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February 23, 2009

Office of Pesticide Programs (OPP)
Regulatory Public Docket (7502P),
Environmental Protection Agency,
1200 Pennsylvania Ave., NW.,
Washington, DC 20460-0001

Re: Petition to Revoke all Tolerances and Cancel all Registrations for the Pesticide 2, 4-Dichlorophenoxyacetic Acid (2, 4-D); Docket Number: EPA-HQ-OPP-2008-0877

Dear Sir/Madam:

Thank you for the opportunity to comment on the petition to revoke all tolerances and cancel all registrations for the pesticide 2, 4-dichlorophenoxyacetic acid (2,4-D), filed November 6, 2008 by the Natural Resources Defense Council (NRDC). Beyond Pesticides would like to formally support the petition submitted by NRDC requesting the cancellation of all 2, 4-D product registrations and the revocation of all tolerances. Beyond Pesticides, and the 41 groups[1] that commented on the agency's Reregistration Eligibility Decision (RED) in 2004, believe that the environmental and human health risks associated with exposures to 2,4-D far outweigh any agricultural or economic benefit that its continued registration may provide, especially since more effective and least toxic alternatives are currently available. Even though the EPA concluded in its RED, published in 2005, that 2,4-D was eligible for reregistration and that levels of concern were not exceeded, significant risks to human health and exposure to 2, 4-D and its products continue to plague homeowners, their children and pets. These concerns are significant enough to warrant a finding of "unreasonable risks to human health and the environment," and the cancellation of 2,4-D's registration and tolerances.

[1] The signatory groups that have called for the phasing out of 2,4-D include Natural Resources Defense Council; TEDX, Inc. (The Endocrine Disruption Exchange); Pesticide Action Network North America; Northwest Coalition for Alternatives to Pesticides; Washington Toxics Coalition; Coalition for Health, Environment and Economic Rights; Cancer Prevention Coalition; The Breast Cancer Fund; Alliance for Healthy Homes; Farmworker Justice Fund, Inc.; Agricultural Resources Center; Institute for Agriculture and Trade Policy; Roseland Organic Farms; Safer Pest Control Project; Defenders of Wildlife; California Safe Schools; Advocates for Environmental Human Rights; Californians for Alternatives to Toxics; New York Public Interest Research Group; New Jersey Environmental Federation; Wyoming Outdoor Council; Alaska Community Action on Toxics; Ecology Center; Citizens' Environmental Coalition; Environmental Research Foundation; Clean Water Action; Toxics Action Center; Informed Choices; National Center for Environmental Health Strategies, Inc.; The Coalition for Alternatives to Pesticides; Texans for Alternatives to Pesticides; Jack B. Richman Environmental Coalition; Colorado Pesticide Network; Grassroots Coalition; Women's Voices for the Earth; Grassroots Environmental Education; No Spray Coalition, Nashville; Students for Bhopal; Citizens' Campaign for the Environment; Connecticut Coalition for Environmental Justice; and the Coalition for Environmentally Safe Communities.

Introduction

2,4-D is one of the most widely used herbicides for the control of broadleaf weeds for commercial agriculture and residential landscapes in the United States. According to the 2005 RED, 46 million pounds of 2,4-D are used annually, with 16 million pounds used on non-agricultural settings, such as golf courses, playing fields, rights-of-ways and residential lawns. 2,4-D is also relatively inexpensive compared to other pesticides on the market and many farmers claim that there is an economic benefit for having 2,4-D on the market. Its heavy use on a wide range of agricultural crops and on turf grass, as well as its high ability to leach through soil has lead 2,4-D to be one of the most frequently detected herbicides in surface and groundwater.[2]

The 2005 RED document approves the uses of 2,4-D and its amines, esters, salts and acid (2,4-D acid, 2,4-D sodium salt, 2,4-D diethyl amine, 2,4-D dimethylamine salt, 2,4-D isopropyl acid, 2,4-D triisopropyl acid, 2,4-D butoxyethyl ester, 2,4-D ethylhexyl ester, 2,4-D isopropyl ester).[3] The effects and toxicities of the salt and ester forms of 2,4-D are similar to those of the acid form; the acid and salt forms are placed in Toxicity Category I (severe eye irritants), and the other forms are listed in Toxicity Category III or IV. Various dietary and water (swimming) standards have been set for each of these forms of 2,4-D. 2,4-D is formulated in over 600 products[4] and in combination with other chemicals, such as dicamba, mecoprop and MCPA.

In previous comments submitted to EPA for the 2005 RED (EPA-HQ-OPP-2004-0167-0072), Beyond Pesticides cited various short-comings in the agency's risk assessment, including the underestimation of dermal absorption of 2,4-D especially in the presence of other agents, such as DEET and sunscreen, and that 2,4-D has also been found to be tracked indoors by humans and pets, where it can stay in the indoor environment on carpets for up to a year, [5] further exposing humans and pets to 2,4-D; removal of the ten-fold additional margin of safety under the Food Quality Protection Act (FQPA), which was instituted to protect children who are especially sensitive and vulnerable to pesticide exposure; failure to acknowledge information that indicates 2,4-D is mutagenic, genotoxic and has endocrine disruptive ability, as well as the failure to assess the combined effects of 2,4-D to other chemicals with which it is so commonly formulated. These deficiencies in the RED contribute to elevated hazards and unreasonable risks to human health and the environment.

I. 2,4-D is Dangerous to Humans And Animals

<u>2,4-D's Toxic Effects Underestimated by the EPA</u>

Our pervious comments have provided the agency with a host of resources illustrating 2,4-D's neurotoxic, mutagenic and genotoxic effects. These effects have been essentially

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[2] Cox, C. 2005. "2,4-D Herbicide Factsheet." *Journal of Pesticide Reform* 25(4): 10-15.

[3] U.S. EPA, 2005. *2,4-D RED Facts.* Office of Prevention, Pesticides and Toxic Substances, Washington DC.

[4] U.S. EPA. 2005. Reregistration Eligibility Decision for 2,4-*D*. Office of Prevention Pesticides and Toxic Substances

[5] Nishioka MG, Burkholder HM, Brinkman MC, Gordon SM. 1996. Measuring lawn transport of lawn applied herbicide acids from turf to home: Correlation of dislodgeable 2,4-D turf residues with carpets dust and carpet surface residues. *Environmental Sci and Tech*. 30:3313-3320.

underestimated by the agency. In sub-chronic laboratory studies, rats exposed to 2,4-D experienced decreases in red cell mass, decreases in ovary and testes weights, increases in liver, kidney, and thyroid weight.[6] A study by Oakes and Pollak (2000) found that 2,4-D is indeed cytotoxic and induces apoptosis via direct effect on mitochondrial membranes.[7] Changes to maternal behavior in rats, along with increased catecholamine levels and a drastic decrease in indolamine levels have also been observed.[8] The induction and frequency of A → G point mutations by 2,4-D (and dicamba) have also been reported. This type of point mutation is important as it is frequently associated with various types of cancer.[9] NRDC's petition, as well as our previous comments to the agency, provides a wealth of citations that the agency should consider. In fact, the scientific literature abounds with evidence detailing the effects of exposure to 2,4-D making it baffling as to why the agency has not taken action to remove this dangerous chemical from the consumer market.

2,4-D is Associated with Endocrine Disruption

Under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act (FQPA) of 1996, EPA must develop a screening program using appropriate validated test systems and other scientific information to assess substances that may have an effect in humans that is similar to effects produced by a naturally occurring estrogen, or other such endocrine effects. EPA has yet to finalize a screening program to assess endocrine disruption for pesticides. According to EPA's RED document, current data "demonstrate effects on the thyroid and gonads following exposure to 2,4-D, there is concern regarding its endocrine disruption potential." The document goes on to state that "there have been no studies on 2,4-D that specifically assess its endocrine disruption potential." However, as noted in the NRDC petition and in previous comments submitted by Beyond Pesticides, there is a wealth of relevant scientific information available indicating that 2,4-D has endocrine disrupting activity.

A study by Garry et al. found a direct correlation of urinary levels of 2,4-D with serum levels of luteinizing hormone (LH) and high testosterone levels at the time of highest exposure suggest a direct effect on hormonal levels by the chlorophenoxy herbicide. [10] LH, produced by the pituitary gland, stimulates the production of testosterone and helps regulate the menstrual cycle and ovulation. Fluctuations in these hormones may affect human fertility. Others found that abnormal sperm[11] and higher rates of birth defects[12] were observed in farmers with long-

[6] Charles, J.M., Cunny, H.C., Wilson, R.D., and Bus, J.S. 1996. Comparative Subchronic Studies on 2,4-Dichlorophenoxyacetic Acid, Amine, and Ester in Rats. *Fundamental and Applied Toxicology* 33, 161-165.

[7] Oakes, D.J., and Pollak, J.K. 2000 The in vitro evaluation of the toxicities of three related herbicide formulations containing ester derivatives of 2,4,5-T and 2,4-D using sub-mitochondrial particles. *Toxicology* 151, 1-9.

[8] Stürtz, N., Deis, R.P., Jahn, G.A., Duffard, R., and Evangelista de Duffard, A.M. 2008. Effect of 2,4-dichlorophenoxyacetic acid on rat maternal behavior. *Toxicology* 247, 73-79.

[9] Filkowski, J., Besplug, J., Burke, P., Kovalchuk, I., and Kovalchuk, O. 2003.Genotoxicity of 2,4-D and dicamba revealed by transgenic Arabidopsis thaliana plants harboring recombination and point mutation markers. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 542, 23-32.

[10] Garry, V.F., Tarone, R.E., Kirsch, I.R., Abdallah, J.M., Lombardi, D.P., Long, L.K., Burroughs, B.L., Barr, D.B., and Kesner, J.S. 2001. Biomarker correlations of urinary 2,4-D levels in foresters: genomic instability and endocrine disruption. *Environmental Health Perspectives* 109, 495-500.

[11] Lerda, D., and Rizzi, R. 1991. Study of Reproductive Function in Persons Occupationally Exposed to 2,4-Dichlorophenoxyacetic Acid (2,4-D). *Mutation Research* 262, 47-50.

time exposure to 2,4-D. Animal studies have also observed the hormone effects of 2,4-D exposure. Xie et al. (2005) observed estrogenic activity in rainbow trout[13] exposed to 2,4-D, while another study found the thyroid glands of laboratory rats were sensitive to 2,4-D as decreases in the thyroid gland transport and production functions, and impairment of hormone iodination in the thyroid were observed after acute exposure.[14] Other studies have found that 2,4-D promotes the proliferation of androgen-sensitive cells by acting synergistically with its main metabolite, 2,4-dichlorophenol (DCP), also known for its endocrine disrupting effects. [15,16]

While the agency recognizes 2,4-D's "endocrine disruption potential" and in light of these data and numerous others cited previously by Beyond Pesticides and NRDC, we urge the agency to adopt the precautionary principle to protect human and environmental health now. It has become clear, over the last 13 years, that EPA believes that it is satisfactory to simply wait for "additional screening and/or testing to better characterize effects related to endocrine disruption" while continuing to endanger human and environmental health. The agency has failed in its responsibilities to test chemicals for endocrine disruption and as such, the RED for 2,4-D violates FQPA. Accordingly, 2,4-D poses unreasonable risks to human health and the environment and must see its registration revoked.

2,4-D Is Dangerous To Residential Pets

Several scientific studies have been presented to the agency that point to 2,4-D's association with cancer, for example non-Hodgkin's lymphoma.[17,18] Nevertheless, the agency concluded that "the data are not sufficient to conclude that there is a cause and effect relationship between exposure to 2,4-D and non- Hodgkin's lymphoma."[19] 2,4-D was then classified as a Group D, not classifiable as to human carcinogenicity. Studies from the National Cancer Institute and other sources have reported an association between exposure to lawn chemicals, like 2,4-D, and adverse impacts in dogs. Reynolds et al. (1994) found that dogs living in and around residences with 2,4-D treated lawns absorb measurable amounts of the herbicide for

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[12] Garry, V.F., Schreinemachers, D., Harkins, M.E., and Griffith, J. 1996. Pesticide Appliers, Biocides, and Birth Defects in Rural Minnesota. *Environmental Health Perspectives* 104, 394-399.

[13] Xie, L.T., Thrippleton, K., Irwin, M.A., Siemering, G.S., Mekebri, A., Crane, D., Berry, K., and Schlenk, D. 2005. Evaluation of estrogenic activities of aquatic herbicides and surfactants using an rainbow trout vitellogenin assay. *Toxicol. Sci*. 87, 391-398.

[14] Malysheva, L.N., and Zhavoronkov, A.A. 1997. Morphological and histochemical changes in the thyroid gland after a single exposure to 2,4-DA herbicide. *Bull. Exp. Biol. Med.* 124, 1223-1224.

[15] Kim, H.-J., Park, Y.I., and Dong, M.S. 2005. Effects of 2,4-D and DCP on the DHT-Induced Androgenic Action in Human Prostate Cancer Cells. *Toxicological Sciences*. 88(1), 52–59 pp. 52-59.

[16] McKinlay, R., Plant, J.A., Bell, J.N.B., and Voulvoulis, N. 2008. Endocrine disrupting pesticides: Implications for risk assessment. *Environment International* 34, 168-183.

[17] Lennart Hardell, and Eriksson, M. (1999) A case-control study of non-Hodgkin lymphoma and exposure to pesticides. *Cancer* 85, 1353-1360.

[18] Ibrahim, M.A., Bond, G.G., Burke, T.A., Cole, P., Dost, F.N., Enterline, P.E., Gough, M., Greenberg, R.S., Halperin, W.E., McConnell, E., and et al.1991. Weight of the evidence on the human carcinogenicity of 2,4-D. *Environmental Health Perspectives* 96, 213-222.

[19] U.S. EPA. 2005. Reregistration Eligibility Decision for 2,4-D. Office of Prevention Pesticides and Toxic Substances. Washington DC

several days after application. Urine concentrations were higher and persisted longer than previous reports.[20]

Glickman et al. (2004) reported that exposure to lawns or gardens treated with phenoxy herbicides was associated with an increased risk of transitional cell carcinoma of the urinary bladder in Scottish Terriers, compared with exposure to untreated lawns or gardens.[21] Several studies have found an association with 2,4-D exposure with canine malignant lymphoma.[22,23, 24] EPA must consider the effects on dogs exposed to 2,4-D from treated residential lawns and eliminate residential uses of 2,4-D.

II. EPA Endangers Children by Removing the FQPA 10X Safety Factor

According to the 2005 RED document, EPA "removed the default 10-fold FQPA special safety factor" citing "the agency has no residual concerns for the effects seen in the developmental toxicity studies." This conclusion is erroneous in light of the science. The purpose of the FQPA 10-fold margin of safety is to "to protect infants and children, taking into account the potential for pre- and post-natal toxicity." 21 USC §346a(b)(2)(C) It is known that children face unique hazards from pesticide exposure. Their developing organ systems, both pre-natal and post-natal, make them more sensitive to toxic exposure. The body of evidence in the scientific literature shows that pesticide exposure can adversely affect a child's neurological, respiratory, immune, and endocrine system, even at low levels. As mentioned in previous comments to the agency, there are several data gaps and toxicity concerns that warrant the 10X safety factor. According to the agency, "There is a concern for developmental neurotoxicity resulting from exposure to 2,4-D. There is evidence of neurotoxicity, including clinical signs such as ataxia and decreased motor activity in pregnant rabbits. . .[T]here is also evidence of developmental toxicity." These observations, by the agency's own admission, mean that there are indeed "residual concerns" that make it critical that the 10X factor is applied across the board to ensure that children are better protected from the impacts of 2,4-D.

The agency is well aware that data on endocrine disruption is extremely critical to children's health. Several of the body's hormones are essential for proper fetal neurological development (eg. the thyroid hormone), failure of which results in lasting effects on learning and developmental behavior. As a result of the evidence against 2,4-D for endocrine disruption and the agency's failure to screen chemicals for endocrine disruption in a timely manner, the 10X

[20]Reynolds, P.M., Reif, J.S., Ramsdell, H.S., and Tessari, J.D. 1994. Canine exposure to herbicide-treated lawns and urinary excretion of 2,4-dichlorophenoxyacetic acid. *Cancer Epidemiology, Biomarkers & Prevention* 3, 233-237.

[21] Glickman, L.T., Raghavan, M., Knapp, D.W., Bonney, P.L., and Dawson, M.H. 2004. Herbicide exposure and the risk of transitional cell carcinoma of the urinary bladder in Scottish Terriers. *Journal of the American Veterinary Medical Association* 224, 1290-1297.

[22] Hayes, H.M., Tarone, R.E., Cantor, K.P., Jessen, C.R., McCurnin, D.M., and Richardson, R.C. 1991. Case-Control Study of Canine Malignant Lymphoma: Positive Association With Dog Owner's Use of 2, 4-Dichlorophenoxyacetic Acid Herbicides. *J. National Cancer Institute, 83:17*pp. 1226-1231.

[23] Hayes, H.M., Tarone, R.E., and Cantor, K.P. 1995. On the Association between Canine Malignant Lymphoma and Opportunity for Exposure to 2,4-Dichlorophenoxyacetic Acid. *Environmental Research* 70, 119-125.

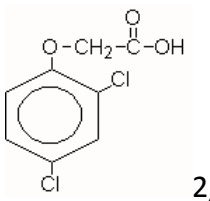
[24]INCHEM. Environmental Health Criteria For 2,4-Dichlorophenoxyacetic Acid. World Health Orgnization, Geneva.

safety factor must be upheld to protect infants and children from the hormone disrupting activity of 2,4-D across the board.

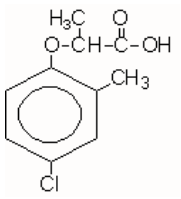
III. 2,4-D is Formulated with Multiple Chemicals Whose Combined Effects Are Not Assessed.

A look at active 2,4-D registered products compiled in the National Pesticide Information Retrieval System (NPIRS)[25]reveals that the majority of products containing 2,4-D also contain other active ingredients. In fact, out of approximately 90 2,4-D products found on NPIRS' database, only 23 contain 2,4-D as the sole active ingredient. The most prevalent combination found was 2,4-D, dicamba and mecoprop-p (MCPP), with over 30 products containing this specific chemical combination. Other combinations observed were 2,4-D and dicamba; 2,4-D and MCPP and 2,4-D and other chemicals, including glyphosate. Since 2,4-D is commonly formulated in combination with other active chemical ingredients, EPA must assess whether 2,4-D in combination with other chemicals, has a different mechanism or level of toxicity.

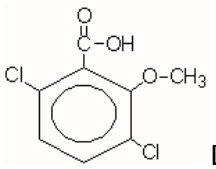
FQPA requires that, when considering whether to establish, modify, or revoke a tolerance, the agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."[26] According to the classification of herbicide modes of action compiled by Weed Science Society of America (WSSA) and the Herbicide Resistance Action Committee (HRAC)- an international body founded by the agrochemical industry- 2,4-D, dicamba and MCPP are classified as growth regulators or synthetic auxins that act like indole acetic acid, (WSSA Group 4; HRAC Group O).[27] Both 2,4-D and MCPP belong to the phenoxy acid chemical family, while dicamba belongs to the similar benzoic acid chemical family. The chemical structures of these chemicals are also similar. Their chemical structures[28] are shown below:



2,4-D



MCPP



Dicamba

According to EPA's "Assessing Pesticide Cumulative Risk" found at http://www.epa.gov/pesticides/cumulative/ as referenced in the RED, common mechanism of toxicity is defined as " two or more chemicals or other substances that cause a common toxic

[25] US EPA/OPP. 1998-2009. The National Pesticide Information Retrieval System (NPIRS). Purdue Research Foundation.

[26] US EPA. 2005. Reregistration Eligibility Decision for 2,4-D. Office of Prevention Pesticides and Toxic Substances, Washington DC.

[27] The Herbicide Resistance Action Committee (HRAC). 2005. Classification of Herbicides According to Mode of Action. http://www.hracglobal.com/Publications/ClassificationofHerbicideModeofAction/tabid/222/Default.aspx

[28] WSSA. 2007. Herbicides: Chemical Structures. Weed Science Society of America

effect(s) by the same, or essentially the same, sequence of major biochemical events (i.e., interpreted as mode of action)."[29]

Since it is known that 2,4-D, dicamba and MCPP have the same mode of action, being synthetic auxins that act like indole acetic acid (growth regulators), the agency has erred in failing to conduct a cumulative risk assessment for these mixtures of chemicals currently formulated together in the majority of 2,4-D end use products on the consumer market. As mentioned in our previous comments to the agency, there is considerable scientific evidence supporting the fact that chemicals with common toxicological modes of action, often predicted by structural similarities, usually have toxicity that is concentration additive.[30] In fact, according to Calamari and Vighi (1992), an additive (cumulative) effect of toxicants in a mixture is likely to be observed when the mode of action of each toxicant is qualitatively identical.[31] Given the apparent structural and mode of action similarities between these chemicals, and given their impacts - which range from reproductive and neurotoxic effects, to surface and ground water contamination, as well as toxicity to various aquatic species - EPA's oversight in conducting the proper cumulative assessment means that the millions of consumers using these products are being directly exposed to toxic mixtures of chemicals that have not been assessed for health and environmental impacts. As a result, 2,4-D and its products should be removed from the marketplace, since there is no "reasonable certainty" of no harm.

IV. Alternatives to 2,4-D Are Available

The reliance on 2,4-D in agricultural and lawn and landscape management is outdated and unnecessary. This further supports the view that the hazards of 2,4-D and deficiencies in the RED make the continued use of 2,4-D unreasonable. It is well known that herbicide-intensive approaches to agricultural production can be replaced by organic production methods that incorporate intercropping, ridge till and mulching systems that eliminate the need for herbicides, improve soil health and productivity, reduces greenhouse gases by sequestering at least two to four times as much atmospheric carbon and reduces fossil fuel use.[32] Similarly, organic lawn management practices eliminate the need for 2,4-D with proper dethatching, aeration, compost fertilization, seed varieties, and adequate watering.[33]

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[29] US EPA. 2008. Assessing Pesticide Cumulative Risk In: Pesticides: Health and Safety. Office of Prevention Pesticides and Toxic Substances Washington DC.

[30] Vighi, M., Altenburger, R., Arrhenius, Å., Backhaus, T., Bödeker, W., Blanck, H., Consolaro, F., Faust, M., Finizio, A., Froehner, K., Gramatica, P., Grimme, L.H., Grönvall, F., Hamer, V., Scholze, M., and Walter, H. 2003. Water quality objectives for mixtures of toxic chemicals: problems and perspectives. *Ecotoxicology and Environmental Safety* 54, 139-150.

[31] Calamari, D., and Vighi, M. 1992. A proposal to define quality objectives for aquatic life for mixtures of chemical substances. *Chemosphere* 25, 531-542.

[32] La Salle, T. and Hepperly, P. 2008. Regenerative 21st Century Farming: A Solution to Global Warming. The Rodale Institute; Hepperly, P. 2007. The Organic Farming Response to Climate Change. The Rodale Institute; Rodale Institute. Farming Systems Trial (FST)

[33] Sachs, P.D. (1996) Handbook of Successful Ecological Lawn Care. Edaphic Press.

Conclusion

Despite the reregistration of 2,4-D as given by the publication of the RED document in 2005, the risk assessment conducted by the EPA is flawed and littered with several deficiencies. These include and are not limited to the disregard of scientific information illustrating that 2,4-D has endocrine disruptive activities and other toxic effects that directly endanger human and animal health; the illegal removal of the 10X safety factor that must be utilized in order the protect vulnerable children; and the failure to conduct cumulative assessments despite evidence which shows that 2,4-D has a common mechanism of toxicity with other chemicals with which it is commonly formulated.

Many arguments will be made that 2,4-D is a valuable herbicidal chemical in the agricultural sector. 2,4-D is cheaper than other chemicals and provides an economic benefit to many farmers. However, based on current science and the deficiencies in EPA's reregistration of 2,4-D, the risks posed by 2,4-D to public health and the environment far outweighs any short-term economic benefit that 2,4-D may provide. Conversely, there are safer alternatives for lawn care and agriculture that have proven effective at controlling weeds, provide long term economic benefit and environmental sustainability. These include organic and sound IPM practices.
It is time the agency put science and the health of the public and the environment first! Beyond Pesticides fully supports the petition submitted by NRDC to cancel the registration of 2,4-D and the revocation of its tolerances.

Thank you for your attention to our comments.

Respectfully,

Nichelle Harriott
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Beyond Pesticides