GM Herbicide Tolerant Crops – Less Equals More

Herbicides needed to support glyphosate and combat resistant weeds: 2,4-D

August 2012

The rapid increase in the number of, and area affected by, weeds resistant to glyphosate (sold as Monsanto's Roundup) in the US and South America has lead to recommendations that farmers should use other herbicides to control weeds in GM crops tolerant to the herbicide (known as or Roundup Ready, or RR, crops).

One such herbicide is 2,4-D, which is now recommended to "burn-off" stubble so that all glyphosate resistant weeds are killed before the next RR crop is drilled.

Specific GM 2,4-D tolerant crops are also on the way. Dow AgroSciences has applied for US approval of a GM maize with 2,4-D tolerance[i] and has an application in the pipeline for US authorisation of a GM soya with three stacked herbicide tolerant (HT) traits (ie, the plants can tolerate applications of 2,4-D plus glyphosate plus glufosinate ammonium).[ii] Herbicides could be applied to GM varieties with several HT traits either in mixtures or in rotation to ensure that glyphosate resistant weeds are killed by the other weedkillers. Recently South Africa has controversially given the green light for 2,4 D tolerant maize.[iii]

This increased use of all chemical weedkillers should put the final nail in the coffin of Monsanto's claim that RR crops would lead to cheaper, easier and safer weed control and demonstrate that on the contrary RR crops are now another proven staging post in the pesticides "arms race" that began in the 1940s.

What is 2,4-D?

2,4-D (2,4-dichlorophenoxyacetic acid) is a systemic broadleaf weedkiller that mimics auxins (a class of plant hormones). It causes plants cells to grow very rapidly and erratically, which brings about damage that ultimately kills the plant. The acid and several salts of 2,4-D are used as herbicides. 2,4-D is notorious as one of the active ingredients in Agent Orange, the defoliant used by the US military during the Vietnam War.

Uses for 2,4-D

2,4-D is used to control a wide range of broadleafed weeds, including in cereal crops, amenity grassland, lawns, orchards and for clearing ground. It is often used in combination with other herbicides, including dicamba (dicamba tolerant GM crops are in the pipeline in the US). The latest pesticide use figures for the UK[iv,v and vi] show 2,4-D use declining on cereal crops, but it is still extensively used on orchard crops, grassland and pasture. In the US its use remains high on grassland, wheat, maize and domestic lawns.

Weed resistance

Weeds resistant to 2,4-D have already been recorded in North and South America, Europe, Australia and Asia.[vii] Resistance to 2,4-D first appeared in 1957 and progressed slowly until the 1990s, after which resistance development accelerated (31 confirmed cases since 1990 compared with 13 before then[viii]).

Contaminants of 2,4-D

The production process for 2,4-D results in some contamination of the final product with dioxins (breakdown and by-products from synthetic chemicals production recognised as some of the most toxic compounds in the world). In 1987 the US Environmental Protection Agency (EPA) confirmed

that 25% of samples contained 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and 37.5% contained 1,2,3,7,8-pentachlorodibenzo-p-dioxin (PCDD). TCDD is the more toxic of the two by-products and has been strongly linked to birth defects and a range of cancers.[ix] In 1995 the US EPA estimated that using 2,4-D contributed 2.6% of the dioxin burden in the US. The companies marketing 2,4-D claim that recent improvements in the manufacturing process mean the chances of dioxins being produced are now much less, although Australian researchers have recently confirmed PCDD to be present in 2,4-D.[x]

Health concerns about 2,4-D

2,4-D is linked to numerous health problems over many decades. Table 1 summarises human health concerns related to 2,4-D hazards.

Table 1 Human health concerns for 2,4-D

General human health issues	Occupational exposure issues
Excessive doses may affect digestive systems. Neurotoxicant. Possible liver and kidney toxicant. Reproductive/development effects. Possible carcinogen. Possible endocrine hormone disruptor.	Irritant to skin, eyes and respiratory tract. Moderate risk of inhalation and dermal exposure, depending on type of personal protection and equipment used.

Source: Compiled from the Pesticide Properties Database (known as FOOTPRINT) maintained by University of Hertfordshire as a readily accessible summary source of data for users in the EU.

PAN International pesticide of concern

2,4-D features in Pesticide Action Network (PAN) International's *Highly Hazardous Pesticide List (HHP*, the modern update to PAN's famous Dirty Dozen of harmful pesticides first published in the 1980s). The PAN HHP List[1] is based on official health and environmental hazard classifications from global, US and EU authorities and serves as PAN's recommendations to the joint UN agencies' initiative for a progressive ban on highly hazardous pesticides.

2,4-D qualifies for inclusion on the PAN HHP List due to chronic human health hazards relating to its ranking as a probable carcinogen by the International Agency for Research on Cancer and its classification by the EU as an endocrine disrupting chemical (EU Category 2).

Carcinogenicity

The US EPA says 2,4-D is "not classifiable as to human carcinogenicity".[xi] However while the overall assessments are not conclusive, various epidemiological and laboratory studies suggest that the risk of certain cancers, including Non-Hodgkins Lymphoma, could increase with exposure to the herbicide.[xii] The presence of dioxins and the use of 2,4-D in mixtures with other herbicides complicates epidemiological studies.

Mutagenic effects

The US EPA[xiii] found 2,4-D "was not mutagenic, although some cytogenic effects were observed".[2] This conclusion appears to be based on the conclusions of 20 unpublished studies – one by Dow Chemicals and 19 by a private US laboratory. However independent researchers have found forms of 2,4-D cause mutations in chromosomes, for example in freshwater snails,[xiv] and human lymphocytes.[xv]

Reproduction and birth defects

Commercial 2,4-D caused teratogenic effects (birth defects) occasionally and decreased foetal viability in laboratory hamsters.[xvi] A human epidemiological study took place in wheat growing areas of the US where 2,4-D is extensively used and showed that, "[I]nfants conceived during April-June – the time of herbicide application – had an increased chance of being diagnosed with

[1] The PAN HHP List and its rationale is available at http://www.pangermany.org/download/PAN_HHP-List_1101.pdf

[2] Mutagenic = induces or increases mutations of genes. Cytogenic = impacts on cell development.

circulatory/respiratory (excluding heart) malformations compared with births conceived during other months of the year."[xvii]

Endocrine disruption
In their 2005 review of 2,4-D the US EPA reported, "[T]here is concern regarding its endocrine disruption potential."[xviii] 2,4-D has an impact on the thyroid gland,[xix and xx] production of the leutinising hormone from the pituitary gland[xxi] and oestrogenic activity.[xxii] Recent research concluded that among subjects with low high density lipoprotein cholesterol (HDL), "[U]rinary 2,4-D was associated with increased [xxiii] levels of triglycerides, insulin, C-peptide, and thyroid stimulating hormone, especially in the susceptible subpopulations," (eg, People with diabetes or hypothroidism) and that exposure to 2,4-D was associated with changes in biomarkers that, "[B]ased on the published literature, have been linked to risk factors for acute myocardial infarction [heart attack] and type-2 diabetes."

Acute toxicity
2,4-D is classed as moderate to low toxicity except for eye irritation, which is classified as high. Ingestion can be fatal.

Residues in food

In the UK data from government and industry monitoring of residues in 2010 found 2,4-D in citrus fruits from several countries, although not above the Maximum Residue Levels (the legally permitted maximum above which products should not be sold). EU monitoring found the herbicide infrequently at low levels, mainly in fruit and vegetables.[xxiv] Direct application to a growing GM crop would lead to an increased chance of residues being detected.

Environmental concerns

Table 2 summarises ecotoxicological rankings of moderate or high concern related to 2,4-D hazards to wildlife.

Table 2 Ecotoxicological concerns for 2,4-D

Mammalian hazard rankings	Other wildlife hazard rankings
High for short-term dietary intake.	Bees (oral): Moderate Earthworms: Moderate Aquatic invertebrates: Moderate Fish: Moderate Birds: Moderate

Source: Compiled from Pesticide Properties Database.

Aquatic toxicity
According to the US Forest Service, "2,4-D acid, salts, and esters are toxic to aquatic animals, with esters having greater toxicity than 2,4-D acid and salts."[xxv] Levels of toxicity vary between different fish and aquatic invertebrate species. In contrast to the views of the USDA Forest Service, a pesticide industry lobby group says, "The acid and amine salts are practically non-toxic to freshwater or estuarine/marine fish," and, "Daphnia was slightly toxic [*sic*] to 2,4-D acid and practically non-toxic to other 2,4-D forms." [xxvi]

Residues in water
The US Department of Agriculture surveyed treated and untreated drinking water in 2009 and found 2,4-D in over 80% of samples, all of which were below the US EPA's maximum concentration level 70,000 parts per trillion[xxvii] (the US EPA maximum concentration level is 700 times higher than the EU's maximum permitted level). In the UK 2,4-D is detected regularly in surface waters. Between 1995 and 2004 between 3.8% and 10% of drinking water samples exceeded the EU 0.1µg/l maximum permitted level,[xxviii] and between 0 and 1.56% of groundwater samples were above this maximum from 1998-2005.[xxix]

Effects on amphibians

Laboratory research showns that 2,4-D can interfere with the development of amphibian embryos.[xxx]

Effects on soil
Research published in 2010 found that 2,4-D had "severe effects" on one species of earthworm, including high levels of mortality and failure to reproduce in laboratory experiments.[xxxi]

Conclusion

An increase in 2,4-D use on GM crops would lead to significant increase in exposure to workers, the public and environment to this dangerous product. It will add to the complexity and costs of weed control for farmers and will eventually lead to more resistance in weed populations. This model of arable crops production is flawed and is now failing.

Integrated Weed Management can greatly reduce dependency on chemical weed control without using GM crops and can provide an important transitional step to agroecological methods of weed management based on crop rotations, break crops, grazing, mechanical weed control and mulches. Such approaches provide safer alternatives and deal with all types of weed – herbicide resistant or not.

Notes

[i] Dow Agro Sciences, press release 8 December 2008. "Enlist™ Corn, Enlist™ Soybeans Successfully Complete FDA Review"
[ii] Dow Chemicals, press release 22 August 2011. "Dow AgroSciences, M.S. Technologies Submit for Approval First Ever Three-Gene Herbicide-Tolerant Soybean"
[iii] Carnie T, 24 July 2012. "Controversial GM Mielies Get the Green Light". *The Mercury*
[iv] Garthwaite DG, Barker I, Parrish G, Smith L, Chippindale C and Pietravalle S, 2011. *Pesticide usage survey report 235 Arable crops in the United Kingdom 2010 (including aerial applications 2010)*. FERA, York
[v] Garthwaite DG, Barker I, Parrish G, and Smith L, 2010. *Pesticide usage survey report 225. Orchards & fruit stores in Great Britain 2008*. FERA, York
[vi] Garthwaite DG, Barker I, Parrish G, Smith L, and Chippindale C, 2010. *Pesticide usage survey report 232. Grassland & fodder crops in Great Britain (including aerial applications 2009) 2009*. FERA, York
[vii] Heap I, 19 December 2011. The International Survey of Herbicide Resistant Weeds
[viii] *Ibid*
[ix] US EPA, 2007. "2,3,7,8-Tetrachlorodibenzo-p-Dioxin (2,3,7,8,-TCDD)"
[x] Holt E, Weber R, Stevenson G and Gaus C, 2010. "Polychlorinated Dibenzo-p-Dioxins and Dibenzofurans (PCDD/Fs) Impurities in Pesticides; A Neglected Source of Contemporary Relevance". *Environmental Science and Technology*: 5409–5415
[xi] US EPA, 2005. Re-registration eligibility decision for 2,4-D
[xii] McDuffie HH, Pahwa P, McLaughlin JR, Spinelli JJ, Fincham S, Dosman JA, Robson D, Skinnider LF and Choi NW, 2001. "Non-Hodgkin's lymphoma and specific pesticide exposures in men: cross-Canada study of pesticides and health". *Cancer Epidemiology, Biomarkers and Prevention* 10:1155-1163.
[xiii] US EPA, 2005. *Op cit*
[xiv] Estevam EC, Nakano E, Kawano T, de Bragança Pereira CA, Amancio FF, and Mendonça de Albuquerque Melo AM, 2006. "Dominant lethal effects of 2,4-D in Biomphalaria glabrata". *Mutation Research* 611: 83-88
[xv] Zeljezic, D and Garaj-Vrhovac V, 2004. "Chromosomal aberrations, micronuclei and nuclear buds induced in human lymphocytes by 2,4-dichlorophenoxyacetic acid pesticide formulation". *Toxicology* 200: 39-47
[xvi] Collins TFX and Williams CH, 1971. "Teratogenic studies with 2,4,5-T and 2,4-D in the hamster". *Bulletin of Environmental Contamination and Toxicology* 6:559-567
[xvii] Schreinemachers DM, 2003. "Birth malformations and other adverse perinatal outcomes in four US Wheat-producing states". *Environmental Health Perspectives* 111:1259-64
[xviii] US EPA, 2005. Reregistration eligibility decision for 2,4-D. EPA 738-R-05-002
[xix] Florsheim WH and Velcoff SM, 1962. **"**Some Effects of 2,4-Dichlorophenoxyacetic Acid on Thyroid Function in the Rat: Effects on Iodine Accumulation". *Endocrinology* 71, 1-16.
[xx] Florsheim WH, Velcoff SM and William AD, 1960. "Some Effects of 2,4-Dichlorophenoxyacetic Acid on Thyroid Function in the Rat: Effects on Peripheral Thyroxine". *Endocrinology* 72:327-333
[xxi] Garry VF, Tarone RE, Kirsch IR, Abdallah JM, Lombardi DP, Long LK, Burroughs BL, Barr DB and Kesner JS, 2001. *Environmental Health Perspectives*, 109: 495-500
[xxii] Meulenberg EP, 2002. "A new test to identify endocrine disruptors using sex hormone-binding globulins

from human serum". *European Journal of Lipid Science and Technology* 109:131-136

[xxiii] Schreinemachers DM, 2010. "Perturbation of lipids and glucose metabolism associated with previous 2,4-D exposure: A cross-sectional study of NHANES III data,1988-1994". *Environmental Health* 9

[xxiv] European Food Safety Authority, 2011. *The 2009 European Union Report on Pesticide Residues in Food*

[xxv] USDA Forest Service, 2006. *2,4-D Human Health and Ecological Risk Assessment FINAL REPORT*

[xxvi] Industry Task Force II on 2,4-D Research Data

[xxvii] USDA, 2011. Pesticide Data Program Annual Summary, Calendar Year 2009

[xxviii] HM Government. "Pesticides in surface water samples: 1995-2004"

[xxix] HM Government. "Pesticides in groundwater samples"

[xxx] Stebbins-Boaz B, Fortner K, Frazier J, Piluso S, Pullen S, Rasar M, Reid W, Sinclair K and Winger E, 2004. "Oocyte maturation in *Xenopus laevis* is blocked by the hormonal herbicide, 2,4-dichlorophenoxy acetic acid". *Molecular Reporoduction and Development* 67:233-242

[xxxi] Correia FV and Moreira JC, 2010. "Effects of glyphosate and 2,4-D on earthworms (Eisenia foetida) in laboratory tests". *Buletin of Environmental Contamination and Toxicology* 85:264-8