



The Herbicide Treadmill in Roundup Ready Crops

EU environment faces huge increase in toxic burden

21 June 2013

Summary

This briefing is part of a series of documents looking at the herbicides that form part of the agri-biotech industry's response to the widespread and growing problem of weeds developing resistance to glyphosate in Roundup Ready (RR) crops in US and South America.¹ It examines the four soil-acting (or residual) herbicides Monsanto and other companies wish to use in the US as part of the RR crop "platform" alongside glyphosate and other herbicides.

Soil-acting herbicides kill weeds soon after they germinate. Monsanto has negotiated with three pesticide companies to include flumioxazin, sulfentrazone and acetochlor in the RR package sold to farmers in the US. A fourth, pyroxasulfone, is also proposed.

All four herbicides pose sufficient risks to health, the environment or water supplies to suggest that their use should not be permitted in the European Union (EU) or elsewhere. Acetochlor has already been refused approval in the EU because of safety concerns (detailed below). Sulfentrazone has no approval in the EU. Flumioxazin has EU approval until December 2015. Pyroxasulfone has only just gained its first approval in the US, and therefore there is very little experience of its use.

If crops genetically modified to tolerate herbicides succeed in gaining EU approval, the precise nature of the array of herbicides used with RR crops to try and prevent resistance developing in EU weeds will be different than that on offer in the US. For example glufosinate ammonium (Bayer CropScience's alternative to glyphosate) is due for reauthorisation in the EU in 2017, but there are doubts about its safety.

The prospective Monsanto herbicide "platform" (seeds, Roundup plus other herbicides targeting glyphosate-resistant weeds) for RR crops in the EU could therefore consist of glyphosate plus 2,4-D, dicamba, glufosinate ammonium and flumioxazin, with the possible addition of pyroxasulfone in the future.

Introduction

Very soon after the mid-1990s introduction of GM herbicide tolerant crops in the US weeds in RR soya, maize and cotton fields began to develop resistance to the main herbicide used on them (Roundup, active ingredient glyphosate). Farmers growing all three crops are now faced with a growing number of problem weeds that Roundup fails to control.²

At least 12 weed species with glyphosate resistance infesting millions of hectares in US soya, maize and cotton crops.³ More than one resistant species can be present in the same crop, making weed control even more difficult. Some resistant weeds now pose a serious threat to crop viability because of the numbers of seeds they produce and their ability to spread. For instance the pigweed Palmer Amaranth is spreading very rapidly in RR cotton crops in the US. Once individual plants get beyond a certain size they can only be controlled by hand pulling to prevent them producing millions of seeds.⁴

The agri-biotech industry response to this failure of RR technology weed control has been to genetically modify crops with yet more GM traits, giving tolerance to other herbicides or using multiple (so-called "stacked") herbicide tolerant traits in the same plant along with the RR traits.

GM Freeze 50 South Yorkshire Buildings, Silkstone Common, Barnsley S75 4RJ
Tel: 0845 217 8992 Email: info@gmfreeze.org Web: www.gmfreeze.org Twitter: @GMFreeze

PAN UK Development House, 54-64 Leonard Street, London EC2A 4LT
Tel: 0207 065 0905 Web: www.pan-uk.org

Crops can then be sprayed with two herbicides at once to ensure all weeds are killed in one operation (in theory), or the herbicides can be used in rotation in an attempt to limit the evolution and spread of resistant weeds.

In the US the three herbicides being promoted for use in this way alongside glyphosate are 2,4-D, dicamba and glufosinate ammonium. None of these herbicides has a good safety record, and the EU approval of glufosinate ammonium beyond 2017 is not certain due to concerns about toxicity.⁵ All three herbicides will add to the toxic burden on the environment, and weeds resistant to them have already been confirmed in the US.⁶ US farmers are also being advised to chemically “burn off” weeds in stubble before with 2,4-D sowing RR crops to reduce the number of glyphosate resistant weeds in the crop.

The escalation in herbicide usage in the US as a result of glyphosate weed resistance developing is put at 239 million kilograms between 1996 and 2011.⁷ This adds to the costs farmers must bear in complete contradiction to the RR technology promise of cheaper, easier weed control. Weed control costs in soya bean fields infested with glyphosate tolerant weeds increased 2.7 times compared to those without tolerant weeds. Weed resistance has increased herbicide expenditure by 64% in Illinois soybean crops and 67% in Iowa maize.⁸

However agri-biotech companies want more products to hand as they struggle to control glyphosate resistant weeds. Monsanto has entered into agreements with other pesticide manufacturers to allow use of their herbicides as part of the “platform” offered to farmers using RR crops. The additional herbicides in the Monsanto “platform” also include soil-acting herbicides that kill weeds soon after they germinate. This briefing examines the toxicity of the three soil-acting herbicides currently used in the developing offer to farmers in the US (flumioxazin, sulfentrazone and acetochlor), plus the new herbicide pyroxasulfone.

The EU and RR crops

No RR crops are currently approved for commercial cultivation in the EU, but there were 14 applications in the EU authorisation pipeline as of May 2013. If the EU unwisely decides to approve RR crops for cultivation, and if Roundup is used in the same way it has been on US RR crops, it is inevitable that weeds resistant to glyphosate will appear fairly soon after their cultivation begins.

There are already five weed species in seven EU states resistant to glyphosate due to previous overreliance on the herbicide in non-GM crops.⁹ A recent Greenpeace study suggests that EU approval of RR crops could result in a massive 800% increase in glyphosate use and a 70% increase in the use of other pesticides.¹⁰

Once glyphosate resistant weeds emerge in the EU it is very likely Monsanto would seek approval for a “platform” of other herbicides for use on RR crops similar to that in use in the US, heralding an unprecedented and untested change to European crop management. The chemical weed control options open to farmers may automatically be limited if the EU does not grant approval for currently unauthorised active ingredients or renew the authorisation for glufosinate ammonium after 2017.

Soil-acting herbicides in the Monsanto “platform”

1) Flumioxazin

Flumioxazin comes from a group of chemicals called N-phenylphthalimides. The main manufacturers are the Valent Corporation and Sumitomo Corporation, with whom Monsanto has agreed a deal to sell it alongside RR seeds and Roundup. Flumioxazin is often traded as Valor in North America and in the EU as Digital, Guillotine and Sumimax.

It is a light-dependent peroxidising herbicide that works by disrupting chlorophyll biosynthesis. This results in an accumulation of toxins in the plant's cells, which irreversibly damages cell membranes leading to the death of the plant. It is a pre-emergent herbicide, meaning it acts in the soil and kills

GM Freeze 50 South Yorkshire Buildings, Silkstone Common, Barnsley S75 4RJ
Tel: 0845 217 8992 Email: info@gmfreeze.org Web: www.gmfreeze.org Twitter: @GMFreeze

weeds as soon as the seedlings emerge into sunlight after germination. Most of the information in this briefing comes from US, Canadian and Australian regulatory safety assessments, along with EU hazard classifications.

Flumioxazin is a relatively new herbicide so weeds have not yet developed resistance to it. Indeed the US Environmental Protection Agency (EPA) justifies its approval as a means to combat the spread of weeds resistant to active ingredients in other weedkillers.¹¹

a) Health Impacts

Flumioxazin features in Pesticide Action Network (PAN) International's Highly Hazardous Pesticide (HHP) List (the modern update to PAN's famous "Dirty Dozen" of harmful pesticides first published in the 1980s) due to chronic human health hazards relating to its ranking as a presumed human reproductive toxicant (EU Category 1B).¹²

Table 1 summarises human health concerns related to flumioxazin hazards. It is one of the 20 or so pesticides known or presumed to be reproductive toxins, and in the EU it warrants the hazard warning phrase "May damage fertility or the unborn child".

Table 1 Human health concerns for flumioxazin

General human health issues	Occupational exposure issues
Chronic toxicity: Reproductive toxin/developmental effects	Skin and eye irritant. Occupational exposure may occur through dermal and inhalation routes.

Source: Compiled from the Pesticide Properties Database (known as FOOTPRINT, see <http://sitem.herts.ac.uk/aeru/footprint/en/>) maintained by University of Hertfordshire as a readily accessible summary source of data for users in the EU.

The following is known about flumioxazin:

- Carcinogenicity: Regulators around the world classify flumioxazin as "not likely" to be a human carcinogen.
- Reproductive impacts: Flumioxazin has been shown to have impacts on reproduction, including that "an increased incidence of foetal death, impaired foetal development and growth retardation was observed in rats, following oral or dermal exposure at levels which were not toxic to the dams".¹³ During gestation, female rats fed with flumioxazin doses at 300 parts per million (ppm) had decreased body weight gain and a red vaginal discharge.¹⁴ A number of those females resorbed embryo implantations and litter sizes were reduced. Consequently Australian labels warn women of childbearing age to avoid mixing, loading or spraying flumioxazin based products.
- Mutations: Flumioxazin is generally thought not to be mutagenic. However in Chinese hamster ovary cells "an increase in cells with aberrations was observed at doses of 1×10^4 M and higher in the presence of S9 [solutions to stimulate *in vitro* metabolism of mutagens]."¹⁵
- Endocrine disruption: There is some evidence that flumioxazin may be an endocrine disrupting chemical based upon "an increased incidence of reproductive organ abnormalities in rats",¹⁶ but other reports from the US EPA say "flumioxazin does not possess oestrogenic or endocrine disrupting properties".¹⁷
- Other effects: Brief and minor irritation of the eyes and skin are possible. Respiratory irritation can occur if inhaled. When doses were repeatedly given to mice, rats and dogs flumioxazin caused liver toxicity, such as alterations in liver function and enzyme activities. Oral and dermal exposure induced anaemia and other blood disorders in rats. "Repeated exposures to Flumioxazin Technical in animals have produced anemia and other blood formation changes, organ weight changes and changes in blood chemistry".¹⁸

b) Environmental Impacts

Flumioxazin has a low toxicity to mammals and birds. For fish it is moderately to slightly toxic, and

GM Freeze 50 South Yorkshire Buildings, Silkstone Common, Barnsley S75 4RJ
 Tel: 0845 217 8992 Email: info@gmfreeze.org Web: www.gmfreeze.org Twitter: @GMFreeze

PAN UK Development House, 54-64 Leonard Street, London EC2A 4LT
 Tel: 0207 065 0905 Web: www.pan-uk.org

for aquatic and estuarine invertebrates it is moderately or highly toxic and impacts on reproduction, growth and survival.¹⁹ It is highly toxic to aquatic plants, including algae, which form an important part of the freshwater food chain, so it could have indirect consequences on organisms that feed on them and further up the food chain. Products containing this herbicide, which can reach surface waters through runoff or spray drift, warrant the EU hazard warnings “Very toxic to aquatic life” and “Very toxic to aquatic life with long-lasting effects”.

Table 2 summarises ecotoxicological rankings of moderate or high concern for flumioxazin hazards to wildlife.

Table 2 Ecotoxicological concerns for flumioxazin

Mammalian hazard rankings	Other wildlife hazard rankings for acute toxicity
None in high or moderate ranking	Bees: Moderate Earthworms: Moderate Aquatic invertebrates: Moderate Fish: Moderate Moderately harmful to some natural enemies tested.

Source: Compiled from Pesticide Properties Database (<http://sitem.herts.ac.uk/aeru/footprint/en/>)

Flumioxazin breaks down in soil and is not thought by regulators to pose a risk of leaching into groundwater to surface waters. However “the potential for the degradation products APF¹ and THPA² to leach to groundwater is high”.²⁰ The mobility of another breakdown product (482-HA³) is unknown. There were also “unidentified residues detected in the aqueous photolysis and anaerobic aquatic metabolism studies”.²¹

c) Residues

Data on the presence of flumioxazin residues in food and water are not generally available as its use is low compared to other herbicides. In the UK and EU flumioxazin has not routinely been sampled in food in recent years. No data from monitoring of the herbicide in water intended for human consumption could be found.

d) Conclusion

Information from independent scientists on the toxicity of flumioxazin is limited. Most of the data quoted in this briefing comes from research carried out for, or on behalf of, the companies that manufacture or market the herbicide. Given Monsanto’s announcement that it will be used as part of the herbicide “platform” to deal with glyphosate resistant weeds in the US, flumioxazin usage is likely to increase over the next few years.

In order to delay the development of glyphosate resistant weeds in the EU if RR crops are introduced, it is likely that Monsanto would seek to include flumioxazin as part of its EU weed control “platform”. Its impact on health, the environment and water quality needs to be fully understood before such a development is permitted, particularly as flumioxazin could be used with several other herbicide active ingredients that have been assessed separately for risks to human and environmental health but not in combination. We simply do not know the risks of exposure to the “cocktail” of herbicides and other pesticides currently applied to crops.

2) Sulfentrazone

Sulfentrazone is an aryl triazolinone herbicide first approved in the US in 1997. The herbicide is often used in combination with other products to control weeds, such as sedges, in amenity grass (playing fields, etc).

Sulfentrazone has never been approved for use in the EU, so no report on its safety by a

¹ APF = 3-oxo-4-prop-2-ynyl-6-amino-7-fluoro-3,4-dihydro-1,4-benzoxazin

² THPA = 3,4,5,6-tetrahydrophthalic acid

³ 482-HA = 7-Fluoro-6-[(2-carboxy-cyclohexenoyl)amino]-4-(2-propynyl)-1,4-benzoxazin-3(2H)-on

regulatory body in a Member State has been published.²² Few independent scientific assessments exist on the safety, toxicity and mobility of sulfentrazone, so most information is available from risk assessments in the US and have been produced by companies applying for approval. The approval of sulfentrazone is currently being reviewed by the USEPA, with final decision on its future use being scheduled for 2015.²³

In October 2010 Monsanto announced that the FMC Corporation agreed to allow its Authority brand herbicide to be used with RR crops as part of Monsanto's offer to farmers struggling with glyphosate resistant weeds.²⁴ Authority brand products are a mixture of sulfentrazone and another herbicide. Table 3 shows mixtures in the four different products covered by the agreement between Monsanto and FMC Corporation.

Table 3 Herbicides used in sulfentrazone products in the US

Product name	Active ingredient with sulfentrazone	Herbicide family
Authority First DF	Cloransulam methyl	Triazolopyrimidine sulfonanilide
Authority MTZ	Metribuzan	Triazinone
Authority XL	Chlorimuron ethyl	Sulfonylurea
Authority Assist	Imazethapyr	Imidazolinone

a) Health Impacts

Table 4 summarises human health concerns related to sulfentrazone hazards.

Table 4 Human health concerns for sulfentrazone

General human health issues	Occupational exposure issues
	Skin and eye irritant.

Source: Compiled from Pesticide Properties Database (<http://sitem.herts.ac.uk/aeru/footprint/en/>)

The following is known about sulfentrazone:

- Carcinogenicity: According to the US EPA sulfentrazone is not carcinogenic.
- Reproductive effects: One study found that sulfentrazone maternal exposure may lead to some neuromuscular and behavioural deficits in nursing rat pups.²⁵ The US EPA states "sulfentrazone caused developmental and reproductive toxicity...at treatment levels that were not maternally toxic, and significant toxic effects were observed primarily in the second generation animals of the reproduction study. Because these animals had been exposed to sulfentrazone *in utero*, the possibility that the observed reproductive toxicity resulted from a developmental and/or genotoxic mechanism was suggested".²⁶

b) Environmental impacts

The herbicide is very soluble in water and very persistent in soil. The US EPA concluded "sulfentrazone is highly mobile and persistent, and has a strong potential to leach into groundwater and move offsite to surface water".²⁷

Sulfentrazone is sufficiently persistent in the soil to cause harm to following crops of cotton and some vegetables (eg, squash, onion and tomato).²⁸ The US EPA reports incidents of crop damage in soya, maize and strawberry cropland affecting over 7,500 acres.²⁹

Table 5 summarises ecotoxicological rankings of moderate or high concern related to sulfentrazone hazards to wildlife and the environment.

Table 5 Ecotoxicological concerns for sulfentrazone

Mammalian hazard rankings	Other wildlife hazard rankings for acute toxicity
Highly toxic for mammalian short-term dietary effects	Bees: Moderate Aquatic crustaceans: Moderate Aquatic invertebrates: Moderate Fish: Moderate No data for natural enemies tested.

Source: Compiled from Pesticide Properties Database (<http://sitem.herts.ac.uk/aeru/footprint/en/>)

Sulfentrazone is slightly toxic to fish and aquatic invertebrates on an acute basis but significantly affects the survival of young fish and adversely affects some young invertebrates at low concentrations. The herbicide is also toxic to marine and estuarine organisms.³⁰

c) Conclusion

Sulfentrazone should not be approved for use in the EU because of its potential risks to health, a high risk of contamination of water and toxic impacts on aquatic and marine organisms.

3) Acetochlor

Acetochlor is a chloroacetanilide herbicide used for pre-emergence control of weeds. In 2010 Monsanto received US approval to use acetochlor-based products for early emergence weed control in cotton,³¹ so it can be used as part of the company's package of options for controlling glyphosate resistant weeds in RR crops.

In December 2011 the European Union announced that acetochlor would not be approved as an active substance under the Plant Protection Products Regulation 1107/2009 due to a series of risks to human health and the environment. The risk assessment found:

- A potential human exposure above the acceptable daily intake in food.
- A potential for human exposure to the surface water breakdown product t-norchloro acetochlor, the genotoxicity of which cannot be excluded.
- A high risk of groundwater contamination for several breakdown products.
- A high risk for aquatic organisms.
- A high long-term risk for herbivorous birds.
- Insufficient data to conclude on the risk assessment for the groundwater contamination for the breakdown products t-norchloroacetochlor and t-hydroxyacetochlor.

EU countries withdrew sales authorisations for acetochlor products in June 2012, with a grace period of 12 months for farmers to use any stocks.³²

a) Health Effects

Acetochlor features in (PAN International's HHP List due to chronic human health hazards relating to its ranking as an endocrine disruptor (EU Category 1) and a possible carcinogen (US EPA). Table 6 summarises human health concerns related to acetochlor. Acetochlor products authorised in the EU until June 2012 warranted the label hazard statements "Causes skin irritation", "May cause an allergic skin reaction", "Harmful if inhaled" and "May cause respiratory irritation".

Table 6. Human health concerns for acetochlor

General human health issues	Occupational exposure issues
Acute toxicity: Slightly hazardous (WHO Class III)	Skin and respiratory tract irritant. Skin sensitiser Dermal absorption possible during handling
Chronic toxicity: Mutagen, liver and	

GM Freeze 50 South Yorkshire Buildings, Silkstone Common, Barnsley S75 4RJ
Tel: 0845 217 8992 Email: info@gmfreeze.org Web: www.gmfreeze.org Twitter: @GMFreeze

PAN UK Development House, 54-64 Leonard Street, London EC2A 4LT
Tel: 0207 065 0905 Web: www.pan-uk.org

kidney toxicant, endocrine disruptor, possible carcinogen	
---	--

Source: Compiled from Pesticide Properties Database (<http://sitem.herts.ac.uk/aeru/footprint/en/>)

The following is known about acetochlor:

- Carcinogenicity: Acetochlor was classified as a probable human carcinogen in 1994,³³ and this was confirmed by the 2006 EU draft assessment report prepared by Spain, which also highlighted the need to provide evidence that the four metabolites (breakdown products) of acetochlor are not carcinogenic.³⁴
- Endocrine Disruption: Acetochlor is a suspected endocrine disruptor,³⁵ and is included on the EU's list of EDCs. It has been shown to influence the metamorphosis of tadpoles at concentrations likely to be found in the environment,³⁶ and to interfere with pubertal development and reproduction in rats.³⁷
- Genotoxicity: Chinese researchers found that acetochlor caused significant concentration-dependent increase in DNA damage in the tadpoles of the Chinese toad.³⁸

b) Environmental Impacts

Acetochlor products containing this herbicide warranted the EU hazard warnings "Very toxic to aquatic life" and "Very toxic to aquatic life with long-lasting effects". Table 7 summarises ecotoxicological rankings of moderate or high concern related to acetochlor hazards to wildlife and the environment.

Table 7. Ecotoxicological concerns for acetochlor

Mammalian hazard rankings	Other wildlife hazard rankings for acute toxicity
Highly toxic for mammalian short-term dietary effects	Bees: Moderate Birds: Moderate Aquatic crustaceans: Moderate Aquatic invertebrates: Moderate Fish: Moderate Earthworms: Moderate Harmful to natural enemies tested. Very persistent in soil and water.
Moderate acute toxicity	

Source: Compiled from Pesticide Properties Database (<http://sitem.herts.ac.uk/aeru/footprint/en/>)

Acetochlor is quickly biodegraded in the soil to form four metabolites: hydroxyacetochlor, t-oxanilic acid, t-sulphonic acid, and t-sulphanylacetic acid.³⁹ However studies suggest that acetochlor could negatively affect soil microbial life and crop health by:

- Stimulating harmful fungi populations, increasing the risk of plant disease grown on soil treated with the herbicide.⁴⁰
- Affecting beneficial nitrogen-fixing rhizobial bacterial populations in GM maize.⁴¹
- Potentially having a long-term negative effect on the diversity of ammonia oxidising bacteria.⁴²

Acetochlor was found to be toxic to earthworms in experiments carried out in China (where it is widely used) and, in combination with the organophosphate methamidophos (which is banned in the EU), synergistic effects were observed.⁴³

Acetochlor is believed to be unlikely to leach into groundwater, but a US monitoring study frequently detected its metabolites at levels above the maximum threshold permitted for pesticides in EU drinking water (0.1 µg/litre, equivalent to 0.1 parts per billion).⁴⁴

c) Conclusion

If acetochlor were to regain EU approval, its use would pose acute and chronic risks to human health and wildlife and contamination of water sources by this herbicide and its breakdown

GM Freeze 50 South Yorkshire Buildings, Silkstone Common, Barnsley S75 4RJ
Tel: 0845 217 8992 **Email:** info@gmfreeze.org **Web:** www.gmfreeze.org **Twitter:** @GMFreeze

products.

4) Pyroxasulfone

Pyroxasulfone is a new active ingredient that has only recently been approved in the US. Pyroxasulfone is a pre-emergence pyrazole herbicide that controls weeds by inhibiting very long chain fatty acid synthesis. It can control broadleaf and grass weeds and is marketed for use on maize and soya crops in the US to help combat glyphosate resistant weeds. Approvals for use in cotton and wheat could follow in 2013. Pyroxasulfone requires a lower dosage to effectively control weeds than other soil acting herbicides in the same chemical family,⁴⁵ It also has a longer half life in the soil, which extends its period of weed control.

Several US manufacturers market products containing pyroxasulfone including Anthem (with fluthiacet-methyl by FMC Corporation), Fierce (with Flumioxazin by Valent/Kumiai Chemical Industry Company) and Zidua (by BASF). In Australia Bayer has approval for a herbicide called Sakura which it claims provides “97% control of resistant annual ryegrass”.⁴⁶

Pyroxasulfone is not approved as an active ingredient in the EU, and the EU Pesticides databases provides no information on its toxicology.⁴⁷ PAN International databases have no data either. The information here draws upon risk assessments carried out in Australia and the US for the approval of the herbicide and are largely based on data supplied by the applicants.

a) Toxicity

Pyroxasulfone is excreted quite quickly and is reported to have “low acute oral, dermal and inhalational toxicity in rats”.⁴⁸ However a number of toxic effects are observed in dogs, rabbits and mice at high doses including:

- Slight eye irritant and developmental effect in rabbits: Pyroxasulfone is not thought to cause birth defects, although it did reduce foetal weights and increase rates of foetal resorption at high doses in rabbits. An Australian evaluation concluded “the observed effects are considered likely to have serious implication for growth and development of foetuses, babies and children”. The product was still recommended for approval but with very large safety margins “to account for the seriousness of the observed health effects”.
- Neurotoxicity: The primary target of toxicity following repeated administration of pyroxasulfone in these species appeared mainly to be the muscular and the nervous systems. The data submitted shows that dogs suffered impaired hind limb function, ataxia (poor coordination and unsteadiness), tremors and degeneration of the sciatic nerve. “(I)n rats, pyroxasulfone was associated with offspring toxicity causing slight but dose related decreases in absolute brain weight accompanied by a decrease in the thickness of the hippocampus, corpus callosum and cerebellum.”⁴⁹
- Developmental toxicity
- Bladder abnormalities
- Liver and kidney toxicity

b) Environmental impacts

Pyroxasulfone is mobile in the terrestrial and aquatic environment, although the US EPA says that 8-25% is bound on soil particles and sediments.⁵⁰ US EPA drinking water modelling predicted drinking water concentrations would peak at 0.210mg/l (210µg/l) – over 2,000 times the EU maximum permitted concentration for a single pesticide. The M1 metabolite was more prone to leaching than the parent product⁵¹. No field data on pyroxasulfone and its metabolites in water are currently available.

Pyroxasulfone has high mobility in soils but binds to organic carbon⁵². Under field conditions pyroxasulfone was found to have limited potential to leach but M-1 had potential under some conditions⁵³.

The following is known about pyroxasulfone:

GM Freeze 50 South Yorkshire Buildings, Silkstone Common, Barnsley S75 4RJ
Tel: 0845 217 8992 Email: info@gmfreeze.org Web: www.gmfreeze.org Twitter: @GMFreeze

PAN UK Development House, 54-64 Leonard Street, London EC2A 4LT
Tel: 0207 065 0905 Web: www.pan-uk.org

- Birds are slightly sensitive to pyroxasulfone, with some effects being shown in the short-term and in reproductive studies on Mallard ducks.⁵⁴
- Fish are not acutely sensitive to pyroxasulfone to the limits of its water solubility in test conditions (2.2 to 2.8 mg/L). However there was a reduction in the wet weight and length of fish exposed to higher concentrations of pyroxasulfone/L during their early life stage.
- Daphnia waterfleas are not sensitive to pyroxasulfone to the limit of its water solubility (1.9 to 4.4 mg/L under test conditions) in acute and sub-chronic studies.
- Green algae are very sensitive and pyroxasulfone is very highly toxic to these species. It also showed inhibitory effects on blue-green algae and marine algae at levels above 0.14 and 0.8 mg/L. The freshwater diatom was insensitive to pyroxasulfone to the limits of its water solubility. However green algae exposed to up to 2 µg pyroxasulfone/L for 72 hours can recover. M-1 and M-3 are slightly toxic to algae. In order to protect aquatic plants, the Australian risk assessment recommended a 160m wide no-spray zone down wind to protect algae and 80m for duckweed.
- Durum wheat is particularly sensitive to pyroxasulfone, and its use on this crop is not recommended.

c) Residues in food

The US EPA lists 23 different metabolites of pyroxasulfone (some short-lived), the main ones identified being:

- M1 = [5-(difluoromethoxy)-l-methyl-3-(trifluoromethyl)-l*H*-pyrazol-4-yl]methanesulfonic acid.
- M3 = 5-(difluoromethoxy)-l-methyl-3-(trifluoromethyl)-l*H*-pyrazole-4-carboxylic acid.
- M25 = [5-(difluoromethoxy)-3-(trifluoromethyl)-1*H*-pyrazol-4-yl]methanesulfonic acid.
- M28 = 3-[1-carboxy-2-(5,5-dimethyl-4,5-dihydroisoxazol-3-ylthio)ethylamino]-3-oxopropanoic acid.
- Metabolite C = 3-[1-carboxy-2-(5,5-dimethyl-4,5-dihydroisoxazol-3-ylthio)ethenylamino]-3-oxopropanoic acid.

Pyroxasulfone and its metabolites have been assessed in maize and soyabeans with varying results. The parent herbicide was found in maize and soya foliage, and residues of pyroxasulfone and its metabolites M1, M3 and M25 were the main residues in maize kernels, but M1 and M25 were not found in soyabean seeds.⁵⁵ Residue tests carried out livestock and poultry showed pyroxasulfone residues in goat milk, meat, liver and kidney and low level residue in egg yolks and whites, liver, muscle, skin and fat of laying hens.

The Acceptable Daily Intake (ADI) proposed by the Australian regulators is 0.002mg/kg of body weight per day,⁵⁶ which is lower than acetochlor (0.0036mg/kg bw/d) or flumioxazin (0.009mg/kg bw/d).⁵⁷

d) Conclusion

Despite the lack of independent research on pyroxasulfone there are several significant safety concerns, including risks to babies and the developing foetus. The large human health “safety” margins and very wide no-spray zones imposed by the Australian authorities on field use of the herbicide to protect non-target plants reveal how serious these risks could be. The introduction of a new active ingredient to the growing arsenal of herbicides being approved to combat glyphosate weed resistance would add another burden to the environment and public health.

Overall conclusions

The four soil-acting herbicides featured in this briefing possess a range of hazards to long-term human health and reproduction, water quality, aquatic ecosystems and wildlife, including beneficial organisms important for pollination, soil nutrient cycling and other ecological services.

If GM herbicide-tolerant crops are introduced in the EU their cultivation is likely to be accompanied by an escalation in herbicide use. There are already concerns about the indirect impact of current

GM Freeze 50 South Yorkshire Buildings, Silkstone Common, Barnsley S75 4RJ
 Tel: 0845 217 8992 Email: info@gmfreeze.org Web: www.gmfreeze.org Twitter: @GMFreeze

levels of herbicide use on biodiversity, particularly in relation to flowering plants around fields and along water courses, and the insects, including pollinators, and birds that rely on these for food and habitat.^{58 and 59} If the EU approves GM RR crops it will come under pressure to authorise herbicides in Monsanto's proposed "platform" to try and contain the inevitable appearance of glyphosate resistant weeds, including to bring back herbicides like acetochlor for which the EU withdrew approval in 2011 for health and environmental reasons. Expanded use of the herbicides in the "platform" would represent a serious and unnecessary burden on the EU environment, bringing additional risks to health, the environment and water quality. Herbicide-related damage also poses an economic burden, including the costs of treating contaminated water supplies, adverse health effects suffered by those exposed to these herbicides and yield losses from reduced pollination.

The herbicides included in Monsanto proposed "platform" for RR crop weed control have not been tested in combinations, so potential additive or synergistic effects between them have not been assessed. The formulations sold to farmers will contain other chemicals (adjuvants) to make them work more effectively, and the toxicity of these commercial products may also differ from the active ingredients alone.

Any EU approval of RR crops in the EU, including the "platform" of associated herbicides, is tantamount to approving a large-scale impact experiment of herbicide combinations in the countryside without regulatory controls.

Granting approval for GM herbicide tolerant crops could also increase the trend to monocultures in arable farming, leading not only to more herbicide use but also further use of insecticides and fungicides to control pests and diseases. Such increases would undermine the efforts of the EU Directive on Sustainable Use of Pesticides to reduce reliance on pesticides and run counter to aims to make European farming more sustainable under the Common Agricultural Policy. The EU should not allow corporate interests to take agriculture down such an unsustainable route and must weigh up the medium- to long-term consequences of increased herbicide use before rushing to approve herbicide tolerant crops.

Europe would be better served by policy support to help farmers adopt agroecological methods using expanded crop rotations, crop diversity, physical and mechanical methods and biological control to ensure pests, diseases and weeds can be managed effectively, safely and sustainably.

Notes

¹ GM Freeze and Pesticide Action Network, 2 August 2012. [GM Herbicide Tolerant Crops – Less Equals More](#). This suite of briefings looks at the herbicides being lined up by the biotech industry (2,4-D, dicamba and glufosinate ammonium) to be used alone or in rotation with glyphosate on GM herbicide tolerant crops to try and prevent weeds with resistance to glyphosate surviving, producing seed and spreading.

² Riley P, 2010. "Resistant weeds cast a shadow over glyphosate resistant crops Pesticides". New 87:3-5

³ Heap I, November 2012. "The international Survey of Herbicide Resistant Weeds". Available at www.weedscience.com

⁴ Steckel L, 2011. "New technology and the future of pigweed control". Presentation to the Pig Posium organised by the University of Arkansas. See www.youtube.com/watch?v=2_iJhIGtOJM&feature=related

⁵ Pesticides Action Network UK and GM Freeze, 2012. *Op cit*

⁶ GM Freeze and Pesticide Action Network, 2 August 2012. *Op cit*

⁷ Benbrook CM, 2012. "Impacts of genetically engineered crops on pesticide use in the US - The first sixteen years". *Environmental Sciences Europe* 2012, 24:24 doi:10.1186/2190-4715-24-24

⁸ *Ibid*

⁹ Heap I, 18 April 2013. *Op cit*

¹⁰ Greenpeace International, 30 October 2012. [Glyphosate tolerant crops in Europe](#)

¹¹ US Environmental Protection Agency, 2008. *Flumioxazin: EPA Petition Response for the Extension of the Exclusive Use Data*

¹² Pesticide Action Network, January 2011. [PAN International List of Highly Hazardous Pesticides](#)

- ¹³ Australian Pesticides and Veterinary Medicine Authority, December 2003. "[FLUMIOXAZIN in the product Pledge 500 WG Herbicide](#)"
- ¹⁴ Australian Pesticides and Veterinary Medicine Authority, December 2003. *Ibid*
- ¹⁵ US Environmental Protection Agency, 31 December 2002. "Flumioxazin: Notice of Filing a Pesticide Petition to Establish a Tolerance for a Certain Pesticide Chemical in or on Food". Federal Register: December 31, 2002 (Volume 67, Number 251)
- ¹⁶ US Environmental Protection Agency, 14 August 2003. "[Flumioxazin: Environmental fate and Ecological Risk Assessment: Cotton, almonds, grapes, sugar cane, container and field ornamentals and Christmas and Deciduous trees](#)"
- ¹⁷ Valent Corporation, undated. "[Material data safety sheet Fierce herbicide](#)"
- ¹⁸ Valent Corporation, undated. *Ibid*
- ¹⁹ US Environmental Protection Agency, 2001. "[Pesticide Fact Sheet Name of Chemical: Flumioxazin Reason for Issuance: Conditional Registration](#)"
- ²⁰ US Environmental Protection Agency, 2002. *Op cit*
- ²¹ US Environmental Protection Agency, 2003. *Op cit*
- ²² European Commission. [Pesticides database](#). Consulted 9 May 2013
- ²³ US EPA, 2009. Sulfentrazone Summary Document Review: initial Docket September 2009.
- ²⁴ Monsanto, 22 October 2010. "[Monsanto, FMC Corporation Announce Crop Protection Collaboration With the Roundup Ready PLUS™ Weed Management Platform](#)"
- ²⁵ de Castro VL, Destefani CR, Diniz C and Poli P, 2007. "Evaluation of neurodevelopmental effects on rats exposed prenatally to sulfentrazone". *Neurotoxicity* 28;1249-59
- ²⁶ USEPA, 27 February 1997. [Pesticide fact sheet: Sulfentrazone](#)
- ²⁷ USEPA, 27 February 1997. *Ibid*
- ²⁸ Pekarek RA, Garvey PV, Monks DW, Jennings KM and MacRae AW, 2010. "Sulfentrazone Carryover to Vegetables and Cotton". *Weed Technology* 24;20-24
- ²⁹ US EPA, 2009. *Op cit*
- ³⁰ USEPA, 27 February 1997. *Op cit*
- ³¹ Monsanto, 2 February 2010. "Monsanto Company Receives Approval for New Acetochlor Herbicide Formulation"
and
Monsanto, undated. [Glyphosate Resistant Weed Biotypes](#)
- ³² European Commission, 22 December 2011. "Commission Implementing Regulation (EU) No 1372/2011 of 21 December 2011 concerning the non-approval of the active substance acetochlor, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Decision 2008/934/EC". *Official Journal of the European Union*
- ³³ US Environmental Protection Agency, 23 March 1994. "Pesticide Tolerances for Acetochlor". *Federal Register* Vol. 59, No. 56. Rules and Regulations
- ³⁴ Spanish Ministry of Agriculture, 2006. Monograph for the inclusion of Acetochlor in Annex 1 Directive 91/414 Volume 1 Report and Proposed Decision
- ³⁵ Pesticides Action Network, 2012. [Pesticides Database – Acetochlor](#)
- ³⁶ Crump D, Werry K, Veldhoen N, Van Aggelen G, and Helbing CC, 2007. "Exposure to the Herbicide Acetochlor Alters Thyroid Hormone-Dependent Gene Expression and Metamorphosis in *Xenopus Laevis*". *Environmental Health Perspectives* 10: 1199-1205
- ³⁷ Rollerova E, Wsolova L and Urbancikova M, 2011. "Neonatal exposure to herbicide acetochlor alters pubertal development in female wistar rats". *Toxicology Mechanism and Methods* 21:406-17
- ³⁸ Yin XH, Li SN, Zhang L, Zhu GN, and Zhuang HS, 2008. "Evaluation of DNA damage in Chinese toad (*Bufo bufo gargarizans*) after in vivo exposure to sublethal concentrations of four herbicides using the comet assay". *Ecotoxicology* 17:280-286
- ³⁹ Spanish Ministry of Agriculture, 2006. *Op cit*
- ⁴⁰ Xin-Yu L, Zhen-Chend Xu L, Cheng-Gang Z, and Hui-Wen Z, 2010. "Assessing the effects of acetochlor on soil fungal communities by DGGE and clone library analysis". *Ecotoxicology* 19:1111-1116
- ⁴¹ Barriusp J, Marin S, and Mellado RP, 2010. "Effect of the herbicide glyphosate on glyphosate-tolerant maize rhizobacterial communities: a comparison with pre-emergency applied herbicide consisting of a combination of acetochlor and terbutylazine". *Environmental Microbiology* 12: 1021-1030
- ⁴² Li X., Zhang H, Wu M, Su Z, and Zhang C, 2008. "Impact of acetochlor on ammonia-oxidizing bacteria in microcosm soils". *Journal of Environmental Science (China)* 20: 1126-1131
- ⁴³ Qi-xing Z, Qjan-ru Z, and Ji-dong L, 2006. "Toxic effects of acetochlor and methamidophos on earthworm *Eisenia fetida* in phaeozem, northeast China". *Journal of Environmental Science (China)* 18:741-745.
- ⁴⁴ Spanish Ministry of Agriculture, 2006. *Op cit*

GM Freeze 50 South Yorkshire Buildings, Silkstone Common, Barnsley S75 4RJ
Tel: 0845 217 8992 Email: info@gmfreeze.org Web: www.gmfreeze.org Twitter: @GMFreeze

PAN UK Development House, 54-64 Leonard Street, London EC2A 4LT
Tel: 0207 065 0905 Web: www.pan-uk.org

-
- ⁴⁵ Hartzler B, 2013. "Factors affecting pyroxasulfone's behaviour in the soil". Iowa State University Extension Service
- ⁴⁶ Bayer CropScience Ltd Australia, 2011. "[Sakura fact sheet](#)"
- ⁴⁷ European Commission. [Pesticides database](#). Consulted 20 March 2013.
- ⁴⁸ Australian Pesticides and Veterinary Medicine Authority, 2011. "Public release summary on the Evaluation of the New Active PYROXASULFONE in the Product SAKURA® 850 WG HERBICIDE"
- ⁴⁹ *Ibid*
- ⁵⁰ US EPA, 31 January 2013 "Memorandum: Pyroxasulfone Human Health Risk Assessment for Use of New Active Ingredient Pyroxasulfone on Soybeans"
- ⁵¹ Australian Pesticides and Veterinary Medicine Authority, 2011. *Op cit*
- ⁵² *Ibid*
- ⁵³ *Ibid*
- ⁵⁴ *Ibid*
- ⁵⁵ *Ibid*
- ⁵⁶ *Ibid*
- ⁵⁷ University of Hertfordshire , 2011. "[Pesticide Properties Database](#)"
- ⁵⁸ Preston CD, Telfer MG, Arnold HR, Carey RD, Cooper JM, Dines TD, Hill MO, Pearman, DA, Roy DB and Smart SM, 2002. "The changing flora of the UK". DEFRA, London
- ⁵⁹ Johnson RM, Ellis MD, Mullin CA and Frazier M, 2010. "Pesticides and Honey Bee Toxicity – USA". *Apidologie* 41 : 312-31