PETITION TO BAN ENDOSULFAN AND REVOKE ALL TOLERANCES AND COMMENTS ON THE ENDOSULFAN UPDATED RISK ASSESSMENT (OPP-2002-0262-0067) BY THE NATURAL RESOURCES DEFENSE COUNCIL

Docket ID: EPA-HQ-OPP-2002-0262

February 19, 2008

The Natural Resources Defense Council (NRDC) submits this petition and these comments on behalf of our 1.2 million members and online activists. NRDC advocates for disclosure of information, regard for scientific inquiry and facts, justice for disempowered people, honesty by government, and corporate accountability. We seek to establish sustainability and good stewardship of the Earth as central ethical imperatives of human society (www.nrdc.org)

Federal Register: November 16, 2007, Volume 72, Number 221, Page 64624-64626. This notice announces the availability of EPA's updated human health and ecological effects risk assessments for the organochlorine pesticide endosulfan, based in part on data recently submitted by endosulfan registrants as required in the 2002 Reregistration eligibility Decision (RED). The Agency is seeking comment on these updated risk assessments as part of EPA's Post-RED process regarding endosulfan. In addition, this notice solicits public comment on EPA's analysis of endosulfan usage information since the 2002 RED, and its preliminary determinations regarding endosulfan's importance to growers and availability of alternatives.[1]

The comment period is extended to February 19, 2008 (FR Jan 2, 2008, Vol 73, No 1, Page 186-187

[1] http://www.epa.gov/fedrgstr/EPA-PEST/2007/November/Day-16/p22385.htm
http://www.epa.gov/fedrgstr/EPA-PEST/2008/January/Day-02/p25277.htm

EPA's FR Notice of its Endosulfan Updated Risk Assessment (HQ-OPP-2002-0262-0067; FR Vol 72, No 221, Nov 16, 2007. p. 64624) documents the following findings and outstanding concerns with endosulfan risks:

> "EPA's updated assessment of the potential human health effects of endosulfan is based on the review of a recently submitted developmental neurotoxicity (DNT) study [HQ-OPP-2002-0262-0058.1], which was required in the reregistration eligibility decision for endosulfan. Based on the toxicological effects observed in the DNT, the Agency selected a different endpoint than used in the 2002 RED assessment to evaluate short- and intermediate-term dermal exposure for occupational handlers. Using the revised dermal endpoint, many of the occupational handler scenarios exceed the Agency's level of concern even with maximum Personal Protective Equipment (PPE) and engineering controls. In addition, for many of the occupational post-application scenarios, the restricted-entry interval (REI) would be several to multiple days longer than the REIs required in the 2002 RED. In addition, EPA has updated the ecological effects assessment for endosulfan based on studies required in the 2002 RED and on additional information drawn from the published literature on endosulfan bioaccumulation, monitoring and transport, and ecological incidence. In general, although preliminary, the new information suggests that parent endosulfan and its sulfate degradate may pose greater risks than the 2002 RED outlined. While the parent may readily undergo degradation under some environmental conditions, the sulfate degradate is persistent and represents a source for endosulfan to enter aquatic and terrestrial food chains. While endosulfan is not expected to biomagnify appreciably in aquatic food webs, the compound does bioconcentrate in aquatic organisms to a significant extent. Also, there is direct evidence (measured residues) that endosulfan bioaccumulates in terrestrial systems and indirect evidence (modeling) that endosulfan has a significant potential to biomagnify in certain terrestrial food webs. In addition, EPA continues to be concerned about endosulfan's volatility and its ability to migrate to sites distant from use areas, such as the Arctic, through various environmental media (air, water, and sediment)." (underlining added for emphasis; FR Notice HQ-OPP-2002-0262-0067).

NRDC Petitions EPA to cancel all registrations of endosulfan and to revoke all tolerances of endosulfan

In our comments on the 2002 RED for Endosulfan, NRDC and World Wildlife Fund asked for cancellation of endosulfan and revocation of all tolerances, because of its persistent, bioaccumulative, and highly toxic nature, and because of the 2002 EPA assessment that there are no or very few benefits for endosulfan uses.[2] Since that time, even more evidence has accumulated supporting our original request. Pursuant to the Administrative Procedure Act, 5 U.S.C. § 551 et seq and 21 U.S.C. § 346a(d), NRDC petitions EPA to cancel all registrations for endosulfan and revoke all tolerances, based

[2] NRDC comments on Endosulfan Reregistration Elegibility Decision. J Sass, G Solomon, T Colborn. Jan 13, 2003. OPP-2002-0262

on evidence summarized in these comments, the arguments made in our earlier comments on the 2002 RED, and the findings and conclusions of the 2007 updated assessment by EPA.

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. §§ 136, et seq, and the Federal Food Drug and Cosmetics Act (FFDCA), 21 U.S.C. § 346a govern how EPA regulates pesticides. Under FIFRA, EPA may not register a pesticide unless the chemical will perform its intended function without causing any "unreasonable adverse effects on the environment." *Id.,* § 136a(c)(5)(C). This effect is defined as "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide." *Id.*, §136(bb).

Under FFDCA, as amended by the Food Quality Protection Act (FQPA), a pesticide may not be used on a particular food unless EPA has set a "tolerance" or a maximum allowable level or grants exemptions from the requirement to set a tolerance. 21 U.S.C. §§ 346a(b) & (c). EPA may "establish or leave in effect a tolerance for a pesticide chemical residue in or on food only if the Administrator determines that the tolerance is safe." *Id.* § 346a(b)(2)(A)(i). The term "safe" means that "there is a reasonable certainty of no harm will result from aggregate exposure" to the pesticide, "including all anticipated dietary exposures and all other exposures for which there is reliable information." *Id.*, § 346a(b)(2)(A)(ii).

To "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue" as required by the FQPA, the Agency must use an "additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure…for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children." 21 U.S.C. 346a(b)(2)(C).

Endosulfan use does not meet the FIFRA standard for safety

Endosulfan use should be cancelled, pursuant to the requirements established under FIFRA. On the one hand, it is a persistent and bioaccumulative toxin (PBT) that is both an endocrine disrupter and a neurotoxicant. On the other hand, its use accrues minimal benefits. Accordingly, it poses an unreasonable adverse effect on the environment and should be cancelled.

<u>Endosulfan is harmful to human health and the environment</u>

Endosulfan is an organochlorine insecticide, in the same general chemical class as DDT. About 1.4 million pounds of this chemical are used in the United States each year on a wide variety of crops. Endosulfan runs off agricultural fields in sediment and contaminates water bodies, where it begins to bioaccumulate in the food chain. Endosulfan (total toxic residues) is found in all environmental compartments: rain, fog, surface water, ground water, and soil. Atmospheric transport of endosulfan has resulted in contamination of sites distant from use areas. Endosulfan therefore presents a risk of

exposure to both urban and rural dwellers, and in areas both near and far from sites of application.

Endosulfan is persistent, bioaccumulative, an endocrine disruptor and a neurotoxicant. [3] EPA's own experts noted that it is expected to be more persistent than was indicated in the 2002 Ecological Risk Assessment, based on data submitted to the EPA on the major degradate of endosulfan, called endosulfan sulfate.[4] Whereas endosulfan parent compound has a half-life in soil of 57 and 208 days for the α and β endosulfan respectively, the half life of the endosulfan sulfate is 1336 days. The degradate is of similar toxicity to the parent compound. Because endosulfan and its major degradate are persistent and toxic, they can remain as hazardous waste in the environment for years or even decades after endosulfan is applied.

Residues of endosulfan are detected on a very wide array of food products, including apples, tomatoes, cucumbers, pickles, zucchini, green peppers, olives, raisins, cantaloupe, prunes, squash, potatoes, french fries, canned pears, spinach, green beans, and butter.[5]

Residues of endosulfan have been detected in multiple human tissues including blood, breast milk, and mammary adipose tissue.[6,7] Over half of women seen at an *in vitro* fertilization clinic seeking care for infertility had endosulfan in their serum.[8] Although the lack of a comparison population in this study makes it difficult to know whether there was an association between endosulfan and infertility, the high prevalence of exposure among women of reproductive age is of serious concern. Pre- and post-natal exposures to endosulfan have been confirmed by measures of residues in human breast milk, placenta, cord blood, and adipose tissue.[5,9,10] One study in Spain demonstrated a significant association between reported consumption of vegetables and residues of endosulfan in

[3] Addendum to the Ecological Risk Assessment of Endosulfan. October, 2007. Document ID No. EPA-HQ-OPP-2002-0262-0063

[4] *Id.* at 2.

[5] Food and Drug Administration. Total Diet Study: Summary of Residues Found Ordered by Pesticide Market Baskets 91-3 – 97-1, June 1999.

[6] Hernandez F, Pitarch E, Serrano R, Gaspar JV, Olea N. Multiresidue determination of endosulfan and metabolic derivatives in human adipose tissue using automated liquid chromatographic cleanup and gas chromatographic analysis. J Anal Toxicol. 2002 Mar;26(2):94-103.

[7] Cerrillo I, Granada A, Lopez-Espinosa MJ, Olmos B, Jimenez M, Cao A, Olea N, Olea-Seranno M. Endosulfan and its metabolites in fertile women, placenta, cord blood, and human milk. Environ Res. 2005 Jun; 98(2):233-9.

[8] Younglai EV, Foster WG, Hughes EG, Trim K, Jarrell JF. Levels of environmental contaminants in human follicular fluid, serum, and seminal plasma of couples undergoing in vitro fertilization. Arch Environ Contam Toxicol 2002 Jul;43(1):121-6.

[9] Campoy C, Jimenez M, Olea-Serrano MF, Moreno-Frias M, Canabate F, Olea N, Bayes R, Molina-Font JA. Analysis of organochlorine pesticides in human milk: preliminary results. Early Hum Dev. 2001 Nov;65 Suppl:S183-90.

[10] Shen H, Main KM, Andersson AM, Damgaard IN, Virtanen HE, Skakkebaek N, Toppari J, Schramm KW. Concentrations of persistent organochlorine compounds in human milk and placenta are higher in Denmark than in Finland. Hum Reprod. 2008 Jan;23(1):201-210.

breast milk of lactating women.[11] These results raise concerns because endosulfan is lipophilic, so when fat stores are metabolized (such as during pregnancy and lactation), the exposure to the developing child during a vulnerable period of development is expected to increase.

Endosulfan has a high bioaccumulative potential with octanol-water partition coefficients (Kow) of 55,500 and 61,400 for the two endosulfan isomers. Endosulfan bioconcentration factors in fish range from 2,400X to 11,000X. (RED p. 26). [12] As with other PBTs or POPs, endosulfan is semi-volatile, travels long distances on global air currents, and has been detected as a contaminant in areas such as the Arctic and high mountain areas, where it was never used.[13] Although levels of many of the organochlorines have declined in the Arctic, levels of endosulfan have actually increased over time.[14]

More telling, endosulfan demonstrates environmental fate and ecological effects similar to its chemical cousins, the cyclodiene-like pesticides. These chemical cousins have been either cancelled (toxaphene, mirex, kepone, dieldrin, aldrin, chlordane) or severely restricted (heptachlor) due to their hazardous nature.

The toxicity of endosulfan on the endocrine system is not included in the selection of toxicity endpoints

It is of serious concern that the toxic effects of endosulfan on the endocrine pathways are poorly evaluated in the 2002 RED. The determination of the toxicological endpoints for endosulfan does not consider the potential for long-term or permanent damage to the sensitive endocrine system. Toxicological endpoints used for risk assessment in the RED include convulsions in rats (acute dietary RfD), enlarged kidneys and glomerulonephrosis in rats (chronic dietary RfD), mortality (dermal toxicity), and decreased leukocyte counts and increased creatinine values (inhalation toxicity).[15] Moreover, chronic toxicity tests used in calculating chronic risk quotient (RQ) values to assess ecological damage are not sensitive to endocrine disrupting endpoints and the RQ values therefore likely underestimate the chronic hazard due to endosulfan.

In the 2002 RED, EPA had determined that endosulfan is a potential endocrine disruptor.[16] The Agency notes the following studies as supportive evidence that

[11] Campoy C, Olea-Serrano F, Jimenez M, Bayes R, Canabate F, Rosales MJ, Blanca E, Olea N. Diet and organochlorine contaminants in women of reproductive age under 40 years old. Early Hum Dev. 2001 Nov;65 Suppl:S173-82.
[12] U.S. EPA. Reregistration Eligibility Decision for Endosulfan. July 31, 2002.
[13] Carrera G, Fernandez P, Grimalt JO, Ventura M, Camarero L, Catalan J, Nickus U, Thies H, Psenner R. Atmospherc deposition of organochlorine compounds to remote high mountain lakes of Europe. Environ Sci Technol. 2002 Jun 15;36(12):2581-8.
[14] Hung H, Halsall CJ, Blanchard P, Li HH, Fellin P, Stern G, Rosenberg B. Temporal trends of organochlorine pesticides in the Canadian Arctic atmosphere. Environ Sci Technol. 2002 Mar 1;36(5):862-8.
[15] U.S. EPA. Reregistration Eligibility Decision for Endosulfan. July 31, 2002. page 15, 17
[16] U.S. EPA. Reregistration Eligibility Decision for Endosulfan. July 31, 2002.

endosulfan is an endocrine disruptor, despite the registrant's conclusions to the contrary:[17]

- "testicular atrophy was reported during a chronic oral toxicity study in rats" (MRID 00004256)
- "increased pituitary and uterine weights were also observed during a multi-generation reproduction study" (MRID 00148264)
- "an increase in the incidence of parathyroid hyperplasia was also reported during the chronic oral toxicity study in rats"
- "other organochlorines (i.e. DDT, DDE, dieldrin, and methoxychlor) have been demonstrated to interact with the endocrine system in spite of differing binding affinities to the estrogen receptor"

A review of the peer-reviewed literature demonstrates that endosulfan is both an endocrine disruptor and a neurotoxicant. In particular, this chemical has been demonstrated to increase the rate of testosterone breakdown and excretion, may decrease the rate of testosterone synthesis, and may affect sex-hormone binding globulin (SHBG) transport of androgens.[18] [19] [20] Numerous studies have consistently demonstrated that endosulfan behaves physiologically as an anti-androgen.[21] The effects of endosulfan are most pronounced in immature animals whose reproductive systems and brains are still developing. In immature (three-week-old) rats, endosulfan causes significant dose-related decreases in sperm counts, and sperm deformities at low exposure levels. The doses that cause these serious testicular adverse effects in immature animals are lower than doses causing effects in older (three-month-old) rats.[22] A National Cancer Institute study also showed testicular atrophy in rats, along with parathyroid hyperplasia.[23] In fish, endosulfan elevates levels of thyroxine and suppresses levels of triiodothyronine (T3), probably by inhibiting the conversion of thyroxine to T3.[24] There is also *in vitro* data reporting that endosulfan causes mast cell degranulation and enhanced immune molecule (IgE) releases, suggesting that it may promote allergic responses.

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[17] U.S. EPA. Endosulfan: evaluation of registrant submission *Endosulfan: Evaluation of possible endocrine effects in mammalian species.* December 11, 2000 MRID 44939102.

[18] Singh SK, Pandey RS. Gonadal toxicity of short term chronic endosulfan exposure to male rats. Indian J Exp Biol. 1989 Apr;27(4):341-6.

[19] Singh SK, Pandey RS. Differential effects of chronic endosulfan exposure to male rats in relation to hepatic drug metabolism and androgen biotransformation. Indian J Biochem Biophys. 1989 Aug;26(4):262-7.

[20] Singh SK, Pandey RS. Effect of sub-chronic endosulfan exposures on plasma gonadotrophins, testosterone, testicular testosterone and enzymes of androgen biosynthesis in rat. Indian J Exp Biol. 1990 Oct;28(10):953-6.

[21] Wilson V, LeBlanc GA. Endosulfan elevates testosterone biotransformation and clearance in CD-1 mice. Toxicol Appl Pharmacol 148:158-168, 1998.

[22] Sinha N, Narayan R, Saxena DK. Effect of endosulfan on the testis of growing rats. Bulletin Environ Contamination Toxicol 58:79-86, 1997. Sinha N, Narayan R, Shanker R, Saxena DK. Endosulfan-induced biochemical changes in the testis of rats. Veterinary and Human Toxicol 37:547-549, 1995.

[23] U.S. National Cancer Institute (1978) Bioassay of Endosulfan for Possible Carcinogenicity. By Division of Cancer Cause and Pre vention, Carcinogenesis Testing Program. Bethesda, Md.: U.S. Dept. of Health, Education, and Welfare. (DHEW publication no. (NIH) 78-1312.

[24] Sinha N, Lal B, Singh TP. Pesticides induced changes in circulating thyroid hormones in the freshwater catfish clarias batrachus. Comparative Biochem Physiol 100C: 107-110, 1991.

Several *in vitro* studies have also indicated that endosulfan has estrogenic and progesterone-mimicking effects.[25] In fact, in one study, endosulfan caused a 2000-fold increase in beta-galactosidase (beta-gal) activity in yeast transformed with the human estrogen receptor whereas estradiol increased beta-gal activity by 5000-fold, indicating that endosulfan was more than 1/3 as potent as estradiol in this assay.[26] Endosulfan also has been shown to activate estrogenic responses through a non-genomic pathway by activating membrane receptors in pituitary cells resulting in increased prolactin secretion.[27] In human cell lines, exposure to endosulfan caused changes in both ER-alpha and ER-beta mRNA steady state levels.[28]

In human studies, endosulfan has been associated with delayed puberty (referenced in Den Hond, 2006[29]). When considered as a part of mixture of total environmental estrogens, endosulfan and other endocrine active pesticides were associated with an increased risk of breast cancer in lean postmenopausal women.[30]

Endosulfan has numerous endocrine disrupting effects, including an anti-androgenic effect, an estrogenic effect, a progesterone-mimicking effect, and an anti-thyroid effect. This extensive evidence of endocrine, reproductive, and developmental toxicity was not adequately represented in the selected data that EPA relied upon for its risk assessment.

The 2002 and 2007 assessments are highly likely to underestimate risk to wildlife and human health through endocrine toxicity. The EFED has recommended that the EPA fully assess the toxicity of endosulfan related to its endocrine disruption activity, when such screening tests are approved.[31] We support this recommendation, and anticipate that such testing will reveal toxic effects on the reproductive capability and behavior of wildlife from current exposure levels, particularly to aquatic species. However, enough is known now to support the cancellation of endosulfan.

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[25] Vonier PM, Crain DA, McLachlan JA, Guillette LJ Jr, Arnold SF.Interaction of environmental chemicals with the estrogen and progesterone receptors from the oviduct of the American alligator. Environ Health Perspect. 1996 Dec;104(12):1318-22.

[26] Ramamoorthy K, Wang F, Chen IC, Norris JD, McDonnell DP, Leonard LS, Gaido KW, Bocchinfuso WP, Korach KS, Safe S.Estrogenic activity of a dieldrin/toxaphene mixture in the mouse uterus, MCF-7 human breast cancer cells, and yeast-based estrogen receptor assays: no apparent synergism. Endocrinology. 1997 Apr;138(4):1520-7.

[27] Watson CS, Bulayeva NN, Wozniak AL, Alyea RA. Xenoestrogens are potent activators of nongenomic estrogenic responses. Steroids. 2007 Feb;72(2):124-134.

[28] Gronfeld HT, Bonefeld-Jorgensen EC. Effect of in vitro estrogenic pesticides on human oestrogen receptor alphaand beta mRNA levels. Toxicol Lett. 2004 Aug;151(3):467-80.

[29] Den Hond E, Schoeters G. Endocrine disrupters and human puberty. Int J Androl. 2006 Feb;29(1):264-71; discussion 286-90.

[30] Ibarluzea Jm J, Fernandez MF, Santa-Marina L, Olea-Serrano MF, Rivas AM, Aurrekoetxea JJ, Exposito J, Lorenzo M, Torny P, Villalobos M, Pedraza V, Sasco AJ, Olea N. Breast cancer risk and the combined effect of environmental estrogens. Cancer Causes Control. 2004 Aug;15(6):591-600.

[31] U.S. EPA. Memorandum from Thurman et al to Stacey Milan. EFED risk assessment for the reregistration eligibility decision on endosulfan (Thiodan). April 13, 2001

Economic benefits of endosulfan justify neither registration nor retention of the tolerances

Contrary to EPA's conclusion that the economic benefits of endosulfan use justify the continued use of this toxic pesticide, [32] in reality, the economic benefits are minimal and are far outweighed by the adverse health and environmental impacts attributable to its use.

As noted earlier, under FIFRA, EPA must consider all the costs and benefits (including the environmental, social, and economic) before registering a pesticide for use. This balance of costs and benefits weighs heavily in favor of cancelling all uses of endosulfan. For food uses, FFDCA only allows the retention (or modification) of tolerances if either the pesticide "protects consumers from adverse effects on health that would pose a greater risk than the dietary risk from the residue" or the use of the pesticide "is necessary to avoid a *significant* disruption in domestic production of an adequate, wholesome, and economical food supply." 21 U.S.C. § 346a(b)(2)(B)(iii). Endosulfan use meets neither of these conditions, and therefore the tolerances should be revoked.

In the 2002 RED, the Environmental Fate and Effects Division staff (EFED) calculated that the use of endosulfan on Florida tomatoes (approximately 34,900 lbs active ingredient (a.i) annually), creates a 90% probability that 60% of aquatic species adjacent to treated fields will suffer a 50% mortality rate from typical use practices. In contrast, the benefits analysis revealed that cancellation of endosulfan for Florida tomatoes would incur a loss of only 0.02 to 0.7% of the total value of production.[33] However, rather than acknowledging that the benefits of endosulfan use are dwarfed by the severity of the predicted environmental harm, EPA registered this use (but reduced the tolerance from 2 ppm to 1.0 ppm). [34]

The impact on tobacco is similarly minimal. The 2002 RED reported that the total value of production of tobacco averages over $2 billion annually; while cancellation of endosulfan on tobacco crops would result in a net loss of less than 0.2% ($4 million) of the total value of production. The benefits analysis predicted that even if endosulfan were replaced with the most expensive alternative, imidacloprid (a neo-nicotinoid and reduced-risk alternative) there would be an estimated decline in net cash returns of only 1.8%.

For cotton, the crop where the most endosulfan is used,[35] cancellation would incur a negligible loss of only 0.1 to 2.4% ($216,000 to $3.8 million) of the total value of production. Despite this finding in the 2002 RED, to accommodate evidence of

[32] Endosulfan, fenarimol, imazalil, oryzalin, sodium actifluorfen, trifluralin, and ziram; Tolerance Actions. Federal Register: September 15, 2006 Volume 71, Number 179, Page 54423-54434. http://www.epa.gov/fedrgstr/EPA-PEST/2006/September/Day-15/p15258.htm

[33] U.S. EPA Biological and economic analysis of endosulfan benefits on selected crops: impacts of cancellation. July 12, 2002.

[34] Endosulfan, fenarimol, imazalil, oryzalin, sodium actifluorfen, trifluralin, and ziram; Tolerance Actions. Federal Register: September 15, 2006 Volume 71, Number 179, Page 54423-54434. http://www.epa.gov/fedrgstr/EPA-PEST/2006/September/Day-15/p15258.htm

[35] U.S. EPA Endosulfan RED. 2002. Page 52

endosulfan residues on cotton gin byproducts that show combined endosulfan residues of concern as high as 27.5 ppm, EPA is establishing a tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on cotton gin byproducts at 30.0 ppm. [36]

Use of endosulfan on broccoli is declining and is estimated to be only 2% of the total acreage. Yet, instead of canceling these meager uses of endosulfan, EPA is increasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on broccoli from 2.0 to 3.0 ppm.[37]

The EPA estimated that uses of endosulfan for cotton, tobacco, Florida tomatoes, New York wine grapes, and Georgia pecans, cumulatively accounts for over 40% of all endosulfan used in the U.S. [38] This report concludes that "[EPA] does not believe that the impacts of a cancellation of endosulfan on these crops would result in important impacts" and that "in all cases, alternatives exist that could effectively replace endosulfan, usually at fairly moderate increases in cost."[39] While the EPA has justifiably revoked all tolerances for grapes and pecans, EPA still allows the tolerances to remain for the other crops. [40]

Loss of tiny percentages of production is not a lawful basis under the FFDCA for retaining these unacceptably risky tolerances. Even absent the FFDCA's strictly health-based standard for tolerances, these tiny production losses cannot justify continued registration of endosulfan in light of its substantial health and environmental risks.

Endosulfan uses must be cancelled and tolerances revoked

The data on the toxicity, persistence, and bioaccumulative properties of endosulfan justify revocation of all tolerances and cancellation of all uses. This is particularly true in light of EPA's own assessment showing very few to no benefits for endosulfan uses.

Based upon the certainty of harm caused by endosulfan, the availability of alternatives, and the insignificant disruption in the food supply, all tolerances for endosulfan should be revoked under the FFDCA. In addition, the risks posed by endosulfan use are enormous, while there are few benefits and equally effective alternatives available, to justify cancellation of all uses.

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[36] Endosulfan, fenarimol, imazalil, oryzalin, sodium actifluorfen, trifluralin, and ziram; Tolerance Actions. Federal Register: September 15, 2006 Volume 71, Number 179, Page 54423-54434. http://www.epa.gov/fedrgstr/EPA-PEST/2006/September/Day-15/p15258.htm

[37] Endosulfan, fenarimol, imazalil, oryzalin, sodium actifluorfen, trifluralin, and ziram; Tolerance Actions. Federal Register: September 15, 2006 Volume 71, Number 179, Page 54423-54434. http://www.epa.gov/fedrgstr/EPA-PEST/2006/September/Day-15/p15258.htm

[38] U.S. EPA Biological and economic analysis of endosulfan benefits on selected crops: impacts of cancellation. July 12, 2002. summary

[39] U.S. EPA Biological and economic analysis of endosulfan benefits on selected crops: impacts of cancellation. July 12, 2002. summary

[40] Endosulfan, fenarimol, imazalil, oryzalin, sodium actifluorfen, trifluralin, and ziram; Tolerance Actions. Federal Register: September 15, 2006 Volume 71, Number 179, Page 54423-54434. http://www.epa.gov/fedrgstr/EPA-PEST/2006/September/Day-15/p15258.htm

Use of old FDA data requires revocation or modification of tolerance

The 2002 RED assessment utilized FDA monitoring data. If a pesticide is not used on the majority of a crop, the typically insensitive detection methods used by FDA are unlikely to pick up residues much below the tolerance level. In addition, much of the monitoring data are based on composited samples which further dilute the results if the entire crop is not treated. To the extent that the 2007 Assessment relies upon FDA monitoring data, FFDCA requires the Agency to obtain confirmatory data within 5 years of the issuance of the RED. 21 U.S.C. § 346a(b)(2)(E). Since the RED was issued early in 2002, the data were due in 2007. The Agency must revoke or modify the tolerance within 6 months of the failure to obtain the necessary data.

FQPA: 10X factor was removed without justification

In its 2007 assessment, EPA removed the 10X FQPA factor that had been applied in the 2002 RED. EPA supports its action to remove the FQPA factor by saying that, "there were no residual uncertainties for pre and/or post-natal toxicity." (HED Addendum at 3). However, this conclusion is not supported by the data or by the analysis of EPA's own experts. The results of the Developmental Neurotoxicity Test submitted by the registrant reported that the rodent pups were more sensitive to endosulfan than the adult rodents. The EPA evaluation of the study reported that the NOAEL for dams is 3.7 mg/kg/day. The LOAEL is 10.8 mg/kg/day based on decrease body weight, food consumption and food efficiency. There was no NOAEL for pups. The LOAEL was the lowest dose tested at 3.74 mg/kg/day based on decreased pup weight at PND 11 and decreased weight gain at PND 4-11. At the medium dose tested, possible delayed preputial separation in males occurred. [41] Therefore, this study strongly supports full retention of the full FQPA factor, because pups are more sensitive than adults, and because there was no identified no-effect-level for the pups.

NRDC points out that the Developmental Neurotoxicity Test (DNT) relied upon by EPA for its decision[42] is not designed to identify or characterize possible regional brain effects, endocrine effects outside of the nervous system, and effects associated with exposures at various time points of development; the study is therefore likely to underestimate the toxicity, particularly for an endocrine disrupting chemical like endosulfan.

NRDC strongly objects to EPA's removal of the full tenfold safety factor for endosulfan, which had a critical impact on the final (2007) assessment. In 2007, EPA determined that "[b]ased on the reduced FQPA safety factor of 10X to 1X and use of the same input files

[41] Data Evaluation Record for the Endosulfan Developmental Neurotoxicity Study in Rat. Sponsor: Endosulfan Task Force. EPA Reviewers: David Anderson, Judy Facey. MRID 46968301. EPA-HQ-OPP-2002-0262-0058.1

[42] Data Evaluation Record for the Endosulfan Developmental Neurotoxicity Study in Rat. Sponsor: Endosulfan Task Force. EPA Reviewers: David Anderson, Judy Facey. MRID 46968301. EPA-HQ-OPP-2002-0262-0058.1

as in the 2002 dietary assessment, the combined dietary exposure to endosulfan residues (food and drinking water) **does not exceed** the Agency's level of concern (>100% of the PAD) for chronic or acute exposures." (HED Addendum at 2). In contrast, in its 2002 assessment (using a full 10X FQPA factor), EPA had determined that for the most exposed population subgroup (children 1 to 6 years old), the percent acute population adjusted dose (aPAD) is 150% at the 99.9th percentile, meaning that children are exposed to excessively high, and therefore unsafe, levels of endosulfan from food consumption alone. Notably, any value above 100% of aPAD is considered unsafe by the EPA. Additional exposures through drinking water indicated that the risk from acute exposures exceeded the Agency's level of concern (LOC) for all populations, including infants, children, and adults. The surface water peak estimated concentration is 23.86 ppb, far exceeding the drinking water LOC of 0 ppb for children and of 3 ppb for the U.S. general population.

If EPA were to apply the full safety factor, as required by FQPA, EPA would be unable to conclude that any endosulfan tolerances are safe and would therefore be required to revoke all tolerances.

FQPA: Vulnerable populations in Arctic not accounted for

In its assessment, EPA failed to fully account for vulnerable populations such as Arctic populations that are over-exposed to endosulfan-contaminated food sources. EPA acknowledges but fails to incorporate evidence that "Since endosulfan has routinely been detected in arctic regions and the Indigenous Peoples of the arctic region of the U.S. (Alaska) rely heavily on subsistence diets (i.e. - fish) as their food source, it is appropriate for the Agency to consider dietary risk and exposure to this specific population subgroup from the worldwide use of endosulfan." (HED Addendum at 2). EPA also acknowledges its obligation to protect these populations, "in accordance with U.S. Executive Order 12898, 'Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations'." (HED Addendum at 2). However, EPA failed to incorporate these outstanding concerns into its assessment, "Since no specific data are available for residues of endosulfan in/on commodities consumed in subsistence diets, the Agency has concerns for dietary exposure of indigenous populations to endosulfan based upon its persistence and potential for bioaccumulation." (HED Addendum at 2).

In the face of an admitted risk which EPA is unable to quantify or even fully qualitatively characterize, EPA cannot properly conclude that endosulfan tolerances that might allow dietary exposures to this population subgroup will be safe. Similarly, the inability of the Agency to quantify and adequately characterize these risks prevents it from determining that continued use of endosulfan will not cause unreasonable adverse effects on the environment. Accordingly, all registrations and tolerances of endosulfan that may contribute to exposure of this sub-population must be cancelled and revoked, respectively.

FQPA: Developmental toxicity

The Developmental Neurotoxicity Test (DNT) is not designed to identify possible regional brain effects, endocrine effects outside of the nervous system, and effects associated with exposures at various time points of development; the study is therefore likely to underestimate the toxicity, particularly for an endocrine disrupting chemical like endosulfan.

Infants and young children are uniquely sensitive to neurotoxic and fetotoxic agents like endosulfan. The developing brain also is affected by endosulfan via altered levels of critical neurotransmitters such as dopamine, noradrenaline and serotonin; the altered neurotransmitter levels are associated with deficits in learning and memory.[43] Rodents dosed with endosulfan prenatally displayed neurodevelopmental toxicity, manifested as increased serotonin binding to the frontal cortical membranes and increased aggressive behavior.[44] Although adults did not display these adverse effects in this study, other researchers have reported chronic deficits in spatial learning in the absence of any overt toxic effects among adult animals exposed to endosulfan. These effects were markedly enhanced when the animals were exposed to low doses of endosulfan and an organophosphate.[45] The combination of endocrine disruption, reproductive toxicity, and neurotoxicity from this persistent, bioaccumulative chemical, means that it cannot be safely used on the food supply or safely be distributed in the environment. The evidence of increased toxicity in immature animals means that endosulfan exposure is unlikely to be safe for fetuses, infants or children, even at low doses.

Exposure underestimated in outdated consumption data

For its assessment of exposure through food sources, EPA relied on consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998 (HED Addendum at 9). However, the USDA consumption data is outdated, fails to reflect current typical current diets, and is particularly weak on diets relevant to Arctic populations. Furthermore, samples collected for the FDA Total Diet Study were collected in supermarkets in only four cities per year, and none in the Arctic regions, leaving the most highly-contaminated regions of the US severely underrepresented in the consumption dataset.

The 2007 assessment provides new evidence that "endosulfan shows appreciable lipophilicity and, therefore, a potential to bioaccumulate in fatty tissues. Since subsistence diets often consist of fish and other traditional subsistence food harvests (e.g., polar bear, walrus, caribou, moose), exposure to tissues into which endosulfan has

[43] Lakshmana MK, Raju TR. Endosulfan induces small but significant changes in the levels of noradrenaline, dopamine and serotonin in the developing rat brain and deficits in the operant learning performance. Toxicology 91:139-150, 1994.
[44] Zaidi NF, Agrawal AK, Anand M, Seth PK. Neonatal endosulfan neurotoxicity: behavioral and biochemical changes in rat pups. Neurobehav Toxicol Teratol. 1985 Sep-Oct;7(5):439-42.
[45] Castillo CG, Montante M, Dufour L, Marti;nez ML, Jimenez-Capdeville ME. Behavioral effects of exposure to endosulfan and methyl parathion in adult rats. Neurotoxicol Teratol 2002 Nov;24(6):797-804.

bioaccumulated is possible." (2007 HED Addendum at 10.) This evidence of bioaccumulation raises the concern significantly that circumpolar (Arctic) populations are likely to have much higher levels of endosulfan contamination in their food sources and their own bodies than the EPA has estimated in its assessment.

In addition to concern for Arctic populations whose diets are high in animal fat contaminated with endosulfan, the well-recognized increase in fat consumption and excessive weight gain in Americans may be relevant to the risk posed by endosulfan because it is lipophilic and accumulates in fatty body tissues. Thus, Americans in 2007 might be consuming and storing more endosulfan residues than would have been the case 10-15 years ago when the CSFII data was compiled.

In the absence of reliable data about Arctic diets and US consumption of animal fat, EPA may not depart from the 10X FQPA safety factor for populations whose exposure to endosulfan is very highly likely to be underestimated in the 2002 and 2007 EPA assessment.

Multiple isomers may have different toxicity profiles

Like the other organochlorine pesticides (OC's), endosulfan is composed of a mixture of isomers. In the cases of its chemical cousins, DDT, aldrin, dieldrin, heptachlor and chlordane, one of the isomers is far more biologically active than the others. In addition, the breakdown (metabolic, photochemical) products are often more toxic than the technical products. Some isomers are more persistent and mobile and convert to more toxic forms than other isomers. Thus, the exact composition of the test substance and the manner in which it is tested is very important. Many of the components of a pesticide will have one or more breakdown products which may be more toxic or more of a problem in the environment. The burden is on EPA to decide whether toxicological or environmental testing needs to be performed on something other than technical product. Is it the same mix of isomers as the marketed product? Are the test animals exposed to the same substance that would be encountered in the environment or in the diet? The issues are similar for environmental fate and effects studies. Testing on the Technical Grade Active Ingredient (TGAI) of pesticides that are mixtures can lead to significantly underestimating toxicity, and therefore risk. If one of the more toxic components is preferentially taken up through the food chain (as was the case for several OC's), toxicity testing on the TGAI may have the effect of diluting the toxicity in an unrepresentative fashion, thus under-estimating the final assessment of risk. If EPA did not aggressively pursue the composition and toxicology of endosulfan, it is possible that the risk assessment understates the risk, and the resultant tolerances for endosulfan are inadequate to protect the public and environment.

EPA assumes the three isomers are equally toxic. In the absence of specific toxicity studies on each of the isomers, EPA has not provided a persuasive scientific basis for this assumption.

Worker risks not addressed

In the 2007 assessment, EPA acknowledges that "with the revised dermal endpoint and level of concern, many of the occupational handler scenarios **exceed EPA-HED's level of concern** even with maximum personal protective equipment or engineering controls. In addition, for many of the occupational post-application scenarios, the restricted-entry interval (REI) would be **several days longer** than the REIs established in the 2002 RED." (emphasis in original; HED Addendum at 2).

The assumptions made regarding the likelihood that workers will use or wear protective equipment are often not substantiated. Even the simplest protective clothing (gloves, long sleeve shirts and long pants) are not likely to be reliably used in hot weather. California is the only state that even makes a symbolic effort to enforce protective clothing requirements. Does EPA have field evidence that the prescribed/recommended/required protective clothing is routinely worn by workers in hot weather? Does EPA believe such requirements to be practical and safe for workers on hot days? Please provide the scientific and factual basis for the answer.

The 3x safety factor for worker intermediate exposure is not supported by a clear scientific rationale. Workers may be exposed for many months at a time, year after year. This is much more akin to a chronic exposure. Accordingly, in the absence of a chronic exposure study, NRDC is skeptical that EPA could bound the risk of occupational exposure with any reasonable level of confidence.

Registering a chemical that puts worker health and safety at risk is inconsistent with EPA's mission to protect human health and the environment.

Percent crop treated assumptions

Historically, EPA dietary risk assessments were based on the simple but conservative assumptions that 100% of the crop was treated and all the resulting food has tolerance level residues. All of the "refinements" adopted since then have been explained as reasonable attempts to portray a more realistic picture of the actual frequency and level of residue levels to which people would be exposed. Thus, percent-crop-treated, processing information and probabilistic analyses have been adopted. The danger with all of these mechanisms is that they will not be adequately protective if they are based on weak data or faulty assumptions. Thus, for example, reliable percent-crop-treated information is virtually non-existent. As far as NRDC is aware, only California requires submission of crop treated data for restricted use pesticides. NRDC understands that most percent-crop-treated estimates are based on proprietary commercial surveys that cannot be fully examined by the public. The reliance on secret sources of data is arbitrary and capricious, unscientific, and does not meet the FFDCA requirement for reliability. 21 U.S.C. § 346a(b)(2)(F). In addition, we are concerned that the food processing factors used by EPA may be based on very limited, informal inquiries of industry sources, sometimes of

the pesticide producer alone. These are not robust data and are likely to be unreliable in a way that cannot be predicted or calculated.

Drinking Water

The drinking water model uses the 90th percentile. The dietary assessment uses 99th percentile. Why did EPA select different percentile estimates? Please provide the scientific and factual basis for the answer.

Label changes for unsupported uses

The "unsupported" uses had not been removed from all labels at the time the 2002 RED was issued. If this has not been done yet, it should be done immediately.

Agency actions to increase food tolerances:

Despite the toxicity, persistence, and bioaccumulative characterization of endosulfan and its major degradates by EPA experts, and other evidence discussed in these comments, EPA has not only maintained tolerances of endosulfan on food products, but it has actually increased the tolerances for many foods, and even added new tolerances.[46] This is in direct contrast to its own experts' assessment, as presented in these comments. The following is a list of the tolerance changes that EPA has published in the Federal Register, including a rationale that increased tolerances are to allow for the level of contaminating residue already detected on food. In other words, because endosulfan already contaminates the food supply, EPA will allow it on food at the levels that it is detected.

- EPA is revoking the tolerances in 40 CFR 180.182(a)(1) on artichoke, globe; beet, sugar, roots; raspberry; safflower, seed; and sunflower, seed.
- EPA is increasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on almond from 0.2 to 0.3 ppm.
- Because detected residues are as high as 0.38 ppm on grains, EPA is increasing the tolerances in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on barley, grain and wheat, grain from 0.1 to 0.3 ppm, and barley, straw and wheat, straw from 0.2 to 0.4 ppm.
- EPA is increasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on blueberry from 0.1 to 0.3 ppm.
- Based on available data on broccoli that show combined endosulfan residues of concern as high as 2.41 ppm, EPA is increasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on broccoli from 2.0 to 3.0 ppm.

[46] Endosulfan, fenarimol, imazalil, oryzalin, sodium actifluorfen, trifluralin, and ziram; Tolerance Actions. Federal Register: September 15, 2006 Volume 71, Number 179, Page 54423-54434. http://www.epa.gov/fedrgstr/EPA-PEST/2006/September/Day-15/p15258.htm

- Based on available data that show combined endosulfan residues of concern as high as 3.1 ppm on cabbage with wrapper leaves, EPA is increasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on cabbage from 2.0 to 4.0 ppm.
- Based on available data on celery that show combined endosulfan residues of concern as high as 7.0 ppm, EPA is increasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on celery from 2.0 to 8.0 ppm.
- Based on available data that show combined endosulfan residues of concern as high as 10.11 ppm in or on head lettuce with wrapper leaves and 5.72 ppm in or on leaf lettuce, EPA is separating the tolerance in 40 CFR 180.182(a)(1) on lettuce into lettuce, head and lettuce, leaf and increasing them for combined endosulfan residues of concern from 2.0 to 11.0 and 6.0 ppm, respectively.
- Based on available data on oat grain, oat straw, rye grain, and rye straw that show combined endosulfan residues of concern as high as 0.30, 0.32, 0.30, and 0.30 ppm, respectively, EPA is increasing the tolerances in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on oat, grain from 0.1 to 0.3 ppm; oat, straw from 0.2 to 0.4 ppm; rye, grain from 0.1 to 0.3 ppm; and rye, straw from 0.2 to 0.3 ppm.
- Available ruminant metabolism data indicate that combined endosulfan residues of concern at 1.1x and 1.7x the maximum dietary burden for beef and dairy cattle, respectively were detected at 0.78 ppm in milk, 12 ppm in fat, 0.85 ppm in kidney, 4.6 ppm in liver, and 2.0 ppm in muscle. Therefore, EPA is increasing the commodity tolerances in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on cattle, fat; goat, fat; hog, fat; horse, fat; and sheep, fat from 0.2 to 13.0 ppm; cattle, meat byproducts, except liver; goat, meat byproducts, except liver; hog, meat byproducts, except liver; horse, meat byproducts, except liver; and sheep, meat byproducts, except liver, from 0.2 to 1.0 ppm; cattle, meat; goat, meat; hog, meat; horse, meat; and sheep, meat from 0.2 to 2.0 ppm; milk, fat from 0.5 to 2.0 ppm; and establish tolerances at 5.0 ppm for cattle, liver; goat, liver; hog, liver; horse, liver; and sheep, liver.
- Based on available data on cantaloupes, cucumbers, and summer squash that show combined endosulfan residues of concern as high as 0.76, 0.66, and 0.25 ppm, respectively, EPA is combining the individual tolerances in 40 CFR 180.182(a)(1) on cucumber, melon, pumpkin, squash, summer; and squash, winter into vegetable, cucurbit, group 9 and decreasing the tolerance for combined endosulfan residues of concern from 2.0 to 1.0 ppm.
- EPA is decreasing the tolerances in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on eggplant from 2.0 to 1.0 ppm and tomato from 2.0 to 1.0 ppm.
- EPA is decreasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on sweet potato, roots from 0.2 to 0.15 ppm.
- EPA is decreasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on apple from 2.0 to 1.0 ppm.
- EPA is establishing a tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on apple, wet pomace at 5.0 ppm.

- EPA is decreasing the tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on pineapple from 2.0 to 1.0 ppm.
- EPA is establishing a tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on pineapple, process residue at 20.0 ppm.
- Based on available data on sweet corn that show combined endosulfan residues of concern as high as 12.0 ppm in or on sweet corn forage and 13.92 ppm in or on sweet corn stover, EPA is establishing tolerances in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on corn, sweet, forage at 12.0 ppm and corn, sweet, stover at 14.0 ppm.
- Based on available data on cotton gin byproducts that show combined endosulfan residues of concern as high as 27.5 ppm, EPA is establishing a tolerance in 40 CFR 180.182(a)(1) for combined endosulfan residues of concern in or on cotton, gin byproducts at 30.0 ppm.

Respectfully,

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