. 56-57. As noted above this complies with PMRA risk assessment policies, which require the use of models when there are no robust water monitoring data capable of identifying the highest concentrations.

- Two generation reproductive toxicity study in rat on ETU
- Developmental neurotoxicity study on ETU
- Occupational information about amount of ETU formed in treated seeds
- Occupational information about dust from treated seeds[35]
- Supervised residue trial study for all registered uses at the Canadian good agricultural practice
- Processed food/feed studies for all uses
- Additional data is required to characterize the potential exposure to ETU through drinking water "confirmatory water monitoring is required to address the determined exposure risk."

The PMRA also gave registrants, users and the public a chance in 2013 to submit additional data for uses proposed to be phased out on apples, pears, grapes, and seed treatment for cereals and potato pieces.[36] The consultation period was extended to 109 days, and during that time the PMRA received new data and information that it used in the final 2018 decision.[37]

After the publication of the proposed decision in 2013, the PMRA did not finalize the decision, nor did it implement the proposed mitigation measures and use cancellations for mancozeb for approximately **five years**. After these extensive delays in addressing a product that the PMRA had already found posed unacceptable risks for nearly all uses, the "final" decision for mancozeb was published in June of 2018 (RVD2018-21). The June 2018 decision noted that no further consideration had been given to "the uses no longer supported by the registrants and those being cancelled due to occupational risks of concern." These were listed as "seed treatment for barley, corn, flax, oat and wheat; potato seed-piece treatment; grapes; greenhouse-grown tomatoes, and orchard crops, including apples and pears." This is important because based on current labels in the public registry, apples and wheat appear to continue to be permitted uses to this day, along with greenhouse tomato uses.

The June 2018 final re-evaluation decision also noted that a revised drinking water EEC was derived from 2002-2003 water monitoring from the United States, data that is now 20 years old and comes from a time when the use of mancozeb was significantly lower.

The main conclusion of the June 2018 final re-evaluation was that **all registrations and uses would be cancelled except for products with uses permitted for foliar application to potatoes**. The cancellation was due to a finding by the PMRA that all other uses of mancozeb posed "unacceptable risks to human health." Label amendments were also required for foliar application to potatoes such as limiting applications to a maximum of 10 applications per year at

[35] PRVD2013-01 p.88.
[36] PRVD2013-01 p.88.
[37] RVD2018-21 p.1, Appendix II.

a maximum rate of 1.69 kg/ha[38] with 7-day application intervals[39] with a one-day pre-harvest interval[40] using aerial or ground spray only. **According to the current labels on the public registry, this change was never implemented, and a much higher application rate is still permitted on potatoes to this day, and none of the other uses have been removed from the label**.

Additional personal protective equipment was required in the final 2018 decision and a restriction on using other EDBC pesticides was to be included in the labels. Since that time, the PMRA has determined that it will allow any tank mix to be permitted on the label without public consultation, so it is unknown if the PMRA intends to reverse the restriction on using multiple EDBC pesticides in forthcoming label amendments.[41] Additional spray buffer zones and limits on the number of aerial applications were to be included on foliar potato applications to mitigate environmental risks. These changes also never happened. The final decision stated that the label amendments had to be completed within 24 months. For the products being cancelled, the registration of the products was to expire 36 months following the publication of the final re-evaluation decision, an event that was to take place in June 2021. None of these changes were ever implemented to protect human health.

It is worth noting that this June 2018 "final" decision aligns with some of the findings of the European Food Safety Authority (**EFSA**) review in 2018-2020 which found that foliar application on potatoes was an exception to various findings of risk.[42]

Registrants were entitled to file a notice of objection under section 35 of the PCPA if they disagreed with the scientific basis of the PMRA's findings. No notices of objection appear on the public registry for mancozeb. Instead, various industry and grower representatives met with PMRA executive director, Richard Aucoin, in 2018.[43] As a result of these meetings, the PMRA withdrew the final decision in the re-evaluation.

It is worth noting that there is no power for the Minister to "withdraw" a decision to cancel pest control products for health and environmental reasons in the *Pest Control Products Act*. Rather, the remedy for a registrant who is unhappy with a final cancellation decision under the PCPA is to either file a notice of objection under section 35 of the PCPA requesting a scientific review panel or, alternatively, to file a new application to register the product with whatever new

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[38] This is the application rate or the rate at which the pesticide may be applied, something that directly relates to the amount of product that ends up on food and in the environment as well as efficacy.
[39] This is the number of days required between applications of the pesticide.
[40] The pre-harvest interval or PHI is the period of time between when application of a pesticide may occur and harvest. The primary objective of the PHI is to prevent high food residues by allowing the product to degrade before it is harvested.
[41] PMRA *Guidance Document, Tank Mix Labelling* (March 2023) https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/policies-guidelines/tank-mix-labelling.html
[42] EFSA peer review of the pesticide risk assessment of the active substance mancozeb. https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2020.5755
[43] https://www.thoroldtoday.ca/local-news/my-face-went-white-the-fight-for-mancozeb-fungicide-3154822

information is needed for that purpose. We note that the 2018 final re-evaluation decision provided for a three-year phase-out, during which growers and registrants could have supplied new information and applied to re-register the products.

Instead of following the legal requirements of the PCPA – the PMRA unlawfully withdrew its decision and negotiated with industry and user groups for two more years. It did not take much for users and registrants to get the PMRA to take the extraordinary decision to withdraw a final registration decision made after more than five years of deliberations and a lengthy consultation period. The PMRA did this in August 2018, only two months after the final published decision. The purported reasons for the withdrawal were a lack of clarity in the 2013 proposed decision about which products were proposed for cancellation.[44] The withdrawal stated that "The proposal should have stated, based on the dietary risk assessment, that all uses were proposed to be cancelled, rather than stating that certain uses were proposed for continued registration with further risk reduction measures proposed." In other words, because there was allegedly a more extensive cancellation in the final 2018 decision than in the proposed decision – a new public consultation was needed. Strangely, the statement describing the risk management decision in the withdrawal notice (cancellation of all uses) does not match the description in either the proposed 2013 decision or the final June 2018 re-evaluation decision.

Only a few weeks after the August 2018 withdrawal of PRVD2018-21, the PMRA posted a new proposed decision (PVRD2018-17) on October 5, 2018. A new and different description of the 2013/2018 risk management proposal was included in that document of "all uses were proposed to be cancelled except greenhouse tobacco". This time, potato uses were to be cancelled.

The October 2018 proposed re-evaluation decision proposed to cancel all uses except greenhouse tobacco. The reasons stated were that:

- Dietary risk from food alone and drinking water alone were identified and found not be acceptable (except for greenhouse tobacco)
- Forestry and woodlot uses are proposed for cancellation due to potential residues in drinking water which are not acceptable
- Occupational risks were found to be unacceptable for potato seed piece treatment, seed treatment for barley, corn, flax, oat and wheat
- Postapplication risks for workers were found to be acceptable for apples, pears, grapes and greenhouse tomatoes only if lengthy restricted-entry intervals (for hand labour) were applied, and these were not believed to be agronomically feasible
- Environmental risks to birds and small wild mammals were identified for foliar sprays of mancozeb on all crops and were found not to be acceptable.

The environmental and human health risks were so serious for all other uses that the PMRA took the extraordinary step of proposing mitigation measures *during* the phase-out of all products. These included re-packaging of wettable powder products, additional protective equipment,

[44] RVD2018-21 was removed from the PMRA website and replaced with a statement to this effect.

longer re-entry intervals, limiting aerial applications to one per season, and a statement warning that ETU may leach into groundwater.[45]

The 2018 proposed re-evaluation noted that the EFSA requested additional data after its most recent (then 2009) evaluation and that American uses on similar crops were subject to lower application rates and additional mitigation measures.[46] Overall, the conclusions of the 2018 proposed decision were similar to those in the 2013 proposed decision.

Despite these alarming findings of risks to human health and the environment, the 2018 proposed decision was not implemented until 2020, when the PMRA made a second "final" decision. At this point the re-evaluation had spanned a decade. It is worth noting that the environmental risk conclusions in the 2020 final risk assessment decision for mancozeb were not significantly different than those in the 2013-2018 risk assessment. The 2020 risk assessment did take into consideration some new information (described in section 3.3.1 of the assessment) however this information merely confirmed that risk quotients for environmental effects were greater than 1 and that levels of concern were exceeded for a wide range of biota. The PMRA's own risk assessment process explains that when risk quotients are greater than 1 this is an indication of unacceptable risk, and that a refined assessment must result in a level below levels of concern for the product to meet the standard under the Act.[47]

The 2020 final re-evaluation decision contained an environmental risk assessment which found that there was a risk from ingestion of pollen based on testing of honey bees (the representative species for all insect pollinators). This was addressed through statements on the label asking users not to apply foliar applications when crops are in bloom. This assessment was based on the LD_{50} (or lethal dose that kills 50% of a test sample) for *Apis mellifera* a species of bee. Sub-lethal effects on bees or other pollinators were not assessed. Although a honey bee field trial was included in the 2020 risk assessment, the PMRA noted several problems in the study in the 2020 risk assessment that were not addressed. Later in 2020, the EFSA peer review reached the conclusion that there were risks of concern for bees, and noted that there were data gaps relevant for all outdoor uses of mancozeb and that, "A colony feeding field study with honey bees was available and indicated a potential concern for colony strength."[48] The PMRA never considered the field study considered by the EFSA and this study provides reasonable grounds to believe that the risks of mancozeb are unacceptable for bees.

The 2020 final PMRA re-evaluation also found that risk quotients for harm to representative species of beneficial arthropods were also exceeded in lower-tier studies and higher-tier studies were "not available for review." Beneficial arthropods are important for soil health. In 2020, the PMRA found that mancozeb poses potential risks to non-target arthropods. This was to be

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[45] PRVD2018-17 p.2.
[46] PRVD2018-17 p.3.
[47] This process is described in the Proposed re-evaluation decision for Azoxystrobin https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/consultations/proposed-re-evaluation-decisions/2023/azoxystrobin/document.html
[48] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7744028/

mitigated with a precautionary statement "to inform users of the potential hazard to beneficial arthropods." However, it is not clear what users are supposed to do with this information, nor is it clear how making the protection of arthropods at the discretion of the user ensures reasonable certainty that no harm will occur to the environment, particularly regarding the biodiversity of soils.

The 2020 risk assessment found that the acute and reproductive levels of concern were exceeded for all bird sizes and feeding guilds. The 2020 risk assessment found that the acute levels of concern for mammals medium and large-sized mammals and reproductive levels of concern were exceeded for all sizes of mammals. These assessments were further refined and showed that mancozeb "may pose a risk to birds and mammals feeding on-field and adjacent to fields where mancozeb is applied". Despite this finding, the PMRA continued to register mancozeb based on unsubstantiated conjecture that "birds may avoid mancozeb treated food items" and that food items contaminated with mancozeb were "short-lived" and therefore acute risks were "not expected". The reproductive risk remained, and the only mitigation measure imposed was a label statement to "inform" the user of the potential hazard. Informing the user of the potential hazard puts the environmental risks of mancozeb at the discretion of the user, and does not ensure that there is reasonable certainty that no harm will occur. Despite all of the findings of risks in the risk assessment, the PMRA reversed its 2013, and two 2018 findings that the risks to birds and mammals were unacceptable, stating in 2020 that the risks to birds and mammals were acceptable.[49]

For aquatic organisms, the 2020 risk assessment found that acute and chronic levels of concern were exceeded for all organisms from spray drift based on all application methods of mancozeb with some narrow exceptions. The risk assessment was unable to model exposure to aquatic organisms from runoff and accordingly the PMRA does not have reasonable certainty that no harm will occur from either spray drift or runoff. This gives rise to reasonable and probable grounds that the risks to aquatic organisms from runoff are unacceptable. Risk quotients for amphibians and aquatic invertebrates also exceeded levels of concern. The 2020 risk assessment acknowledged that ETU was an endocrine disruptor, and without explanation stated that "the refined risk assessment indicates amphibians are not expected to be at risk." However, no refined risk assessment is included in the 2020 document. It is well-known that amphibians can be particularly vulnerable to endocrine disruptors and that endocrine disruptors are also typically carcinogenic.

In short, there were numerous serious environmental risks associated with predicted mancozeb exposures and these were not mitigated by anything other than advisory statements, placing risk management, if any, at the full discretion of users. Despite this, in a complete reversal of three previous decisions and risk assessment conclusions, the PMRA continued the registration of mancozeb, inclusive of uses that it had previously found posed unacceptable environmental risks and without material changes to the scientific understanding of the environmental risks of mancozeb.

[49] RVD2020-12 p.54-55

The 2020 re-evaluation included an incomplete assessment of occupational and cancer risks

According to the 2020 decision, registrants submitted a variety of new toxicological information that was submitted only after the 2018 proposed decision was released.[50] This included information that was not new, and that should have been submitted in response to the 2013 proposal. Despite the registrants failing to provide data requested or identified as deficient in 2013 the PMRA took two years to review the data and revised the toxicology endpoints for protection of human health from mancozeb and ETU based on this information. These updates are located in Appendix V of the 2020 re-evaluation decision.

For example, as the result of the submission of a developmental neurotoxicity (DNT) study in 2020 the uncertainty factor added for this missing data was modified. This increased the acute reference dose for females for mancozeb by 2.5 times. An acute neurotoxicity study was considered, leading to an increase in the acute reference dose for the general population. However, it is unclear if this study is the same one referenced in the 2013 risk assessment, which did not identify a dose at which there was no effect.[51] The result was that the "dose response was not clear as there was significant variability in the data."[52] If so, it was not really a new study and it is not clear why the PMRA changed its conclusions. Alarmingly, the acute reference dose for all treatment related effects was based on this lowest effect level for neurotoxicity and not on the lowest effect level found in female rats which was much lower. The PMRA appears to have allowed industry submissions from the Mancozeb Task Force to influence its consideration of the science in this regard. The use of a level that is not the lowest no adverse effects level is not conservative and may underestimate human health risks.[53] As a result the PMRA would lose reasonable certainty that no harm will occur at these doses. It is notable that the PMRA did not change the acute reference dose for ETU in 2020.

For chronic risks from mancozeb, expressed as the acceptable daily intake (ADI)[54] the submission of immunotoxicity and developmental neurotoxicity studies resulted in a reduction in the "database – missing data" uncertainty factor and a resulting significant increase in the acceptable dose from 0.0006 mg/kg to 0.023 mg/kg for all populations. In 2020 the PMRA

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[50] RVD2020-12 p.6.
[51] RVD2020-12 p.35 discusses how the study did not identify a no adverse effect level (NOAEL).
[52] RVD2020-12 p.36.
[53] PMRA (2021) Framework for Risk Management of Pest Control Products, explains that the starting point for calculating the reference dose or value is the lowest level of exposure that causes no adverse effects (NOAEL). The NOAEL is "typically selected from the test species that exhibits the greatest sensitivity to the toxic effects of the pesticide." This is also explained in PMRA (2008) SPN2008-01 "The application of uncertainty factors and the PCPA factor in human health risk assessment of pesticides" this states that the selection of the most appropriate NOAEL takes into consideration which human subpopulations may be exposed, the route of exposure and the anticipated duration and/or frequency of exposure and that the critical effect is "typically the first adverse effect that occurs in the toxicity database with increasing dose."
[54] The ADI is effectively the chronic reference dose, below which the risks would be acceptable because there would be reasonable certainty that no harm would occur. This is because the ADI reflects the lowest NOAEL plus uncertainty factors.

created a separate chronic risk ADI for ETU – for which uncertainty factors remained and the ETU chronic risk factor remained roughly the same.

Inexplicably, the PMRA did not create a chronic or acute reference dose for children, who are usually treated as a separate sub-population in accordance with PMRA risk assessment policies. These policies appear to have been ignored for mancozeb.

Overall, the changes to the toxicology reference doses do not explain the changed conclusions in the 2020 human health evaluation. Most reference doses revised in 2020 were more protective with the exception of the acute general population and female acute reference doses for the parent compound mancozeb.

For the 2020 human health re-evaluation, PMRA considered submissions from the mancozeb task force (MTF) a group of registrants who made non-public submissions about how the PMRA should revise the proposed 2018 re-evaluation decision to cancel all uses except tobacco. In order to reduce the use pattern considered in the re-evaluation, the MTF task force submitted that the following uses, formulations and application methods of mancozeb would be voluntarily cancelled:

- All seed treatments (including potato seed piece treatment), greenhouse uses (in other words, tobacco, tomatoes), use on pears, carrots, celery, lettuce, watermelon, lentils, wheat, alfalfa grown for seed, as well as ornamentals and forestry uses.
- All applications using any handheld equipment.
- All end-use (commercial class) wettable powder or dust formulations.[55]

Accordingly, the 2020 final decision was far narrower in scope and in the scope of assessment than any of the prior decisions of the PMRA. We note that all of the above uses are still on the published labels in the PMRA public registry. When we wrote to the PMRA on September 11, 2023, asking why the labels were not updated following the 2020 decision, we did not receive a response. We reminded the PMRA again of this question in late September and continued to not receive a response.

The 2020 human health decision found unacceptable risks from the remaining uses – the same uses that are still allowed without any changes on the published labels. To mitigate those risks to protect workers, bystanders and the general public from occupational, residential and dietary exposure a large number of risk reduction measures had to be implemented for agricultural uses on a wide variety of crops, by lowering the application rates and maximum applications per year, additional personal protective equipment requirements, prohibition of the use of handheld equipment, longer re-entry intervals, prohibition of use in residential areas, and changes to the maximum residue limits on crops. These mitigation measures are set out in Appendices I and II

[55] RVD2020-12 p.2.

and X of the 2020 decision.[56] As noted, these mitigation measures do not appear to have ever been implemented, based on the published labels in the public registry as of September 2023.

The proposed 2018 registration decision (similar to the decisions in 2013 and earlier in 2018) found that to protect workers from pesticide residues from mancozeb, they would have to be prevented from entering the field for unrealistic periods of time that were not "agronomically feasible." The period of time where workers cannot do hand labour in a field is known as the restricted-entry-interval (REI).

A re-entry interval is the interval during which hand labour (weeding, pruning, picking) is not permitted after pesticide application. REIs are referenced, but are not on pesticide labels, and PMRA guidance on what activities are prohibited during REIs are also very unclear.[57] It is our opinion that REIs, without clear definitions on the labels, are too vague and unenforceable to provide reasonable certainty that no harm will occur to human health.

The prohibition on hand-labour alone – as set out only in PMRA guidance and not on the label - does not explicitly prevent people from entering the fields and being exposed to inhalation and dermal contact with pesticides on foliage. This includes people engaged in watering, moving around equipment, or simply passing through. Even where the PMRA guidance stipulates what is intended by a "restricted entry interval" or hand labour this guidance is completely unclear about what tasks or entry are actually allowed.[58]

This interval could not plausibly be enforced when it is not described or defined on the label. Moreover, the PMRA guidance provides standardized REIs that are not consistent with those on the mancozeb labels. The PMRA guidance defining an REI is not enforceable as a condition of registration under section 6 of the *Pest Control Products Act* because it is not defined on the label, and an REI is therefore not an appropriate consideration for determining acceptable risk, since that risk must be based on the conditions of registration under section 2(2) of the Act.

Despite all of this, in the 2020 re-evaluation, the PMRA re-considered whether the REIs for mancozeb were agronomically feasible. This was based on the smaller use pattern (i.e. the smaller variety of crops, application rates and other uses that were now part of the 2020 risk assessments). The risk assessment of the remaining uses covered apples, cucumbers, potatoes,

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[56] RVD2020-12 p.26-28.

[57] PMRA – understanding restricted entry intervals for pesticides. https://www.canada.ca/content/dam/hc-sc/documents/services/consumer-product-safety/reports-publications/pesticides-pest-management/fact-sheets-other-resources/fs-restricted-entry-intervals.pdf

[58] For example, the published Guidance "Restricted Entry Intervals" indicates a default REI of 12 hours without clarity around label requirements, and also allows "certified applicators" a term unknown to the PCPA and its associated regulations, to enter within 4 hours. It states that "hand labour" involves contact with treated surfaces and that activities "can include" thinning, weeding etc. This definition does not clearly prohibit spraying workers, or require workers to wear any specific PPE while spraying occurs for example. Many labourers may be unclear about whether the REI applies to them based on this very vague definition. It only refers to "treated surfaces" and not air exposures from volatile compounds.

pumpkin, squash, sugar beets and field tomatoes.[59] It also used revised toxicology endpoints based on the new data that were submitted on various human health issues. For mixers/loaders and applicators the occupational risks were controlled with engineering controls and additional PPE. However, the only mitigation measures for occupational risks for post-application workers remained the REIs. The risk assessment did not explain why the PMRA reversed its assessment that the REIs were feasible from 2018.

Specifically, the 2018 proposed decision stated that the REIs for apples, pears, grapes, and greenhouse tomatoes were not agronomically feasible and risks were not acceptable.[60] The REIs referenced as being not agronomically feasible in the 2018 proposed decision are set out in table 4 on page 67 of that assessment. They can be compared to the REIs required in the 2020 assessment to mitigate occupational risk that were now said to be feasible:

Crop	Activity	Formulation	REI (days) not feasible in 2018	REI (days) feasible in 2020
Tomatoes	Harvesting	DF, WG, WP	27 (greenhouse)	**30**
	Other activities	DF, WG, WP	27 (greenhouse)	12 hours
Apples (terrestrial food crops)	Hand thinning	SN, WP	59	35
		DF, WG	56	
	Hand harvesting	SN, WP	34	**77**
		DF, WG	32	
	Hand-line irrigation	SN, WP	24	12 hours
		DF, WG	22	
	All other activities	DF, WG, SN, WP	12 hrs	
Grape	Girdling, cane turning	WP	81	21
		WG	53	21
		DF	41	21
	Hand harvesting	WP	60	**66**
		WG	34	**66**
		DF	28	**66**
	Hand line irrigation	WP	8	1
		WG	2	1
		DF	12 hrs	**1**
	All other activities	WP	15	12 hours
		DF, WG	12 hrs	12 hours
Pear			65	Use to be cancelled
			40	

[59] RVD2020-12 p.11.
[60] PRVD2018-17 p.56.

			30	
			5	

Although the final 2020 decision stated that greenhouse uses for tomatoes had to be removed from the label, "tomatoes" were still listed as having a re-entry interval in the appendix providing for changes to the label. It is unclear if after 2018, there was a registration added for field tomatoes, and the REI proposed in 2020 was new, or whether the 2020 decision is internally contradictory on the issue of whether greenhouse tomatoes were cancelled versus mitigated with a changed REI and a different (higher) application rate.[61] Field tomatoes are not discussed in the 2018 decision but do appear as a "supported use" in the 2020 decision.[62]

The significant increase of the REI for harvesting outdoor grown apples to 77 days (when 32-34 days for harvesting had previously been stated to be not agronomically feasible) cannot be fully explained by other mitigation measures in 2020 since the maximum application rate for apples from 2018 was unchanged at 4.5 kg per hectare.[63] The number of applications per year was limited to four applications in 2020, whereas previously the risks were assessed in 2018 based on six applications.[64] However it is not clear how a change to the maximum number of applications would impact on post-application exposure estimates, nor how more than doubling the number of days in the re-entry interval is consistent with four applications per year (it would have to be spread out over 308 days which is longer than the growing season for apples). This was not explained in the 2020 decision. Take for example the 77-day harvesting interval, this would mean that apples – typically harvested in late August and September – would have to be sprayed with mancozeb no later than the end of May to protect post-application workers. Due to the 35-day interval for hand thinning – no workers could go into the fields and conduct this work in June. The label instructions for apples indicate that it is to prevent cedar apple rust and quince rust and should be applied "in protective schedule from green tip to second cover spray". The second cover spray would be post-bloom. However, apple blossoms typically bloom from early spring to late summer. Hand-thinning would typically take place four to six weeks after bloom. In light of this it is unclear how this interval is feasible. In the response to comments in the 2020 assessment it was stated that the BC ministry of agriculture indicated that it "may be" feasible for up to two to three weeks, not the full 35 days on the label. Confusingly, the PMRA responded to this comment stating that "as much as possible growers should apply mancozeb after thinning, which may be possible with the reduction in the number of applications for apples."[65] It is not clear how this is compatible with a 77-day harvest interval. A comment from Ontario Apple Growers on the risk assessment apparently argued for changes to these mitigation measures to

[61] RVD2020-12 Appendix X, Table 1 shows a higher maximum application rate for tomatoes (2.44 kg of active per hectare) than was considered in the 2018 risk assessment for greenhouse tomatoes (1.8 kg of active ingredient per hectare) see PRVD2018-17 p.83.
[62] RVD2020-12 p.2.
[63] RVD2020-12, Appendix X, Table 1 shows the maximum rate for apples remained at 4.5 kg a.i./ha compared to PVRD2018-17 p.85 which shows that for most products the application rate was the same at that time.
[64] *Ibid*.
[65] RVD2020-12 p.51.

make them feasible. In response, the PMRA noted that they had no way to study exposure to post-application workers in high-density orchards.[66]

For grapes, the REI was also increased significantly in 2020, even though the lower number of days was previously said to be not agronomically feasible. This is also not fully explained by mitigation measures. The 2018 application rate for grapes was only 1.5 and 1.6 kg/ha for DF and WG products, which was **increased** to 2.25 kg/ha in 2020.[67] The maximum number of applications for grapes was reduced only for DF from six to one per year, but remained unchanged for WG at one application per year.

It is entirely unclear how the PMRA determined that these *higher* REIs were suddenly agronomically feasible and how the PMRA determined that these changes could have improved exposure to workers, given the approval of *higher* application rates in many cases. Given the earlier conclusion that these were not agronomically feasible periods of time to prevent agricultural workers from going into their fields – stretching into months – this alone gives rise to reasonable and probable grounds to believe that the risks of mancozeb are unacceptable.

The 2020 re-evaluation decision also noted that the re-entry interval does not prevent workers including certified pesticide sprayers from entering treated areas for short-term tasks involving hand labour after only four hours. It is not clear how the risks to these workers were mitigated and there are reasonable grounds to believe that a certified sprayer who is not required to comply with the re-entry interval may be exposed to unacceptable risks from exposure to mancozeb and its breakdown products.[68]

In 2018, the cumulative exposure to ETU from mancozeb breaking down and the breakdown of other EDBC fungicides was considered. The cancer qi of 0.0601 mg/kg bw/d was based on incidences of liver tumors in the combined chronic carcinogenicity reproduction study. The chronic exposure to ETU estimated by drinking water modeling of ETU exposure resulted in a cancer risk estimate of four in a million – without considering dietary risks from food residues.[69] In 2018, drinking water modelling was conducted with regional scenarios and region-specific weather data for a variety of crops. This resulted in an acute drinking water EEC of 16 µg/L and a chronic drinking water EEC of 2.9 µg/L (as reported in PRVD 2018-17).[70] These values were used as the concentrations that people would be exposed to for the cancer risk assessment for ETU.

The 2020 re-evaluation decision changed the cancer risk assessment conclusions for ETU in drinking water by relying on selective water monitoring concentrations from US monitoring data submitted by the registrants. The monitoring dated from 2001-2002, more than two decades ago, when as noted earlier in this submission, sales of mancozeb were far lower. The monitoring data

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[66] RVD2020-12 p.50.
[67] RVD2020-12 Appendix X, Table 1 compared to PVRD2018-17 p.86.
[68] RVD2020-12 p.49-50.
[69] PRVD2018-17 p.34-36.
[70] RVD2020-12 p.134.

were not from Canada, but from the US. Over two years, there were 231 sites sampled a total of 3,971 times. This averages only 17 samples per site over two years, so not even once per month. The low frequency of this sampling is not discussed in the 2020 re-evaluation decision. There is no comment in the re-evaluation decision on whether the sites selected had some contextual basis to demonstrate that they would have high concentrations of ETU, nor is there any discussion of whether the sampling protocols used would have been expected to identify peak concentrations. Moreover, the 2020 decision notes that some sample sites were "large watersheds draining into the Great Lakes" which would presumably be of very little value for identifying peak concentrations from small drinking water sources. The PMRA admits in the 2020 decision that "the data does not allow for the calculation of chronic EEC values as sampling was infrequent."[71] The result of this should have been that the PMRA continued to use the 2018 chronic modelled EEC of 2.9 µg/L. Instead, the PMRA makes the unsubstantiated and unscientific comment that "the use of a peak value from the monitoring data set provides a very conservative estimate of chronic drinking water concentrations." This peak concentration value was 0.57 µg/L from New York State, a level approximately six times lower than the modelled level of drinking water exposure. Instead of using this peak concentration, the EEDBC/ETU task force of registrants, convinced the PMRA to use an even lower figure, that of 0.21 µg/L.[72] This level is so low, that it is approaching the level of quantification for mancozeb (0.1 µg/L) as identified by the EFSA.[73] The PMRA provided no reasons or rationale for using this other than that the US EPA used it in their assessment.

These concentrations appear to be lower than the concentrations of ETU modelled from currently allowed uses of mancozeb in Canada. As a result of incorporating the water monitoring data and ignoring the models, the PMRA reduced the finding of cancer risks from ETU from the 8 in a million finding from 2013-2018 to below one in a million.[74] This method runs contrary to the requirements in PMRA policies noted above.

The revised estimated concentrations in the 2020 risk assessment are not clear. The PMRA appears to be using actual monitored data from another country with unknown context, contrary to its own published policies requiring monitoring to be used to improve the drinking water models, not to ignore it. The limitations of the new monitoring data are not discussed – including that they are from another country.

The 2020 risk assessment was limited to crops that continued to be supported by the registrant "Mancozeb Task Force" and did not include all crops currently permitted on mancozeb labels. Further, the food residue of mancozeb was assumed to be zero.

This assumption appears to be incorrect. It is not clear if this assumption was validated with Canadian Food Inspection Agency (CFIA) food residue monitoring data as this is not mentioned.

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[71] RVD2020-12 p.134.
[72] RVD2020-12 p.135.
[73] https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2020.5755
[74] RVD2020-12 p.9-11.

A 2017 review of CFIA data sampled from Canadian fruits and vegetables found that total dithiocarbamate food residues (**without** considering drinking water or other dietary exposures) would lead to a cancer rate of 3.25 in a million when combined with other pesticide food residue exposures (imazalil, deildrin and mirex). This is 39 new cancer cases annually and was described by the authors as "non-negligible". The authors also found that the non-cancer risks of food residue exposure to dithocarbamates exceeded risk quotients by significant amounts (the RQ of 1 was exceeded with values ranging from 2.52 to 13.14).[75] These findings point to unacceptable cancer risks from dithiocarbamate exposures due to their common breakdown carcinogenic product ETU. It is not clear why the PMRA did not consider this published, peer reviewed 2017 study of CFIA data, and there is no mention in the risk assessment of any PMRA analysis of the original CFIA data.

The 2020 re-evaluation noted that although a threshold value was used to estimate cancer risk, there was no threshold for the liver tumours induced by ETU and that although there was a liver tumour mode of action study underway in 2020, it was not yet available to the PMRA.[76] The PMRA does not have reasonable certainty that no harm will occur as a result of the liver tumour-inducing properties of ETU exposure – a breakdown product of mancozeb. Any reasonable certainty is undermined by the lack of relevant Canadian monitoring data as well as the lack of any threshold for liver tumour effects to support the cancer dose of 0.0601 mg/kg. The PMRA should include a cancer reassessment – including a review of whether a threshold dose can be used where none are identified in animal studies. This issue should be within the scope of the special review we are requesting. There were also apparent problems with the estimates of the percentage of mancozeb that degraded to ETU. Health Canada used 6.8% even though the percentage converted in some studies was as high as 16.6%.[77]

The 2020 risk assessment imposed a large number of mitigation measures on all uses in order to support a reversal of the finding of unacceptable risks from the three previous assessments. Many of these mitigation measures were very clearly not realistic.

Current status of mancozeb products

As of September 2023, there were 27 products containing mancozeb listed on the public registry in Canada. Three of these are technical active ingredient registrations and one is for manufacturing only. The remaining product registrations are end-use products. Thirteen of these are listed as "phase-out" and 14 are listed as "full registration".

Product labels include registrations in several "use-site" categories. Detailed descriptions of the use pattern permitted on the label for Dithane DG 75 fungicide are included in Appendix III. We

[75] Valcke M., Bourgault M.H., Rochette L., Normandin L., Samuel O., Belleville D., Blanchet C., Phaneuf D. Human health risk assessment on the consumption of fruits and vegetables containing residual pesticides: A cancer and non-cancer risk/benefit perspective. Environ. Int. 2017; 108:63–74. doi: 10.1016/j.envint.2017.07.023 at p.66, 68.
[76] RVD2020-12 p.35.
[77] RVD2020-12 p.57.

reiterate that none of the mitigation measures required in 2020 appear to have been implemented on the labels.

Regulation of mancozeb in other countries

From 2021, with a grace period which ended in January 2022, mancozeb use as pesticide has been banned within the whole European Union (EU) due to the observed reproductive toxicity and endocrine-disrupting properties. The EU also issued a 2022 notification of final regulatory action under Article 5 of the 1998 Rotterdam Convention, to which Canada is a signatory.

EU Member States had to withdraw all authorizations for plant protection products containing mancozeb as active substance by July 4, 2021 at the latest. Disposal, storage, placing on the market and use of existing stocks of plant protection products containing mancozeb was prohibited as of January 4, 2022.

Update to the Screening Assessment of ETU by Environment Canada

In January 2023, Environment Canada conducted a risk assessment of the exposure of Canadians to ETU in the environment under the chemicals management plan (CMP) as part of the implementation of the *Canadian Environmental Protection Act*.[78] This risk assessment explicitly excluded all exposures to ETU from pesticides which the assessment states "were not characterized further." The standard used in these assessments is not whether there is reasonable certainty of no harm, as in the *Pest Control Products Act*, but rather whether there is evidence that the chemical is entering the environment in a quantity or concentration that may constitute a danger to human life or health. The standard of constituting a danger is more permissive than the standard in the *Pest Control Products Act*.

The assessment explains that there was biomonitoring data available in 2019 that the PMRA failed to consider in its human health risk assessment, noting that as part of the fifth and six cycles of the Canadian Health Measures Survey, which samples the blood and urine of about 3,000 individuals in Canada aged 3-79. ETU was measured in the urine samples of 97% of 2,704 individuals in the fifth cycle, and 99% of 2508 individuals in the sixth cycle. The screening risk assessment states that: "While these data may not capture acute or unique intermittent exposure, they support that there are potential chronic exposures to ETU in the general Canadian population, likely from use of multiple EBDC pesticides."[79]

The PMRA failed to consider biomonitoring data or to attempt to establish biomonitoring levels of concern (biological exposure limits) for ETU exposures. The reference doses mentioned earlier are expressed in milligrams per kilogram and cannot be directly translated into a concentration in blood or urine to assess if actual health effects can be expected (a biological

[78] https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance/ethylene-thiourea.html
[79] CMP ETU screening, p.7.

exposure limit). A biological exposure limit/level or BEL can be computed to assess whether the reference dose has been exceeded, which can then be compared to the amount in blood and urine.

In a published study from May 2020, researchers attempted to establish biological exposure limits for mancozeb using urine samples vineyard pesticide applicators from northern Italy. They calculated that the maximum allowable body burden of mancozeb is approximately 2.45 mg, and 0.92 mg of ETU.[80]

The 2023 Canadian chemicals management policy screening risk assessment for ETU also identified a biological exposure limit (expressed as a biological equivalent) of 0.7 micrograms per litre,[81] which compared to the geometric mean from the Canadian Health Measures Survey of 0.42 micrograms per litre. The *geometric mean* from the Canadian Health Measures Survey was more than 50% of the biological exposure limit using the CMP's own calculations.

This also means that the geometric mean amount that is found in actual blood or urine samples is **twice** what the PMRA estimates will be found in drinking water for its cancer risk assessment. Given that drinking water was the main route of exposure for ETU, this seems implausible at best unless ETU is bioaccumulating in humans. In other words, there are serious problems with the previous drinking water assessment for ETU and related cancer risk assessment.

The conclusion of the CMP screening assessment was that "this indicates that exposures for the Canadian General population are below the current level of concern." However, this screening assessment did not take into account the increasing use of mancozeb and other EDBC fungicides over time in Canada. Taking into consideration the absence of a threshold for liver tumor cancer risks identified in the studies that the PMRA looked at, this level is of potential concern. The PMRA does not have reasonable certainty that exposure to ETU is not causing liver tumors in Canadians. The screening risk assessment noted that "overall confidence in the exposure and datasets for ETU is moderate" and that there was uncertainty for the durations and frequencies of exposure to ETU. This uncertainty entails a loss of reasonable certainty and the risks of exposure to ETU are not acceptable.

Canada is not the only country that has conducted biomonitoring of ETU. The US Centres for Disease Control summarized existing biomonitoring in 2017. It was noted that Hispanic pregnant women and children residing in the California Salinas Valley (an agricultural region where

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[80] https://www.medrxiv.org/content/10.1101/2020.05.12.20098939v1.full

[81] Biological exposure monitoring is the measurement of pesticides or their biotransformation products found in the body, or eliminated therefrom, (this is what is monitored in blood and urine in the Canadian Health Measures Survey). Biological exposure limits are used to estimate the amount of a chemical or metabolite in a biological specimen that is consistent with an existing exposure guidance value such as a tolerable daily intake or a reference dose. In this case, the CMP biological exposure limit was based on the reference doses set by the Pest Management Regulatory Agency.

mancozeb is used) had a geometric mean concentration of urine ETU of 0.71 µg/L (detection frequency, 22.6%) – or right at the biological equivalent identified in the CMP.[82] In other countries, workers exposed to mancozeb applications had levels ranging up to 100 µg/L.[83] Thus, without looking at samples from agricultural workers, or other populations that are highly exposed, the exposure to ETU from mancozeb may be underestimated considerably. The PMRA should include an assessment of biological exposure data from agricultural workers in the special review.

Grounds for special review

Section 17(2) of the Act

Member states in the EU withdrew all authorizations for plant protection products containing mancozeb as of July 4, 2021[84] due to reasons pertaining to human health and the environment. Additionally, the herbicide received a Rotterdam ban notification that came into force as of December 2022.[85]

The October 2020 non-renewal decision of the EU highlighted the following concerns:

1. Mancozeb is classified as toxic to reproduction and exposure is non-negligible.

2. Mancozeb has endocrine-disrupting properties for humans and for non-target organisms.

3. Mancozeb poses a high risk to birds, mammals, non-target arthropods, soil macro-organisms as well as for aquatic organisms.

4. Estimates of occupational and bystander exposure exceed reference values.

1) Mancozeb is classified as toxic to reproduction and exposure is non-negligible.

The European Food Safety Authority (EFSA) peer-review noted that mancozeb is classified for developmental toxicity as Repr. 1B; H360D (ECHA, 2019), based on malformations observed in the rat developmental toxicity studies leading to a critical area of concern with regard to the EU approval criteria.[86] A 2017 systematic review of mancozeb as a reproductive and developmental hazard concluded that:

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[82] https://www.cdc.gov/biomonitoring/ETUPTU_BiomonitoringSummary.html
[83] *Ibid*.
[84] EC Renewal Report – October 2020. Available at: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/active-substances/details/277
[85] Rotterdam Convention Ban. Available at: https://www.pic.int/Procedures/NotificationsofFinalRegulatoryActions/Database/tabid/1368/language/en-US/Default.aspx?tpl=std
[86] EFSA Mancozeb Peer Review, (June 2019) https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2020.5755

> Results from *in vitro* studies provide evidence that Mancozeb may indirectly disrupt or impair reproduction at the cellular level and should be regarded as a reproductive toxicant. Animal studies confirm reproductive and developmental toxicity in mammals and suggest that males chronically exposed to Mancozeb experience significant changes in physiological, biochemical, and pathological processes that may lead to infertility. Epidemiological studies were limited to indirect methods of exposure assessment and examined the effect of fungicides more broadly during pre-conception, pregnancy, and birth, yielding mixed results. … High confidence ratings from in vitro and animal studies, in combination with moderate confidence ratings from epidemiologic studies employing indirect methods of exposure assessment, provide evidence that Mancozeb should be regarded as a suspected developmental hazard and a presumed reproductive hazard in humans.[87]

The PMRA did not adequately assess the reproductive toxicity of mancozeb in the 2018-2020 re-evaluation. The PMRA also did not evaluate all of the evidence that was before the EFSA in its review and the PMRA should launch a special review to obtain the additional evidence considered by the EFSA.

2) Mancozeb has endocrine-disrupting properties for humans and for non-target organisms

The EFSA peer review concluded that mancozeb meets the criteria for endocrine disruption for humans through the T-modality based on effects observed in the thyroid (thyroid follicular cell hypertrophy, increased thyroid weight, thyroid follicular cell hyperplasia and tumours of the thyroid gland (adenomas and carcinomas)). Based on the available information, the EFSA concluded that the approval criteria on the endocrine disrupting potential for mancozeb as set out in point 3.6.5 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, are met leading to a critical area of concern.

The PMRA did not adequately assess the endocrine-disrupting properties of mancozeb in the 2013-2020 re-evaluation. The PMRA also did not evaluate all of the evidence that was before the EFSA in its review and the PMRA should launch a special review to obtain the additional evidence considered by the EFSA on endocrine disruption, particularly given the gaps for amphibians that are evident in the 2020 risk assessment. The PMRA should also consider published literature published since 2020 on the endocrine disrupting properties of mancozeb.[88] This literature concluded that:

> The existing data demonstrate that MCZ possesses significant endocrine-disrupting properties in the thyroid and gonads, inducing its effects through toxic damage to hormone-producing cells, inhibition of the enzymes involved in hormone biosynthesis, modulation of hormonal receptors, as well as dysregulation of the hypothalamus-pituitary-gland axis. At the same time, an increasing body of data demonstrates that other

[87] Runkle et al "A systematic review of mancozeb as a reproductive and developmental hazard".
[88] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9390121/

> endocrine tissues, including adipose tissue and adrenals, may be the targets of MCZ toxicity. In addition, due to the role of hypothalamic structures in central control of endocrine system functioning, it has been proposed that MCZ neurotoxicity may at least partially contribute to endocrine disrupting effects of the fungicide. However, further studies are required to unravel the mechanisms of MCZ endocrine-disrupting activity and overall toxicity.[89]

The endocrine-disrupting properties of mancozeb mean that it may not follow a dose-response curve that is amenable to an acute or chronic reference dose based on high dose testing particularly in terms of thyroid toxicity.[90] Non-monotonic dose response curves have been demonstrated in the literature for many pesticides.[91] This could have the result of toxicity at much lower levels than the PMRA is utilizing in its risk assessment. Since this hazard, and whether it follows a linear, or even monotonic dose-response curve is fundamental to the safety profile of mancozeb, it alone warrants a special review. With so much uncertainty about the toxicity and hazards of mancozeb the PMRA must review them. This review must use a transparent method to address the endocrine-disrupting properties of mancozeb and its breakdown products.

3) Mancozeb poses a high risk to birds, mammals, non-target arthropods, soil macro-organisms as well as for aquatic organisms.

The EFSA found that the tier 1 risk assessment for the representative species selected indicated **a high risk to non-target arthropods** for the representative uses to vines and potatoes. The resulting tier 2 risk assessment indicated a high in-field risk. Several higher-tier field studies were available and discussed at the experts meeting. It was agreed by expert peer-reviewers that the available data were not sufficient to demonstrate the potential for recovery and consequently a high in-field risk to non-target arthropods was concluded for the representative uses in cereals, grapevines and potatoes. As a high risk to in-field populations of non-target arthropods has been indicated for all representative uses this leads to a critical area of concern.

In the PMRA risk assessments, the risk quotients exceeded acute levels of concern for on-field uses for arthropods at all proposed application rates, with the risk quotients (where the acceptable level is 1) ranging from 13 to 68. For apples the off-field risks to arthropods was identified as ranging up to 6.3 times the acceptable level. There were no higher tier studies considered – in contrast to the higher tier studies reviewed by the EFSA. Even with the higher-tier studies the EFSA concluded that there was not enough information to establish that arthropods would recover. The PMRA needs to include these higher tier studies in its review, since it concluded that arthropods would recover after one season for a single application and noted that "there is uncertainty as to whether recovery extends beyond a season for multiple

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[89] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9390121/
[90] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6137554/
[91] *Ibid*. and https://pubmed.ncbi.nlm.nih.gov/37553404/ and https://pubmed.ncbi.nlm.nih.gov/33834149/ and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6915086/

applications particularly at the highest rates" and found that "mancozeb poses a potential risk to non-target arthropods."[92] There was no mitigation proposed other than a notification to users. Putting risk management at the discretion of users does not result in reasonable certainty that no harm will occur and the PMRA made no such finding in the 2020 risk assessment. As the conclusion of the 2020 risk assessment is inconsistent with a finding of reasonable certainty that no harm would occur to beneficial arthropods, the PMRA should conduct a special review of this impact.

The EFSA reviewed chronic toxicity data for earthworms and other soil macroorganisms. The EFSA concluded there is a high chronic risk to other soil macroorganisms for all representative outdoor uses. An interim report for an ongoing field study investigating the effects on collembolans and soil mites was available. The available results indicated an effect on several taxa with no clear recovery by the final available sampling date (167 days after treatment). The results of the final assessment were not yet available and therefore it is unknown whether recovery will occur within one year. Consequently, a high risk to soil macroorganisms was concluded for the representative uses to wheat, grapevines, potatoes, and tomatoes in open protected greenhouse structures. The EFSA concluded that as a high risk to soil macroorganisms has been indicated for all representative uses this leads to a critical area of concern.

The PMRA failed to assess the risks to other soil macroorganisms in its assessment and did not look at the field study for collembolans and soil mites that was considered by the EFSA. The EFSA conclusion provides reasonable grounds to believe that the environmental risks of mancozeb to soil macroorganisms are unacceptable.

The EFSA tier 1 long-term risk assessment for grapevines and potatoes indicated a high risk to birds and mammals from both mancozeb and ETU. A comprehensive refined risk assessment considering specific focal species relevant for the representative uses was discussed at the experts' meeting. When considering all of the refinements, a high long-term risk was concluded for the majority of the specific focal species for birds and mammals for the representative uses to wheat, grapevines and potatoes. This conclusion is applicable to both mancozeb and metabolite ETU. This finding of the EFSA aligns with the previous findings of the PMRA in their 2013-2018 risk assessments inclusive of the 2020 final decision, which concluded that the acute and reproductive levels of concern were exceeded for all bird sizes and feeding guilds, and that for mammals the acute level of concern was exceeded for medium and large sized mammals and that the reproductive level of concern was exceeded for all size classes and feeding guilds.[93] The conclusion of the 2020 assessment was that the refined acute risk to birds and mammals existed for areas on and adjacent to fields where mancozeb is applied.

The PMRA did not have any evidence for the statement that "birds may avoid mancozeb treated food items". The PMRA simply critiqued but did not revise or further refine the risk assessment to mammals and birds, but nevertheless concluded – without any scientific basis in its own

[92] RVD2020-12 p.17
[93] RVD2020-12 p.18.

modeling – that "acute risks to birds and mammals "are not expected." Only a warning to users was provided as a mitigation measure. The standard in the Act of reasonable certainty that no harm would occur was not met. This gives rise to reasonable grounds to believe that the risks of mancozeb to the environment are unacceptable. Moreover, the PMRA has not assessed the risks of metabolites other than ETU for birds and mammals. The EFSA found that a risk assessment was not available to identify and assess the risk to birds and mammals from metabolites other than ETU. This gap in the data means that the PMRA cannot have reasonable certainty that no harm to the environment, specifically birds and mammals, will occur.

The EFSA concluded that there was a high chronic risk to fish from grape uses. It also concluded that there was a chronic risk to aquatic invertebrates. The EFSA reviewed information that the PMRA did not include in its 2018-2020 risk assessment process, such as the pulsed exposure fish early-life stages study and mesocosm studies.[94] The mitigation measure of a spray buffer zone used by the PMRA is not scientifically supported to mitigate the risks from runoff of mancozeb to freshwater invertebrates and fish from ground applications.

In summary, the outcome of the EFSA aquatic risk assessment for mancozeb was driven by the chronic risk to fish for which a high risk was concluded. While the 2013-2020 re-evaluation made similar findings, the PMRA did not evaluate the studies assessed by the EFSA and did not explain how the findings were consistent with the reasonable certainty of no harm standard in the PCPA, the PMRA also did not evaluate all of the evidence that was before the EFSA in its review and the PMRA should launch a special review to obtain the additional evidence considered by the EFSA regarding aquatic risks.

4) Estimates of occupational and bystander exposure exceed reference values.

The EFSA peer review concluded that operator exposure estimates exceed the acceptable occupational exposure limit (AOEL) even considering the highest level of personal protective equipment (PPE) for the use on potatoes, cereals, and grapevine. This finding aligns with the problems highlighted earlier in this submission about the use of extended REIs on grapes in the PMRA's 2020 re-evaluation and the limitations of knowledge about the effectiveness of PPE to protect workers.[95]

Considering the combined exposure to ETU and mancozeb the EFSA found that no representative products demonstrated exposure estimates below the acceptable occupational exposure limit (AOEL/AAOEL) for operator, worker, bystander and/or resident. The EFSA referred to this as a critical area of concern.

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[94] The predicted exposure profile for the representative use grapevines was not covered by the exposure in the refined pulsed exposure study; therefore, a high chronic risk to fish was concluded for all focus surface water scenarios for grapevines (refer to Appendix A of the EFSA review for details).
[95] https://www.sciencedirect.com/science/article/pii/S0925753519321381?via%3Dihub

The PMRA did not adequately assess the occupational exposure of mancozeb in the 2013-2018 re-evaluation. Specifically, the feasibility of the re-entry intervals and the exposure of non hand-labourers post and during application, as well as exposure to certified sprayers, was not evaluated. The PMRA had inadequate information on exposure to workers in high density orchards. The PMRA also did not evaluate all of the evidence that was before the EFSA in its review and the PMRA should launch a special review to obtain the additional evidence considered by the EFSA, to re-evaluate the REI finding of agronomic feasibility, and to assess the real-world effectiveness of PPE for protecting mixer/loader/applicators and others.[96] Without this information the PMRA does not have reasonable certainty that no harm will occur.

5) Other aspects of concern raised by the EFSA assessment which the PMRA should include in a special review.

The EFSA found that more investigations of the phototoxicity potential of mancozeb should be provided, considering the contradictory results in two valid *in vitro* studies and the absence of test at wavelengths (UVB) where mancozeb showed significant absorption (since there is no OECD test for UVB absorber). Phototoxicity was not addressed in the PMRA's 2020 risk assessment.

The EFSA assessed drinking water risks that the PMRA did not assess. Information on the risk to human or animal health through the consumption of drinking water containing *N*-chloro derivatives of hydantoin (e.g. 1,3-dichloro hydantoin) have the potential to be formed from the chlorination of surface water that might contain hydantoin was not available. It was identified that the drinking water treatment process of chlorination might produce 1,3-dichloro hydantoin when surface water is treated to produce drinking water. As the risk to human or animal health through the consumption of drinking water containing 1,3-dichloro hydantoin was not adequately addressed, this led to the EFSA risk assessment being not finalised. The PMRA should include drinking water risks from this metabolite of mancozeb in the special review. The PMRA does not have reasonable certainty that no harm will occur from this transformation product. Without this the PMRA has reasonable grounds to believe that the risks are unacceptable.

[96] https://www.sciencedirect.com/science/article/pii/S0925753519321381?via%3Dihub

Section 17(1) of the Act

The Minister has reasonable grounds to believe that the health and environmental risks of mancozeb are unacceptable based on the three previous re-evaluation decisions of the PMRA leading it to just this conclusion and the EFSA conclusion that the risks are unacceptable. In addition, there are several areas that the PMRA has reasonable grounds to believe that mancozeb risks are unacceptable based on newer literature.

For example:

The Minister has not addressed that absence of a threshold for the liver tumors identified in the 2020 final risk assessment, nor has the Minister considered the new mode of action study for ETU liver tumors.[97]

A 2023 study concluded that low level mancozeb exposure causes copper bioaccumulation in the renal cortex of rats, leading to tubular injury.[98] The researchers concluded that "[t]hese findings demonstrate that low-dose Mancozeb exposure is a potential risk for kidney injury due to copper overload and warrants further in vivo and human population-based investigations." The doses were only 100 mg/kg/day.

Another 2023 study found that exposure to Mancozeb presented side effects by changing the composition of the microbiota in rats, increasing bacterial diversity, reducing the interaction patterns of the microbial communities, and changing microbial metabolic pathways.[99] This effect was seen regardless of the doses used. The researchers noted that:

> Among the adverse effects that Mancozeb may cause, dysbiosis is of primary relevance for host health, but its clinical implications were not yet characterized. Dysbiosis is a condition in which the gut bacteria become imbalanced, leading to a wide range of diseases including inflammatory bowel disease (IBD), obesity, allergic disorders, Type 1 diabetes mellitus, autism, obesity, and colorectal cancer in both human and animal models (DeGruttola et al., 2016; Belizário and Faintuch, 2018). Several recent studies have shown that fungicides can disrupt the functioning of the gut microbiota, affecting its composition and diversity (Xu et al., 2014; Jin et al., 2017; Meng et al., 2019; Yuan et al., 2019; Kong et al., 2020; Meng et al., 2021). In addition, specific bacteria in the gut can regulate metabolites and metabolic pathways, further affecting the health of the host (Liu et al., 2017; Djekkoun et al., 2021). Overall, these studies indicate that the gut microbiota may be one of the primary targets of fungicide-induced toxicity and that changes in the

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[97] PRVD2020-12 p.35.
[98] Mumtaz Akhtar, Louis D. Trombetta, "Low level mancozeb exposure causes copper bioaccumulation in the renal cortex of rats leading to tubular injury," Environmental Toxicology and Pharmacology, Volume 100, 2023, https://doi.org/10.1016/j.etap.2023.104148. (https://www.sciencedirect.com/science/article/pii/S138266892300090X)
[99] Pezzini et al "Changes in the gut microbiota of rats after exposure to the fungicide Mancozeb" Toxicology and applied Pharmacology (May 2023) Vol 466 (1).

> gut microbiota may be used as early indicators for monitoring the health risk of the host exposed to fungicides.

Another 2023 study addressed mancozeb-induced cytotoxicity in human erythrocytes. It concluded that mancozeb induces oxidative stress in human erythrocytes, impairs the antioxidant defense system, oxidizes cellular components, that will adversely affect erythrocyte structure and function. This study noted that a growing body of evidence suggests that pervasive usage of mancozeb may harm human health, increasing the urgency with which we must investigate its toxicological effects.[100]

A 2021 study found that the pesticide mancozeb exerts higher cytotoxicity than its metabolite ETU by suppressing trophoblastic spheroid attachment onto endometrial epithelial cells at levels 100 times less than ETU. The study summarized the current literature on endocrine disruption from mancozeb as follows:

> Growing epidemiologic evidence indicates that Mancozeb may affect the reproductive system by impairing female fertility. Several studies reported that women exposed to Mancozeb were more likely to experience abnormal menstrual cycles and spontaneous abortions (Arbuckle et al., 2001, Garry et al., 2002, Farr et al., 2004). In line with this, some *in vivo* and *in vitro* studies revealed Mancozeb exposure disrupted the structure of human granulosa cells, decreased healthy follicles in rats, blocked ovulation by inhibiting luteinizing hormone (LH) secretion, reduced oocyte fertilization, declined progesterone synthesis in bovine luteal cells, and caused mouse fetal malformation (Bhaskar and Mohanty, 2014; Miranda-Contreras et al., 2005; Palmerini et al., 2018; Rossi et al., 2006a). In our previous work, Mancozeb was found to impair the embryo implantation, but no detail mechanism of Mancozeb on endometrial cells was described (Akthar et al., 2020).[101]

They concluded that "our study supports the notion that Mancozeb can reduce MUC1 and ITGB3 protein expression in endometrial cells, leading to a non-receptive condition resembling recurrent implantation failure in patients."

Additionally, a 2022 study assessed mancozeb exposure and oxidative damage in greenhouse farmers.[102] The study found that some workers had much higher exposure levels and that stricter

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[100] Quds et al "Mancozeb-induced cytotoxicity in human erythrocytes: enhanced generation of reactive species, hemoglobin oxidation, diminished antioxidant power, membrane damage and morphological changes." Pesticide Biochemistry and Physiology (June 2023) Vol 193. https://www.sciencedirect.com/science/article/abs/pii/S0048357523001189

[101] Wang et al "the fungicide mancozeb reduces spheroid attachment onto endometrial epithelial cells…" Ecotoxicology and environmental safety (Jan 2021) Vol 208. https://www.sciencedirect.com/science/article/pii/S0147651320314433

[102] Costa et al. "Assessment of mancozeb exposure, absorbed dose, and oxidative damage in greenhouse farmers" (2022) International Journal of Environmental Research and Public Health 19(17) https://www.mdpi.com/1660-4601/19/17/10486

control and more effective adherence to PPE and other safety operational procedures were needed.

These effects have not been previously assessed by the PMRA and require review.

The PMRA also lacks any reasonable monitoring of mancozeb (total dithiocarbamates) and ETU in drinking water and surface and groundwater sources in Canada. The PMRA has failed to ensure that registrants provide acceptable monitoring data. It is unacceptable that the PMRA changed key findings about cancer health risks based on confidential monitoring from the registrants, focused on 20-year-old US monitoring data.

In recent years, Brazilian legislation was adopted to allow a concentration of 8 µg/L of mancozeb in drinking water in Brazil. Researchers concluded on a study in zebrafish in 2023 that the concentration of manozeb allowed in drinking water is not safe for aquatic organisms.[103] Published research has identified that mancozeb use can lead to the accumulation of manganese and ETU in channel sediment and water, and that this can result in exceedances of threshold values for drinking water by nearly 140 times.[104]

The low levels at which mancozeb may cause environmental harm, coupled with the uncertainty in the PMRA's cancer risk assessment which was based on infrequent samples in the United States and no independent monitoring, and used a threshold value for liver tumors which does not exist also gives rise to reasonable grounds to believe that mancozeb may cause unacceptable risks.

The PMRA should study post-application risks to workers in high-density orchards as part of the special review since they cannot have reasonable certainty that no harm will occur to post application workers without this information.[105]

The PMRA should include up to date information on the potential for PPE to reduce applicator exposure and reduced post-applicator exposure using real-world data on PPE use.[106]

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[103] Leandro et al. "Permissible concentration of mancozeb in Brazilian drinking water elicits oxidative stress and bioenergetic impairments in embryonic zebrafish" (Sept 2023) Environmental Pollution vol 333 https://www.sciencedirect.com/science/article/abs/pii/S0269749123010151

[104] Melgar et al "Occurrence of pollutants in drainage channels after long-term application of mancozeb to banana plantations in SE Mexico" (Aug 2008) Journal of Plant nutrition and Soil Scoemce 171(4):597 https://onlinelibrary.wiley.com/doi/abs/10.1002/jpln.200700171

[105] RVD2020-12 p.50-51.

[106] RVD2020-12 p.48-49 specifically highlighted the lack of adequate data for glove wearing.

Submissions on the *Pest Control Products Act*

Recently we requested that the PMRA update its 2023 workplan; the PMRA did so. In reviewing the workplan we asked why mancozeb was not included since the European Union submitted a Rotterdam notification for mancozeb in December 2022. The PMRA responded as follows:

> PMRA uses a systematic approach to special reviews, starting with a preliminary analysis. A detailed overview of all steps, including the preliminary analysis is outlined in *PMRA Guidance Document, Approach to Special Reviews of Pesticides*. The PMRA is aware of the EU decision for mancozeb and consequently, a preliminary analysis is currently under way. Upon completion of the preliminary analysis, a decision on whether a special review is warranted and initiated will be made public, as per the requirements of the PCPA.

It is our submission that the PMRA has no discretion under section 17(2) to determine "whether a special review is warranted." The provisions of this section are mandatory based on the ban in the European Union, something that was confirmed by the Federal Court in *Équiterre v. Canada (Health)*, 2016 FC 554. Recent amendments to the *Pest Control Products Act* do not permit the PMRA to avoid a special review of mancozeb given that the previous re-evaluation did not address the aspects of concern identified in the European Union ban, which took place after the 2020 re-evaluation decision. Even if the Minister finds that some aspects of the European Union ban were addressed in the 2020 re-evaluation decision, the requirements of subsection 17.1(2) of the *Pest Control Products Act* are conjunctive – namely the minister must also find that there is no additional information in relation to the health or the environmental risks of mancozeb or any of its end-use products that provides the minister with reasonable grounds to believe that the risks may be unacceptable. As the PMRA did not assess the information that was before the EFSA in December of 2020 on critical issues of concern the criteria in subsection17.1(2) are not met.

In this case, reasonable grounds are clearly present based on the 2013-2018 risk assessment conclusions of the PMRA alone. It is clear that the PMRA revised the mancozeb risk assessment in response to complaints by user groups – not based on scientific considerations. While some minor scientific points of analysis were updated, the PMRA merely changed its conclusions without updating the science on most issues, inclusive of issues that led to the ban in the European Union.

A reasonable interpretation of subsection 17.1(2)(b) must interpret the phrase "aspect of concern" to refer to the actual scientific information considered by the other OECD regulator, in this case the European Union. This means that if the PMRA is aware of scientific information considered by the European Union that led to the ban of mancozeb there, and which the PMRA did not consider, inclusive of the EFSA risk assessment and December 2020 EFSA peer review documentation, the PMRA does not have discretion to refuse to initiate a special review of mancozeb products. A broader interpretation of this discretion would not be reasonable given that such information can also result in reasonable grounds to believe that the product results in unacceptable risk. Any interpretation of the discretion in subsection 17.1(2) must accord with the

primary purpose of the Act to prevent unacceptable risks, the purpose of section 17 as a whole, to ensure that new information about risks is considered, and the ancillary purposes of the Act including transparency and public participation. Given the stark reversal between the 2018 and the 2013 decisions and the 2020 final re-evaluation, and the fact that the public was never consulted on the new conclusions in the 2020 final decision – a special review is clearly warranted. A special review is also warranted because the PMRA never implemented the 2020 risk assessment decision and never imposed the required mitigation measures.

Consistent with the purposes of the Act, the threshold for reasonable grounds to believe that risks may be unacceptable must be a low one and does not require any new evidence. This was confirmed by the Federal Court in *Wier v. Canada (Health)*, 2011 FC 1322 which held at para 88 that evidence supporting a special review request does not need to be "significant" or "new" evidence. Further, the court held at para 101 that where there are opinions within the regulatory agency on both sides of a question of whether a product poses a risk, the precautionary principle requires that the Minister initiate a special review. Opinions on both sides are clearly present given the previous final June 2018 decision and other decisions of the PMRA regarding this active ingredient. The fundamental standard in the Act of reasonable certainty that no harm will occur means that the Minister will have reasonable grounds to believe that the risks are unacceptable for the purpose of section 17(1) whenever the Minister has reasonable grounds to believe that reasonable certainty is lost. Accordingly, risks may be unacceptable due to uncertainties or methodological issues that have not been addressed in a previous assessment, as is the case here.

The primary purpose of the *Pest Control Products Act* is to prevent unacceptable risks, and acceptable risks are defined as reasonable certainty that no harm will occur to human health or the environment. It is obvious that the PMRA lacks reasonable certainty based on the low-quality monitoring data for human cancer risks, the failure to consider biomonitoring data that contradicts the cancer assessment, the alarming findings and lack of mitigation measures in the environmental risk assessment in addition to new peer-reviewed and published scientific literature on risks of metal accumulation, oxidative stress, and changes to the microbiome.

A new special review is also warranted because the PMRA failed to consult the public on the revisions to the 2018 re-evaluation decision. While a new 2018 proposed re-evaluation was published, this merely proposed the same thing that was decided in 2018. There was no public consultation on the significant revisions to the risk assessment that led to the 2020 re-evaluation decision. This is alarming because the initial 2018 re-evaluation was reversed on the basis that the public consultation was flawed from the perspective of users and registrants. Why this same courtesy was not granted to the public prior to the publication of the 2020 final re-evaluation decision is not clear.

The public never had an opportunity to comment on the revisions to the revised exposure estimates from the American water monitoring provided by registrants. This information is still protected as confidential data and there is no readily available description of the data or why it was considered reliable. When the PMRA engages in material changes to the risk assessment as

a result of public consultation – changes that alter the ultimate conclusion of the risk assessment – the PMRA should publish an update an provide the public with an opportunity to comment on those changes and the new revised proposal before making a final decision. The PMRA did not do this with mancozeb, but instead altered the risk assessment and made a final decision with no public consultation on those changes. While this does not directly engage with the question of acceptable risk, the Minister must assess whether there is reasonable certainty consistent with and in furtherance of the ancillary objective of the Act set out in section 4(2)(c) which is to encourage public awareness in relation to pest control products by informing the public, facilitating public access to relevant information and public participation in the decision-making process.

Conclusion

Aspects of concern that should be included within the special review

All of the aspects of concern identified above in the European Union review by the EFSA should be included in the scope of the special review. Additionally, the PMRA should include metal accumulation, new research on oxidative stress and reproductive harms such as failed implantation and potential harm to aquatic organisms along with all of the other risks and uncertainties identified above within the scope of the special review. The PMRA should incorporate up-to-date human studies of worker exposure to mancozeb and published research on potential accumulation of ETU and manganese in sediments and include all relevant drinking water metabolites. The PMRA needs to re-assess the occupational risks and risks from drinking water exposure, particularly cancer risks and re-assess whether it should eliminate the threshold approach to cancer risks in light of the high levels found in Canadian biomonitoring. These aspects, along with other aspects listed in the text of this request, should be included.

It is our position that the Minister does not have jurisdiction to renew any products containing mancozeb in light of the reasonable scientific uncertainty raised by the above submissions and we request confirmation that the products will not be renewed by the PMRA until the PMRA can confirm, utilizing current science, that there is reasonable certainty that no harm will occur. Additionally, we note that the PMRA lacks jurisdiction to renew products unless the labels have been amended in accordance with the 2020 re-evaluation decision since it has found that the previous label conditions presented unacceptable risks. Any labels must be immediately amended, and where the label amendment conditions of the 2020 re-evaluation have not been complied with the PMRA should immediately cancel the registrations under section 25 of the Act.

We remind the Minister of the statutory obligation in subsection 17(5) of the Act to respond to this request "within a reasonable time." This is a legal requirement that supersedes any service standards or guidance of the PMRA. That the time must be "reasonable" is not a *carte blanche* to delay the review of the application. We ask that you confirm **forthwith** that a review team has been assigned to this request. As the purpose of the review is limited to determining whether a special review is itself warranted, this review would in our view be unreasonably delayed if it exceeds six months. If the review of a special review request requires more than six months to complete, it is our position that the PMRA is at that point doing the substantive work that the legislature intended to be the substance of a special review. In that instance, the special review is clearly warranted and should be granted so that it follows the proper process set out in the Act including the transparency requirements of the Act.

Sincerely,

Jane McArthur, Toxics Program Director, Canadian Association of Physicians for the Environment (CAPE)

Lisa Gue, National Policy Manager, David Suzuki Foundation

Laura Bowman, Staff Lawyer Ecojustice

Cassie Barker, Toxics Senior Program Manager,
Environmental Defence

Beatrice Olivastri, CEO, Friends of the Earth Canada

Meg Sears PhD, Chair, Prevent Cancer Now

Mary Lou McDonald, LL.B., President, SafeFoodMatters.org

Appendix I – organizations submitting this letter

The **Canadian Association of Physicians for the Environment** (CAPE) is a national physician-led organization working to better human health by protecting the planet. CAPE collaborates with other organizations, nationally and internationally, to work effectively and build power together. We support physicians to be advocates for healthier environments and ecosystems. We take action to enable health for all by engaging with governments, running campaigns, conducting research, and drawing media attention to key issues.

The **David Suzuki Foundation** is a leading Canadian environmental non-profit organization, founded in 1990, with offices in Vancouver, Toronto and Montreal. We collaborate to find solutions to create a sustainable Canada through scientific research, traditional ecological knowledge, communications and public engagement, and innovative policy and legal solutions. Our mission is to protect nature's diversity and the well-being of all life, now and for the future.

Ecojustice uses the power of the law to defend nature, combat climate change, and fight for a healthy environment. Its strategic, public interest lawsuits and advocacy lead to precedent-setting court decisions and law and policy that deliver lasting solutions to Canada's most urgent environmental problems. As Canada's largest environmental law charity, Ecojustice operates offices in Vancouver, Calgary, Toronto, Ottawa, and Halifax.

Environmental Defence is a leading Canadian advocacy organization that works with government, industry and individuals to defend clean water, a safe climate and healthy communities.

Friends of the Earth Canada is the Canadian member of Friends of the Earth International, the world's largest grassroots environmental network campaigning on today's most urgent environmental and social issues.

Prevent Cancer Now is Canada's science-based, public advocacy voice for primary cancer prevention. This involves making informed, least-toxic choices individually, and by regulators and governments, for healthy food, water and environments.

Safe Food Matters works in the regulatory and legal arenas to ensure our food is safe from harmful inputs like pesticides.

Appendix II

Table 1 – products containing mancozeb with full registration in Canada (Sept 2023)

REG NO.	PRODUCT NAME	EXPIRY DATE	MARKETING TYPE	Permitted use site categories
31181	AGROSOLAN LIQUID FUNGICIDE	12/31/2026	COMMERCIAL	Manufacturing uses only
29221	DITHANE DG 75 FUNGICIDE	11/19/2023	COMMERCIAL	4-forest and woodlots, 5-greenhouse food crops, 6-greenhouse non-food crops, 7-industrial oil seed & fibre crops, 27-ornamentals outdoor, 13-terrestrial feed crops, 14-terrestrial food crops
20552	DITHANE F-45 FUNGICIDE	11/19/2023	COMMERCIAL	5-greenhouse food crops, 7-industrial oil seed & fibre crops, 10-seed treatments food & feed, 13-terrestrial feed crops, 14-terrestrial food crops
20553	DITHANE RAINSHIELD FUNGICIDE	12/31/2028	COMMERCIAL	13-terrestrial feed crops, 14-terrestrial food crops
20734	DITHANE TECHNICAL FUNGICIDE	12/31/2025	TECHNICAL ACTIVE	Manufacturing uses only
26842	GAVEL DF FUNGICIDE	12/31/2026	COMMERCIAL	13-terrestrial feed crops, 14-terrestrial food crops
19788	MANCOZEB TECHNICAL FUNGICIDE	12/31/2026	TECHNICAL ACTIVE	Manufacturing uses only
33292	MANZATE DISPERSS	12/31/2026	COMMERCIAL	4-forest and woodlots, 5-greenhouse food crops, 6-greenhouse non-food crops, 7-industrial oil seed & fibre crops, 27-ornamentals outdoor, 13-terrestrial feed crops, 14-terrestrial food crops
33299	MANZATE MAX	12/31/2026	COMMERCIAL	4-forest and woodlots, 5-greenhouse food crops, 27-ornamentals outdoor, 13-terrestrial feed crops, 14-terrestrial food crops
28217	MANZATE PRO-STICK FUNGICIDE	12/31/2026	COMMERCIAL	4-forest and woodlots, 5-greenhouse food crops, 6-greenhouse non-food crops, 7-industrial oil seed & fibre

				crops, 27-ornamentals outdoor, 13-terrestrial feed crops, 14-terrestrial food crops
25397	PENNCOZEB 75DF FUNGICIDE	12/31/2027	COMMERCIAL	5-greenhouse food crops, 7-industrial oil seed & fibre crops, 13-terrestrial feed crops, 14-terrestrial food crops
30241	PENNCOZEB 75DF RAINCOAT FUNGICIDE	12/31/2023	COMMERCIAL	5-greenhouse food crops, 7-industrial oil seed & fibre crops, 13-terrestrial feed crops, 14-terrestrial food crops
25166	PENNCOZEB TECHNICAL FUNGICIDE	12/31/2023	TECHNICAL ACTIVE	4-forest and woodlots, 5-greenhouse food crops, 6-greenhouse non-food crops, 7-industrial oil seed & fibre crops, 27-ornamentals outdoor, 10-seed treatments food & feed, 13-terrestrial feed crops, 14-terrestrial food crops
28893	RIDOMIL GOLD MZ 68WG FUNGICIDE	12/31/2027	COMMERCIAL	13-terrestrial feed crops, 14-terrestrial food crops

Source: PMRA public registry ***https://pest-control.canada.ca/pesticide-registry/en/***

Appendix III – detailed use pattern for Dithane DG 75 Fungicide

Note – this does not include the changes required by RVD2020-12 to application rates, re-entry intervals or pre harvest intervals or the number of applications because the PMRA has failed to confirm that these label changes were made or update the label on the public registry to the current label requirements since making that decision.

Forest and woodlot:

Note: it was assumed these are woodlot uses since it was specified not to use for ornamentals

Use	Application method	Application rate	# of times per year	Time of year typically applied	Other notes
Arborvitae, Juniper, Douglas Fir	Spray by ground or aerial	2.75-3.5 kg per 1000 L water (per ha not specified on label)	Spray at 10-14 days intervals April to early June	April to early June to protect new growth	Not for use on ornamental trees or in ornamental nurseries.
Ash, Oak, Sycamore	Ground spray or aerial	2.75-35 kg per 1000 L water	Spray at 10-14 day intervals	Beginning just prior to bud burst and continue as long as wet weather persists in spring	Not for use on ornamental trees or in ornamental nurseries.
Pine	Ground spray or aerial	2.5 kg per 1000 L of water	Every 2-3 weeks	During July, August and September	Not for use on ornamental trees or in ornamental nurseries.

Greenhouse food crops:

Use	Application method	Application rate	# of times per year	Time of year	Restricted re-entry interval	Pre-harvest interval	Other notes

				typically applied			
Greenhouse tomatoes		2.4 kg/ha	Every 7 to 12 days to keep new growth covered		Use not removed from current label as required by RVD2020-12	7 days	

Greenhouse non-food crops:

Use	Application method	Application rate	# of times per year	Time of year typically applied	Restricted re-entry interval	Pre-harvest interval	Other notes
Greenhouse tobacco		50-100 g in 25 to 50 L of water per 100 square metres	2x per week until transplanting starting when plants are 1.5 cm "across"	seedlings	Use not removed from current label as required by RVD2020-12		

Outdoor ornamentals:

Note: it is not clear on the label whether they are outdoor or greenhouse – it was assumed that if greenhouse was not specifically mentioned it was not permitted.

Use	Application method	Application rate	# of times per year	Time of year typically applied	Restricted re-entry interval	Pre-harvest interval	Other notes
Hawthorn		2.75-3.5 kg in 1000 L water	Spray at 10-14 day intervals as required	beginning with bud burst in spring			

Holly		1.8 to 2.5 kg in 1000L water	Spray as required especially during wet season			Avoid applications close to harvest to avoid visible residues.	
Ivy		1.25 to 2.5 kg. in 1000 L water	Spray as required as required especially during the wet season				
Honeysuckle	Apply only as dilute foliar spray, ground application	Unclear	3 applications per year at 10-14 day intervals	At green tip to half inch green leaf			2kg per 1000 L of water.

Industrial oilseed & fibre crops:

Crop	Application method	Application rate	# of times per year	Time of year typically applied	Restricted re-entry interval	Pre-harvest interval	Other notes
Alfalfa grown for seed		1.46 kg/ha	Max 3, every 7-10 days	Prior to 50% bloom			Do not use for human or animal consumption Do not graze treated crop or cut for hay Do not use on alfalfa for human consumption do not use seed crop residue for animal consumption.

Terrestrial food and feed crops:

Note: label gives general instructions for spraying by ground or aerial application. Label does not specify spray method (eg. Nozzle) or whether aerial or ground for each

application. It is unclear which are food vs. feed crops and some (eg. Carrots) appear to be for cover-cropping only but it is not clear on the label.

Crop	Application method	Application rate	# of times per year	Time of year typically applied	Restricted re-entry interval	Pre-harvest interval	Other notes
Apple	Ground spray	6 kg/ha			Not yet amended to include as required by 2020 re-evaluation decision	45 days	Ground only tank mix with Vangard 75 WDG, Nustar with >70 day PHI
Carrots	ground spray	2.25 kg/ha	Unlimited, repeat at 7 to 10 day intervals	When disease is first reported in the area	Not yet amended to include as required by 2020 re-evaluation decision	7 days	"do not use treated crops for feed or food"
Celery	ground spray	2.25-3.25 kg/ha	Unlimited repeat at 3 to 5 days in bed and at 7 day intervals after plants set.	At emergence		14 days	Remove residues by stripping, trimming and washing.
Field cucumbers	Aerial or ground spray	2.25-3.25 kg/ha	Repeat at 5 to 7 day intervals as needed	When plants begin to vine	Not yet amended to include as required by 2020 re-evaluation decision	14 days	

ginseng		4.4 kg/ha		When disease first appears with five sprays at 2 week intervals	Not yet amended to include as required by 2020 re-evaluation decision	30 days	Do not feed treated ginseng roots or foliage to livestock
Onions (dry bulb)	ground spray	2.25-3.25 kg/ha	Repeat every 7 to 10 days.	When disease first reported in area	Not yet amended to include as required by 2020 re-evaluation decision	10 days (15 days for tank mix)	Do not use on green bunching onions Allowed in tank mix with rovral WP or Rovral WDG "as a preventative treatment" at same application rate beginning in mid-june or when conditions are favourable for disease infection.
Onions (dry bulb)	Granular-infurrow	4.4-8.8 kg/ha	One per year	At seeding time	Not yet amended to include as required by 2020 re-evaluation decision	100 days	Specific to control of onion smut
Potatoes	ground spray	1.1-2.24 kg/ha	Repeat at 7 to 10 day intervals	When plants 10-15 cm high	Not yet amended to include as required by 2020 re-	Day before harvest	During periods of wet weather spray may be reduced to 5-6 days. Tank mixes allowed with Kocide

					evaluation decision		2000 and Curzate 60 DF Fungicide
Field tomatoes	ground spray	1.75-3.25 kg/ha	Repeat every 7 to 10 days	When disease first reported in area	Not yet amended to include as required by 2020 re-evaluation decision	7 days	
Sugar beets	ground spray	2.25	Repeat every 7 to 10 days	When disease first threatens	Not yet amended to include as required by 2020 re-evaluation decision	21 days	Do not use treated tops for food or feed.
Wheat (all varieties including durum)	Aerial or ground spray	Early spray 1.1 kg/ha And/or Late spray 2.25 kg/ha	Do not make more than 2 applications per season	At specific early growth stages At later growth stages prior to flowering	Not yet amended to include as required by 2020 re-evaluation decision	40 days	For ground spray with flat fan nozzles, use 100 L water /ha at a pressure of 345kPa do not graze or cut for hay. Use 40 L water/ha for aerial applications
Lentils	Aerial or ground spray	2.25 kg/ha	Before bloom and at mid bloom 10-14 days later, third application 10-14 days	Before bloom when bud evident	Not yet amended to include as required by 2020 re-	35 days	For ground spray with flat fan nozzles, use 100 L water /ha at a pressure of 345kPa do not graze or cut for hay.

			later no more than 3 applications per season		evaluation decision		Use 40 L water/ha for aerial applications

Sprays
(Ground or aerial equipment) - Use Dithane DG 75 Fungicide at the rate shown; ensure good coverage by using 200-1000 L per ha for ground equipment and 50-80 L/ha for aircraft. A spreader-sticker may be used if needed. Coarse sprays are less likely to drift, therefore, avoid combinations of pressure and nozzle type that will result in fine particles (mist).

Aerial
Apply only at the rate recommended for aerial application on this label. Where no rate for aerial application appears for the specific use, this product cannot be applied by any type of aerial equipment. Apply only under conditions of good practice specific to aerial application as outlined in the National Aerial Pesticide Application Manual, developed by the Federal/Provincial/Territorial Committee on Pest Management and Pesticides.

Environmental, bystander precautions and other instructions
Do not apply to any body of water. Avoid drifting of spray onto any body of water or to other non-target areas. Specified buffer zones should be observed.
Apply only when meteorological conditions at the treatment site allow for complete and even crop coverage. Do not spray when the wind is blowing towards a nearby sensitive crop, garden, terrestrial habitat (such as shelterbelt) or aquatic habitat.

Mixer /loader requirements
Do not allow the pilot to mix chemicals to be loaded onto the aircraft.
Loading of premixed chemicals with a closed system is permitted
The field crew and the mixer/loaders must wear chemical resistant gloves, coveralls and goggles or face shield during mixing/loading, cleanup and repair.

All personnel on the job site must wash hands and face thoroughly before eating and drinking. Protective clothing, aircraft cockpit and vehicle cabs must be decontaminated regularly.