ROUNDUP - GLYPHOSATE

environmental exposure, toxicity and mechanisms of action

Innovation Lectures (INNOLEC)
Masaryk University, May 2012

Roundup – identity, use

Herbicide (pesticide targetting plants)

- **Glyphosate-based chemical**
- **used in home garden care, sidewalks, highways, …**
- **Used in large scale agriculture**
- **Used in siviculture**

Most widely used agricultural chemical globally

Dobson, Giesy and Solomon, 2003

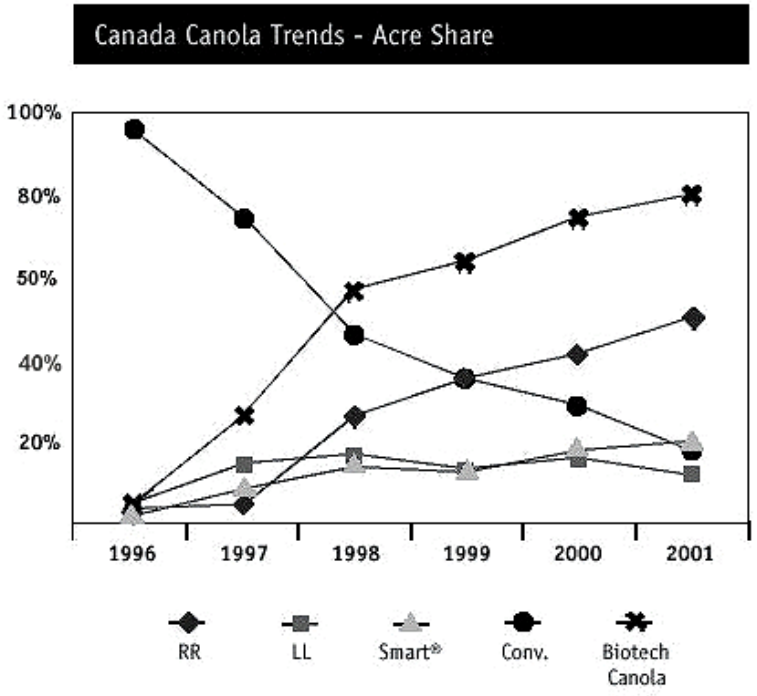
Roundup - key issues

- RR (Roundup Ready) crops
- Exponential increase in use of Roundup in large scale agriculture
- Impact on environment
- Potential impact on health of biota and human
- Control of food production by one company

Genetically modified – GM crops


Grown
for
Biofuel

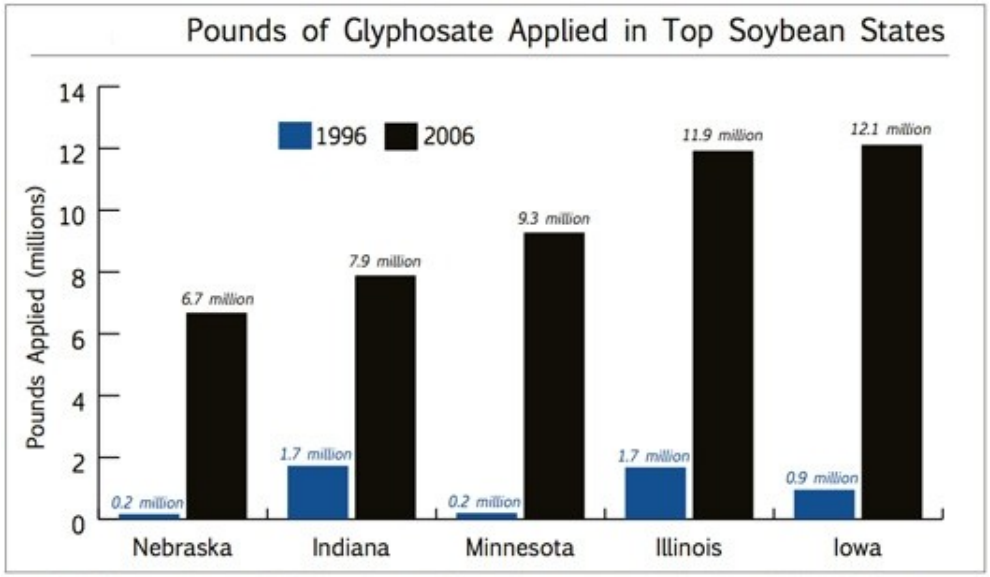
Greater use of Glyphosate herbicides linked to GM (RR) crops



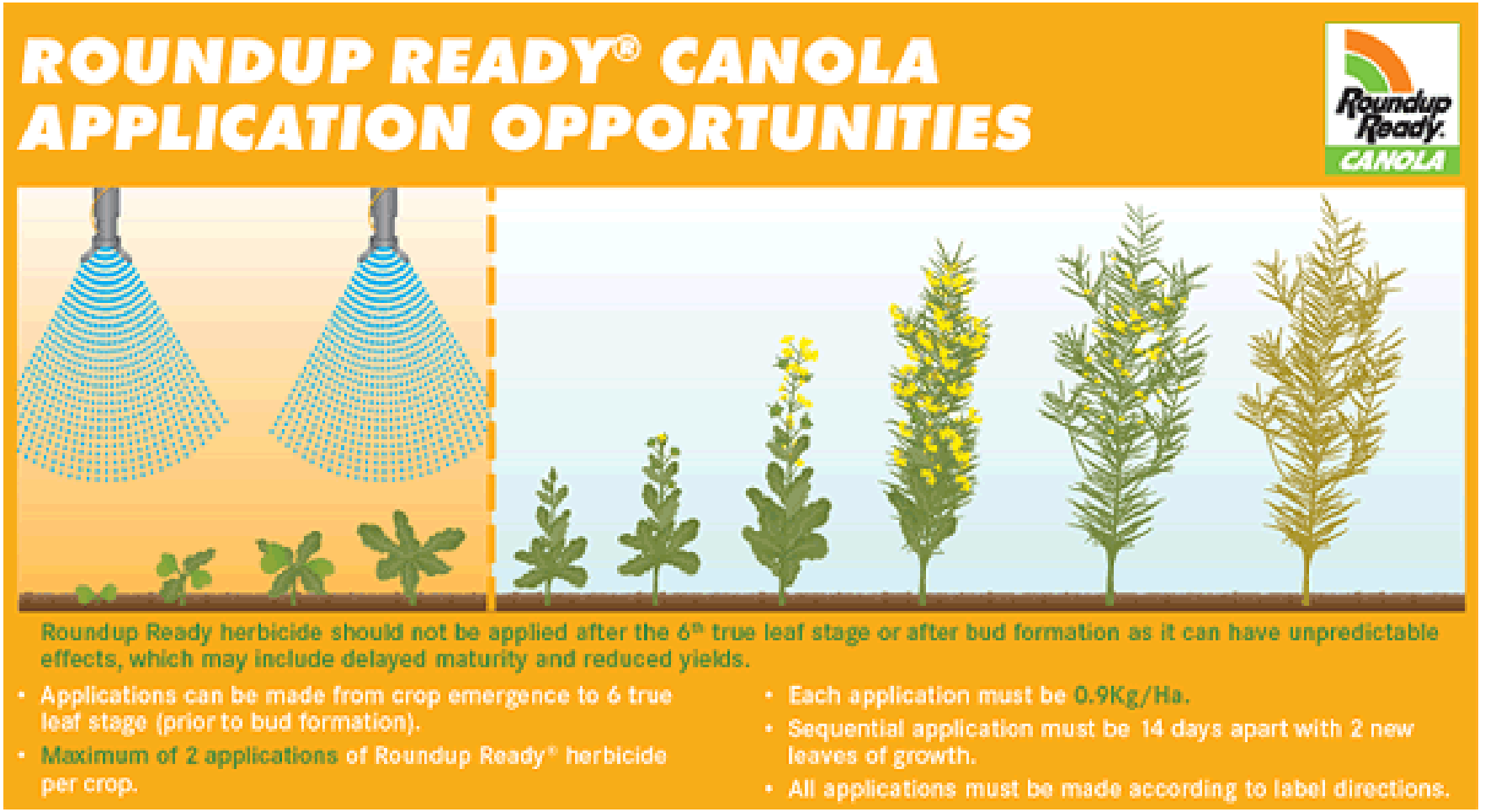
RR = *Roundup Ready*
LL = LibertyLink®

LibertyLink® is a registered trademark of Aventis.
Smart® is a registered trademark of American Cyanamid.

Source: Ipsos Reid Market Watch, 2000

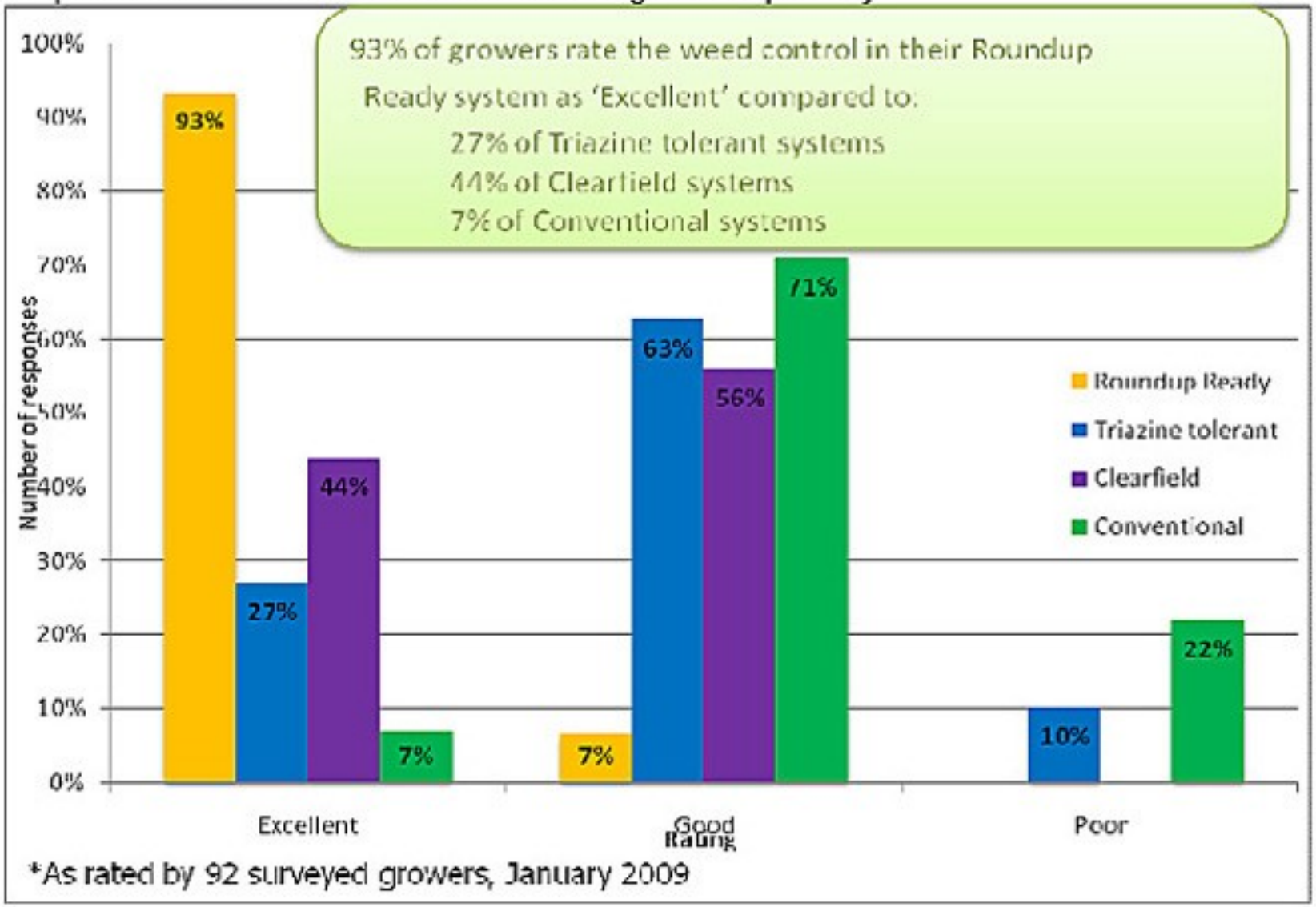


Source: USDA/NASS, Agricultural Chemical Usage 2006 Field Crops Summary, May 2007 at http://usda.mannlib.cornell.edu/usda/nass/AgriChemUsFc//2000s/2007/AgriChemUsFc-05-16-2007_revision.txt; Agricultural Chemical Usage 1996 Field Crops Summary, September 1997 at http://usda.mannlib.cornell.edu/usda/nass/AgriChemUsFc//1990s/1997/AgriChemUsFc-09-03-1997.txt.



- **Roundup applied at specific time intervals**
- **RR genetically modified plants grow but weeds are killed**
- **Greater productivity of RR crops**

Graph A. Effectiveness of Weed Control using Roundup Ready



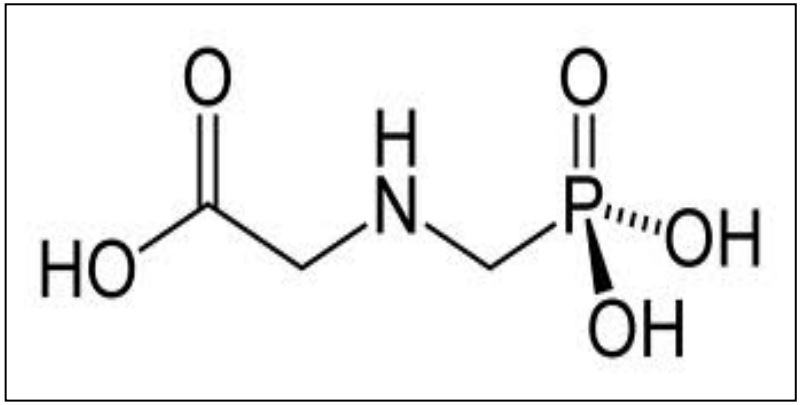
Roundup Ready (RR) crops have good yields

21 Biotech Crop Countries and Mega-Countries*, 2005

* 14 biotech mega-countries growing 50,000 hectares, or more, of biotech crops.

Source: Clive James, 2005

1. Identity and mode of action of RU



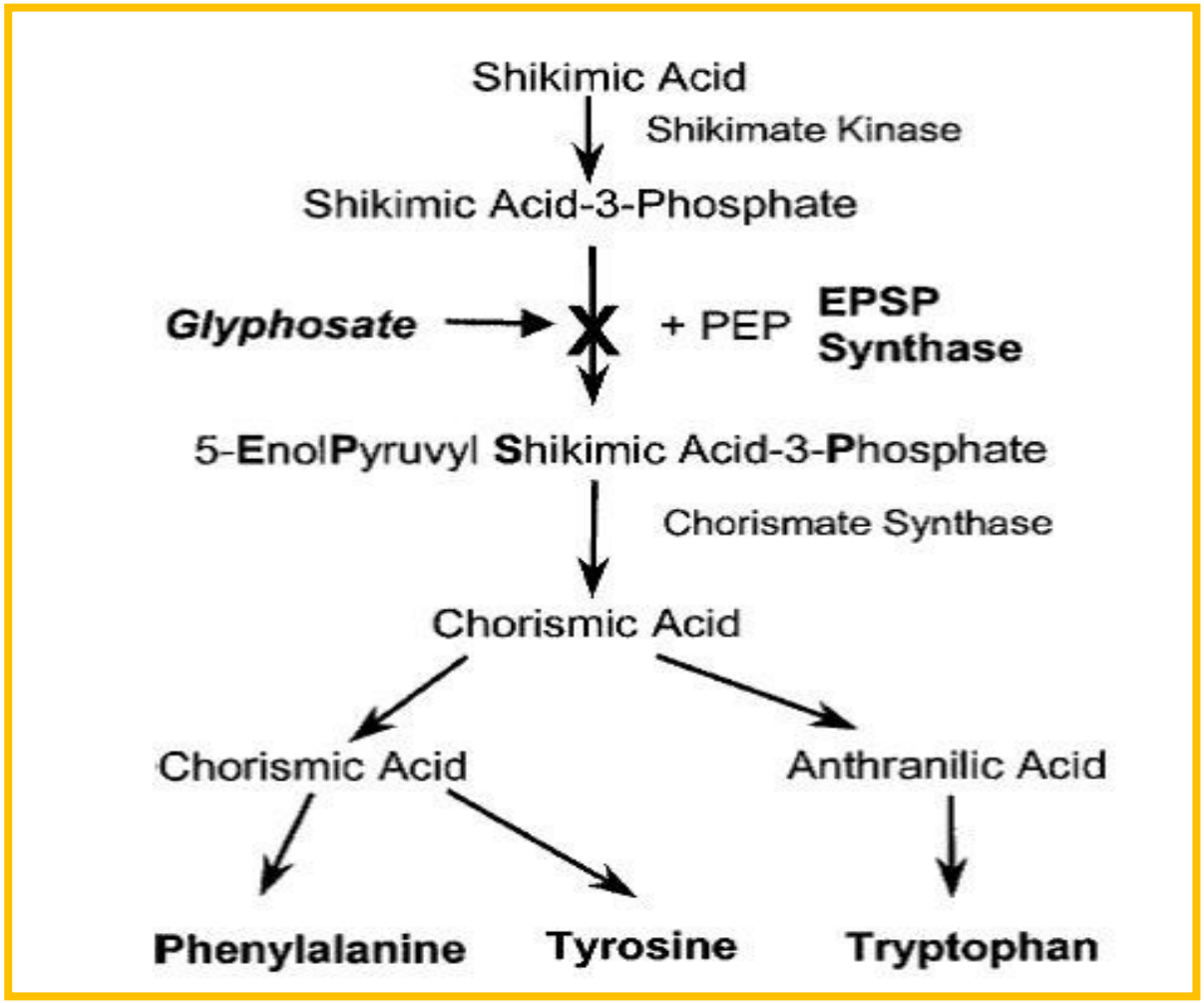
glyphosate

- **Glyphosate - active ingredient of Roundup**
- **weak organic acid, *N*-(phosphonomethyl)glycine**
- **non-selective herbicide**
- **herbicidal action**

  inhibition of synthesis of aromatic amino acids
- **Roundup=glyphosate, surfactants, water, …**

Herbicidal action of glyphosate inhibition of EPSPS

(5-EnolPyruvyl Shikimic acid-3-Phosphate Synthase)



2. Degradation products of Glyphosate

AMPA
Aminomethyl-phosphonic acid

N.B.
Surfactant(s)
POEA
Polyethoxylated tallowamine used in commercial glyphosate preparations

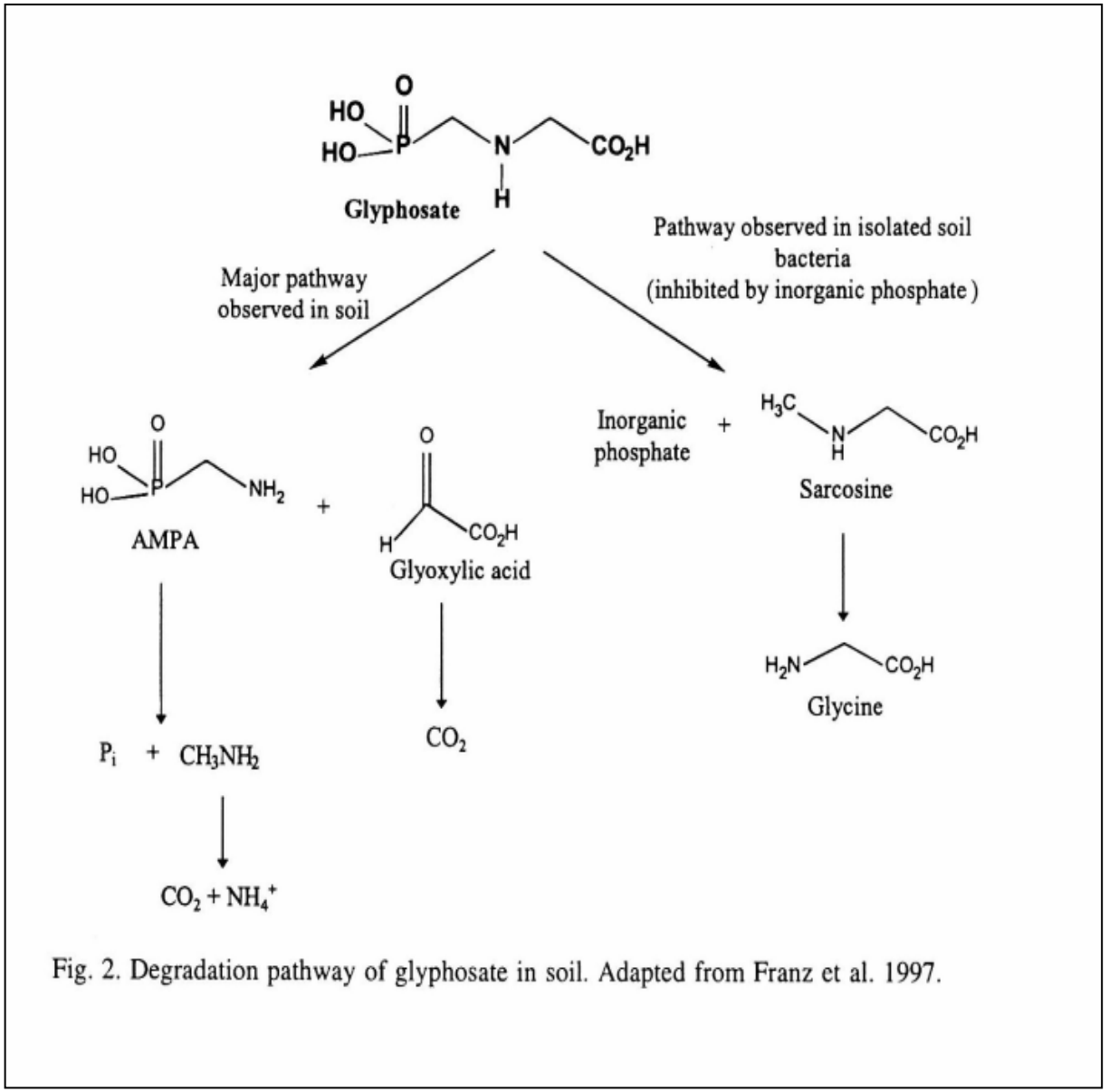


Fig. 2. Degradation pathway of glyphosate in soil. Adapted from Franz et al. 1997.

2. Roundup - Glyphosate Exposure

Sorption, degradation, leachability of GL

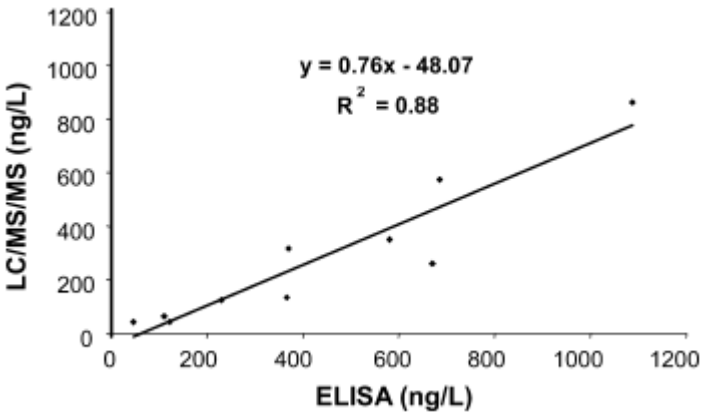
- **strong sorption of GL to soil particles**
- **contamination of ground water limited**
- **leaching of GL to surface waters during rain events**
- **spraying over water, spray drift**

Byer et al. 2008 Environ Sci Technol

TABLE 1. Comparison of LC/MS/MS and ELISA for Glyphosate in Urban Creeks (ng/L)

	Highland Creek			Mimico Creek			Indian Creek		
	LC/MS/MS		ELISA	LC/MS/MS		ELISA	LC/MS/MS		ELISA
sampled	AMPA	Gly.	Gly.	AMPA	Gly.	Gly.	AMPA	Gly.	Gly.
17-Apr-07	nd	nd	bl	61.7	nd	bl	nd[a]	nd	nd
14-May-07	nd	nd	nd	81	nd	(74)tc	42.6	nd	nd
16-May-07	115	42.7	123	167	42.2	(47)tc	219	132	367
16-Jul-07	59	124	231	591	350	581	351	316	371
19-Jul-07	972	11800	12000	324	862	1090	102	575	686
21-Aug-07[b]	85	nd	bl	1270	63	111	85.6	20.8	bl
							57.7	nd	bl
							65.3	27.9	bl
							nd[c]	nd[c]	nd[c]
17-Sep-07	73	nd	nd	2080	260	670	108	32.6	bl
							nd[c]	nd[c]	nd[c]
							nd[d]	nd[d]	nd[d]
							nd[e]	nd[e]	nd[e]

[a] nd = value <20 ng/L for LC/MS/MS, and "no detect" for ELISA; bl = < 3 × MilliQ; tc = trace level, > 3 × MilliQ < MDL. [b] On Aug 21 samples were collected in triplicate from Indian Creek. [c] Represents field blank. [d] Represent travel blank. [e] Represent laboratory blank.



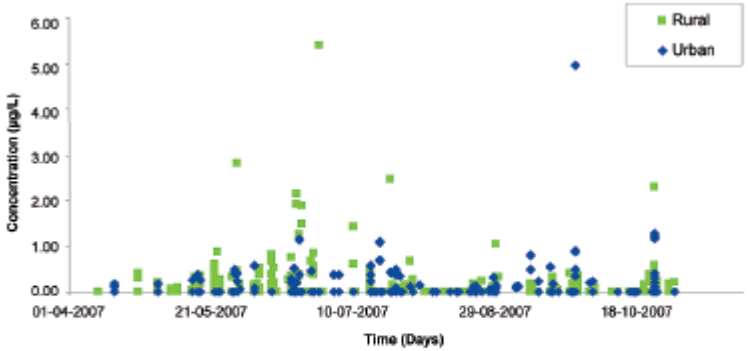
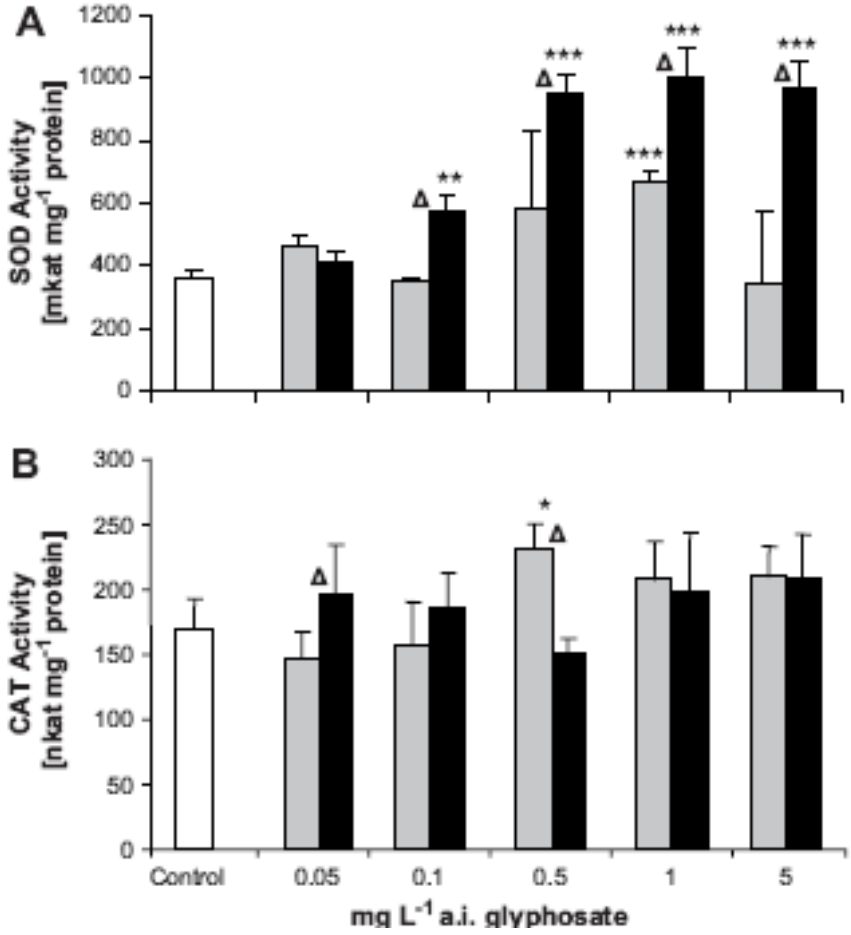


FIGURE 4. Glyphosate occurrence in surface water samples in Ontario from April to October 2007. A sample with concentration 12.0 µg/L collected on July 19 during a precipitation event in an urban creek is not shown.

Toxicity of Roundup - Glyphosate

- **invertebrates**



Contardo-Jara et al. 2009
Environ Pollution

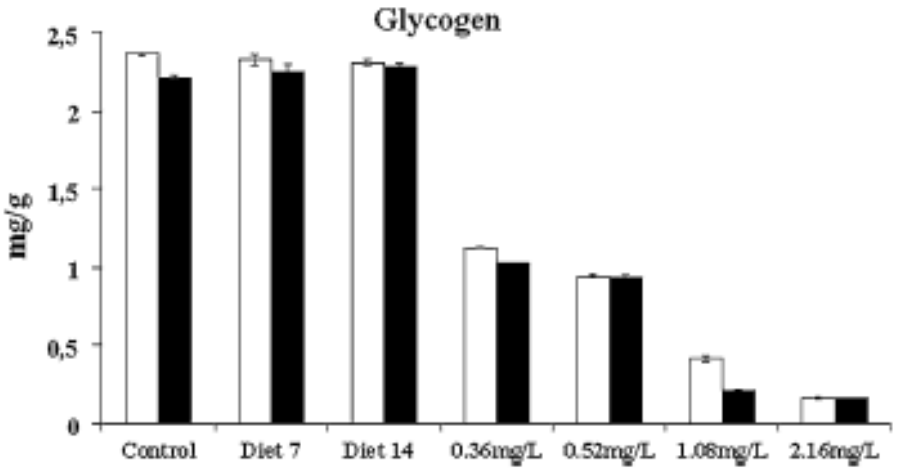
Exposure to GL in *Lumbricus* - link to oxidative stress

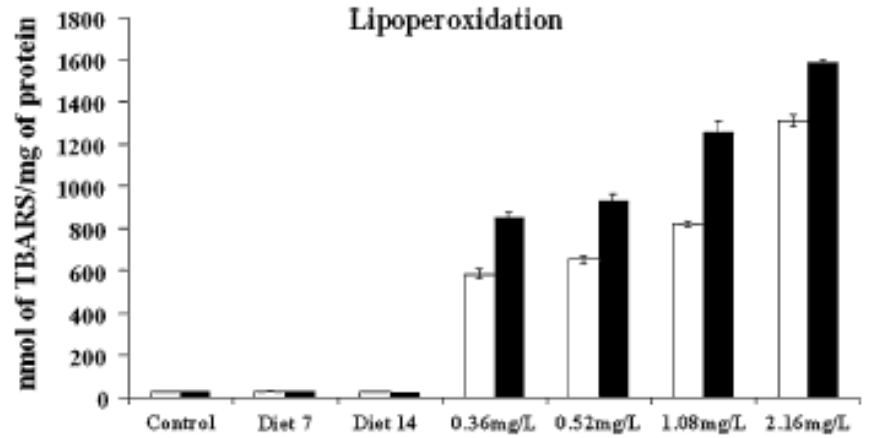
Toxicity of Roundup - Glyphosate

- **invertebrates**

Table 1 Number of mating pairs and ovigerous females of *Hyalella castroi* exposed to different treatments

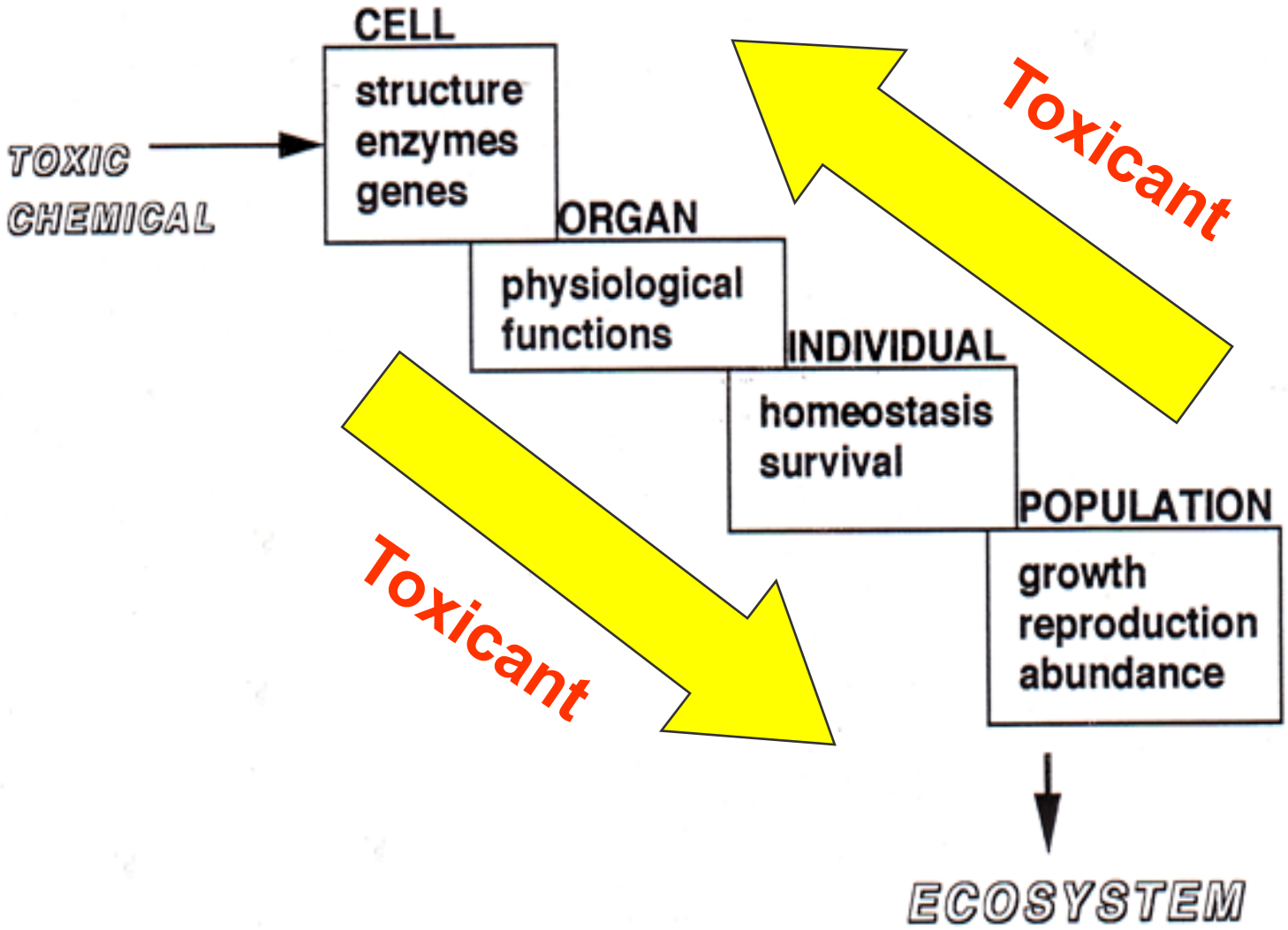
	Number of mating pairs	Ovigerous females	Mean number of eggs
Control (wild-caught)	–	20	30 ± 6
Diet			
7 days	18	15	30 ± 4
14 days	17	13	32 ± 7
Glyphosate I	4	0	0
Glyphosate II	0	0	0
Glyphosate III	0	0	0
Glyphosate IV	0	0	0





Effect of RU on energetic status, lipid peroxidation, reproductive fitness of *Hyalella* *Dutra et al. 2011Ecotoxicology*

Effects at different levels of biological organisation



Mechanistic links between exposure and effects

Toxicity

- **Fish**

Toxicity:

RU >GL
Surfactant > GL

Folmar et al. 1979

Table 6. Effects of pH on toxicity of Roundup, glyphosate, and the surfactant to rainbow trout and bluegills

Chemicals, organism, and pH	LC50 (mg/L) and 95% confidence limits	
	24 h	96 h
Roundup		
Rainbow trout		
6.5	14 (12–17)	7.6 (6.4–9.1)
7.5	2.4 (2.0–2.9)	1.6 (1.2–2.2)
8.5	2.4 (2.0–2.9)	1.4 (1.2–1.7)
9.5	2.4 (2.0–2.9)	1.4 (1.2–1.7)
Bluegills		
6.5	7.6 (6.4–9.1)	4.2 (3.5–5.0)
7.5	4.0 (3.2–5.0)	2.4 (2.0–2.9)
8.5	3.9 (3.1–4.9)	2.4 (2.0–2.9)
9.5	2.4 (2.0–2.9)	1.8 (1.3–2.5)
Glyphosate		
Rainbow trout		
6.5	240 (200–290)	140 (120–170)
9.5	240 (200–290)	240 (200–290)
Bluegills		
6.5	240 (200–290)	140 (120–170)
9.5	230 (190–280)	220 (170–280)
Surfactant		
Rainbow trout		
6.5	7.4 (6.2–8.9)	7.4 (6.1–9.0)
9.5	1.4 (1.2–1.7)	0.65 (0.54–0.78)
Bluegills		
6.5	4.2 (3.1–5.7)	1.3 (1.1–1.6)
9.5	3.0 (2.2–4.1)	1.0 (0.72–1.4)

Toxicity of Roundup - Glyphosate

- **Human placental cells JEG3**

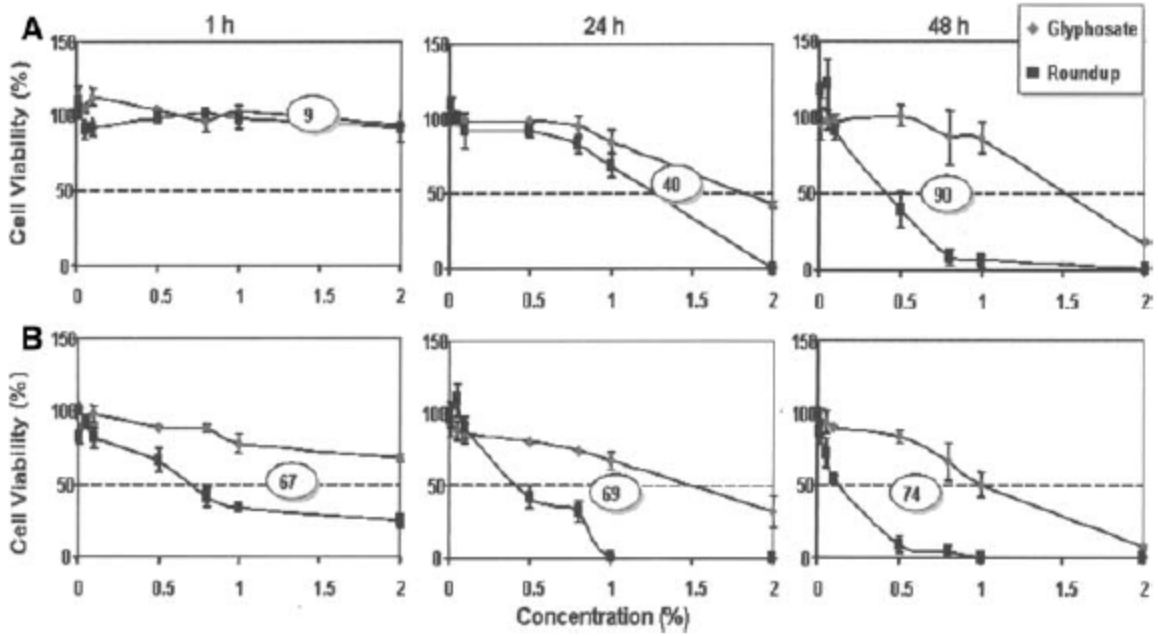


Fig. 2. Effects of Roundup and equivalent quantities of glyphosate on JEG3 cell viability in serum-containing medium (***A***) or in serum-free medium (***B***) for various times (1, 24, 48 h). The other details are indicated in the legend of Figure 1

Compare

- **toxicity in serum-containing and serum-free medium**
- **toxicity of RU and GL**

Benachour et al. 2007 Arch Env Contam Toxicol

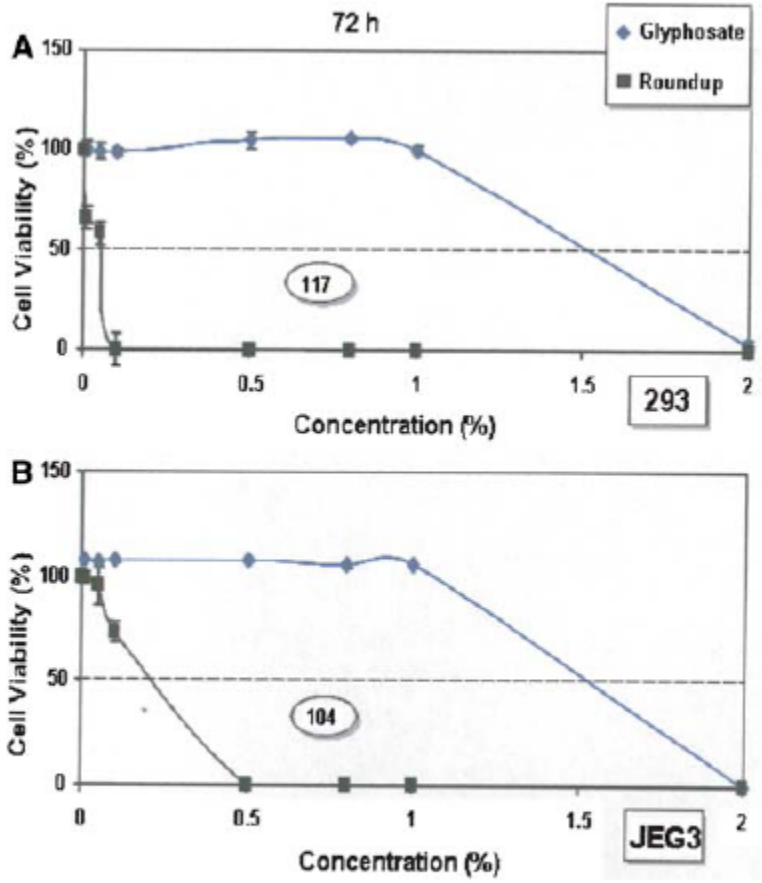


Fig. 3. Effects of Roundup and equivalent quantities of glyphosate on 293 (*A*) and JEG3 (*B*) cell viability in serum-containing medium for 72 h. Without serum, the cells do not survive 72 h. The other details are indicated in the legend of Figure 1

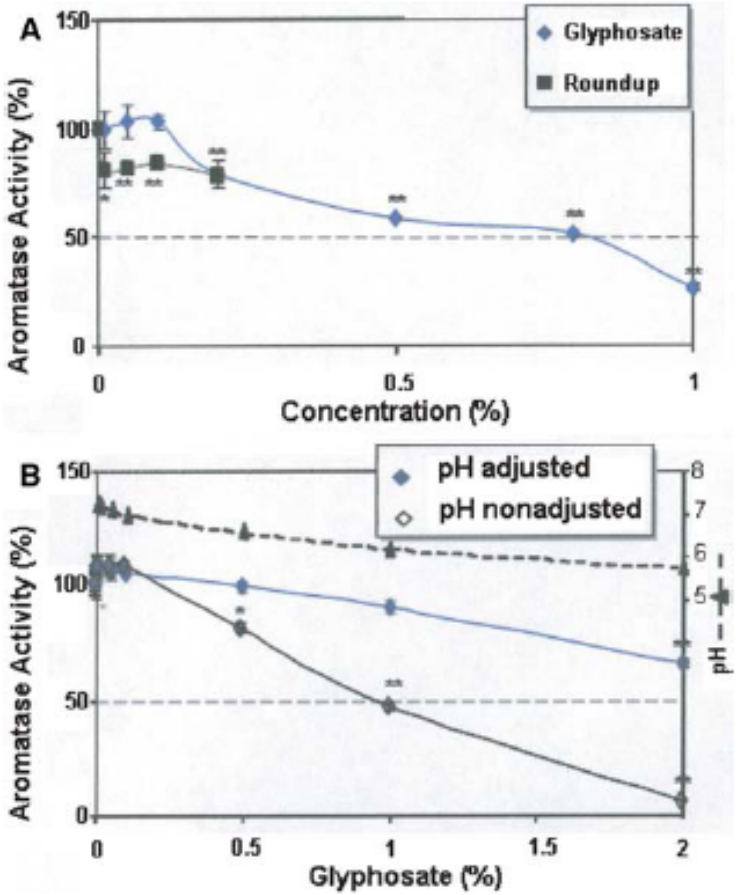
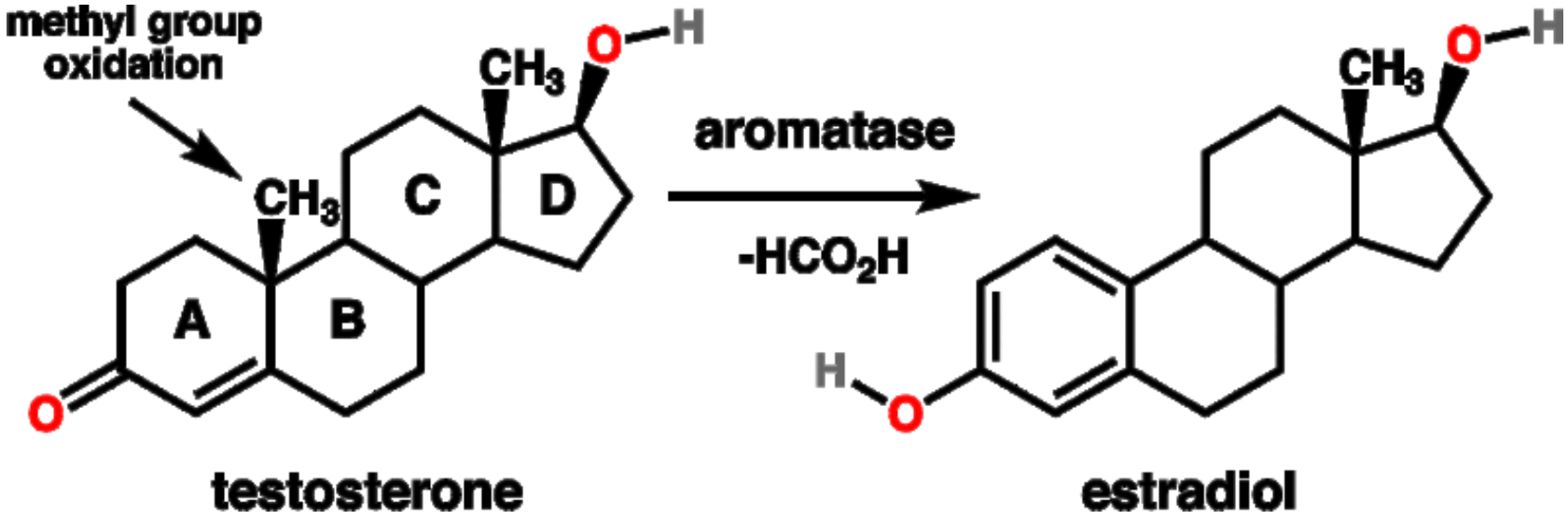


Fig. 4. Effects of glyphosate and equivalent quantities of Roundup on human aromatase activity in 293 cells in serum-free medium after 24 h (*A*) at nontoxic concentrations below 0.2 and 1% for Roundup and glyphosate, respectively. Effects of glyphosate alone on human aromatase activity in placental microsomes after 15 min and at 37°C (*B*) at pH adjusted (to the Roundup pH, - -▲- -) or nonadjusted, decreasing to pH 2.96 at 2%

Toxicity of RU >> Toxicity of GL
similar results with HepG2 cells

Role of aromatase in steroidogenesis



Toxicity of Roundup - Glyphosate

Roundup inhibits steroidogenesis in rats by disruption of StAR protein expression

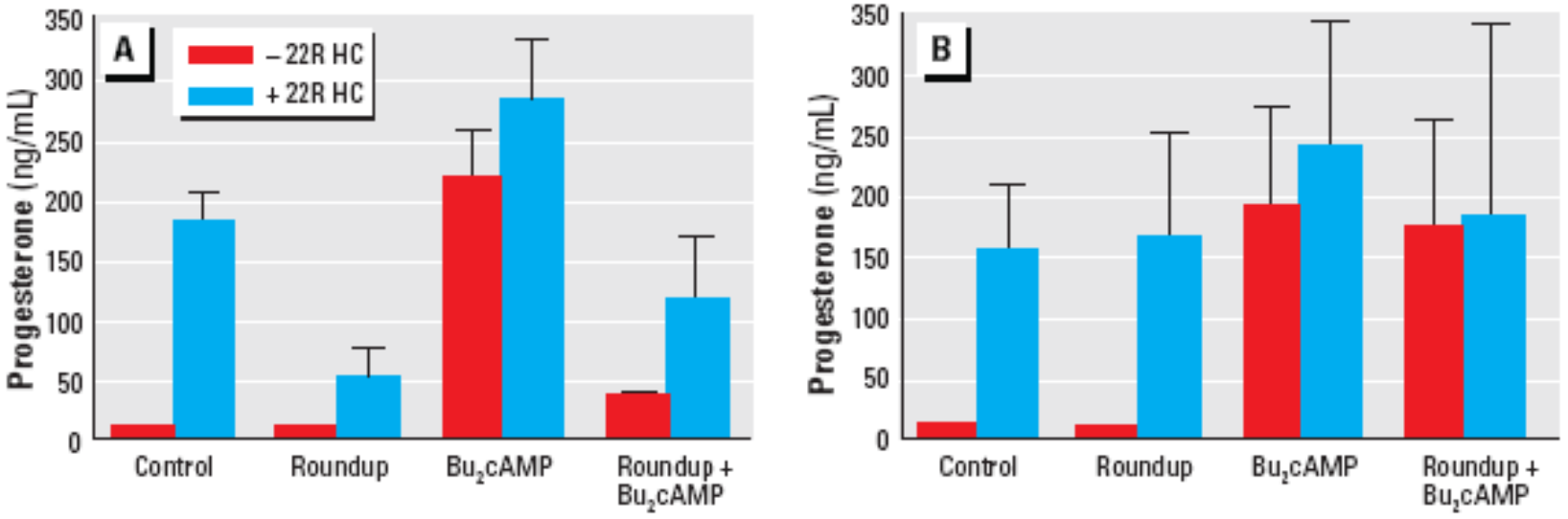
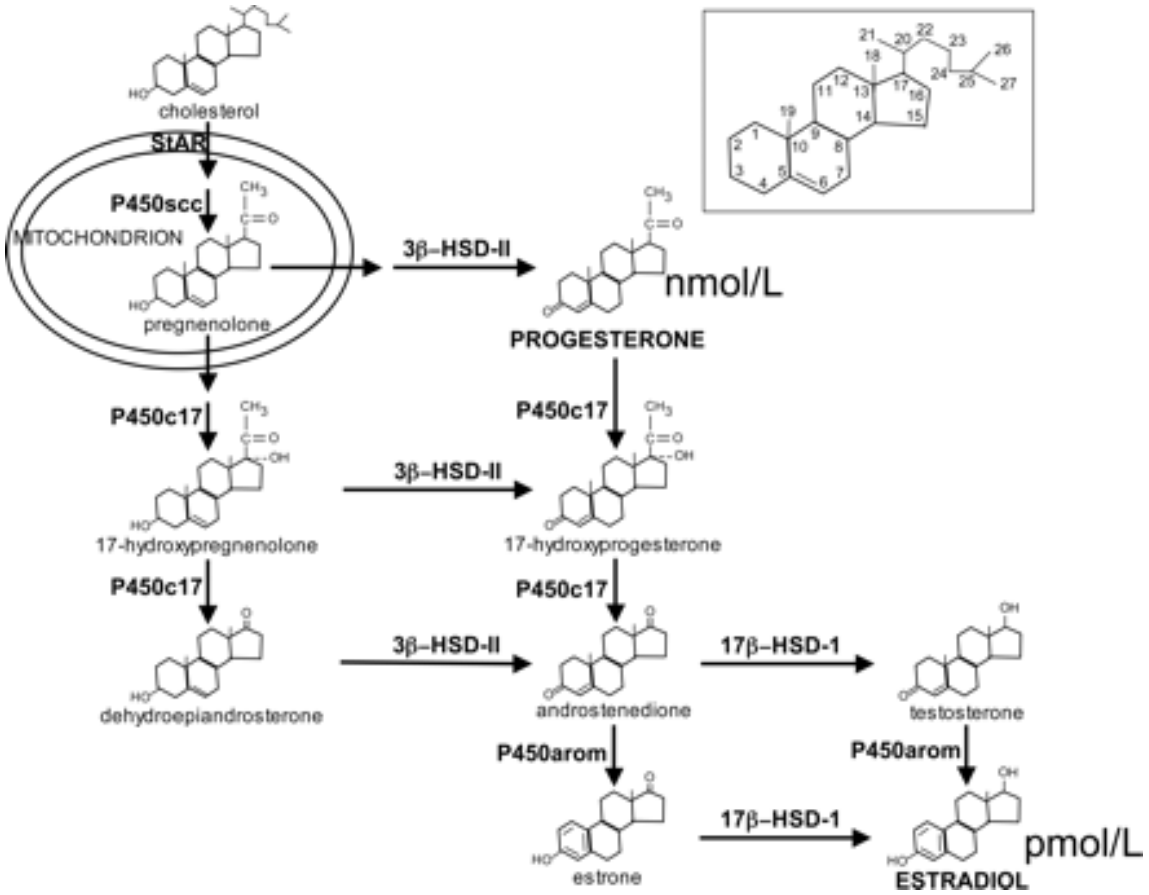


Figure 2. Effects of Roundup on P450scc and 3β-HSD enzyme activity and steroidogenesis in MA-10 cells. (*A*) Effects of 2-hr treatment with Roundup on progesterone production. The difference between $(Bu)_2$cAMP and Roundup + $(Bu)_2$cAMP was statistically significant ($p < 0.01$). (*B*) Effects of 2-hr treament with Roundup on progesterone production after a 24-hr recovery.

Walsh et al. 2000

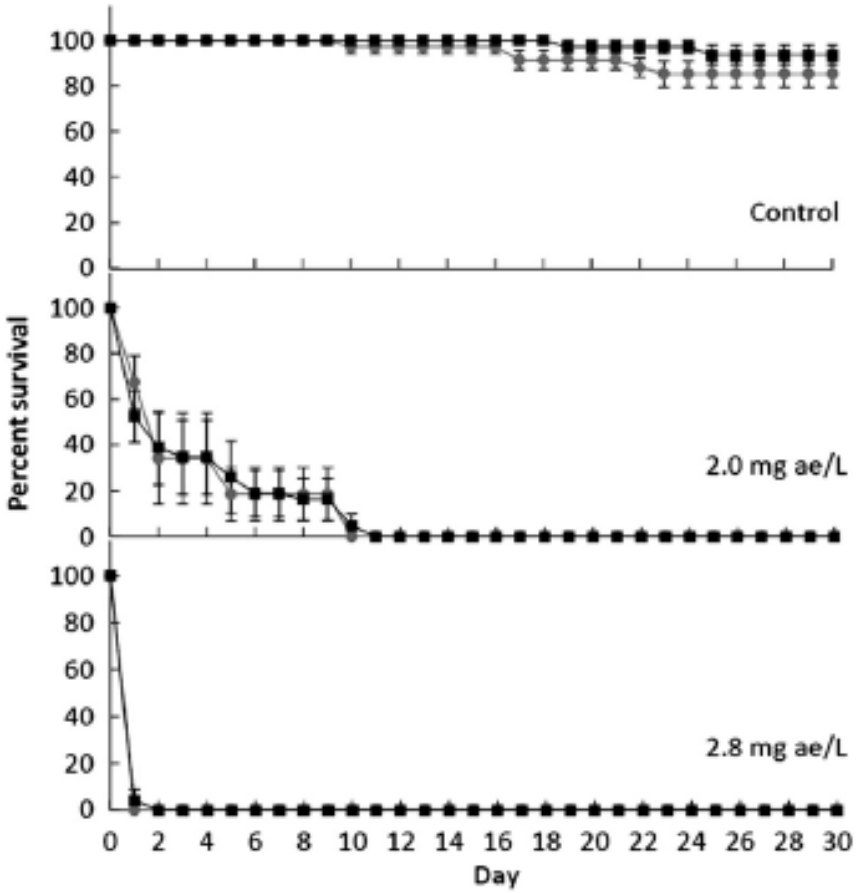
Role of StAR (Steroid Acute Regulatory Protein) in steroidogenesis



Stocco, 2000

Toxicity of Roundup - Glyphosate

- **Amphibians**



- **very sensitive to RU-GL**

Dinehart et al. 2010 Env Poll

studies by Relyea controversy

[chronic toxicity] ≃ [environmental]
HQ (Hazard Quotient) analysis

HQ analysis = Exposure level : toxicity reference value

HQ < 1.0 **no risk, acceptable risk**

HQ > 1.0 **need for further evaluation**

HQ > 100 **definite risk**

Giesy, Dobson and Solomon, 2000
Ecological Risk Assessment for Roundup Herbicide
Rev Environ Contam Toxicol 167: 35-120

Toxicity of Roundup – Glyphosate

- **Health concerns**

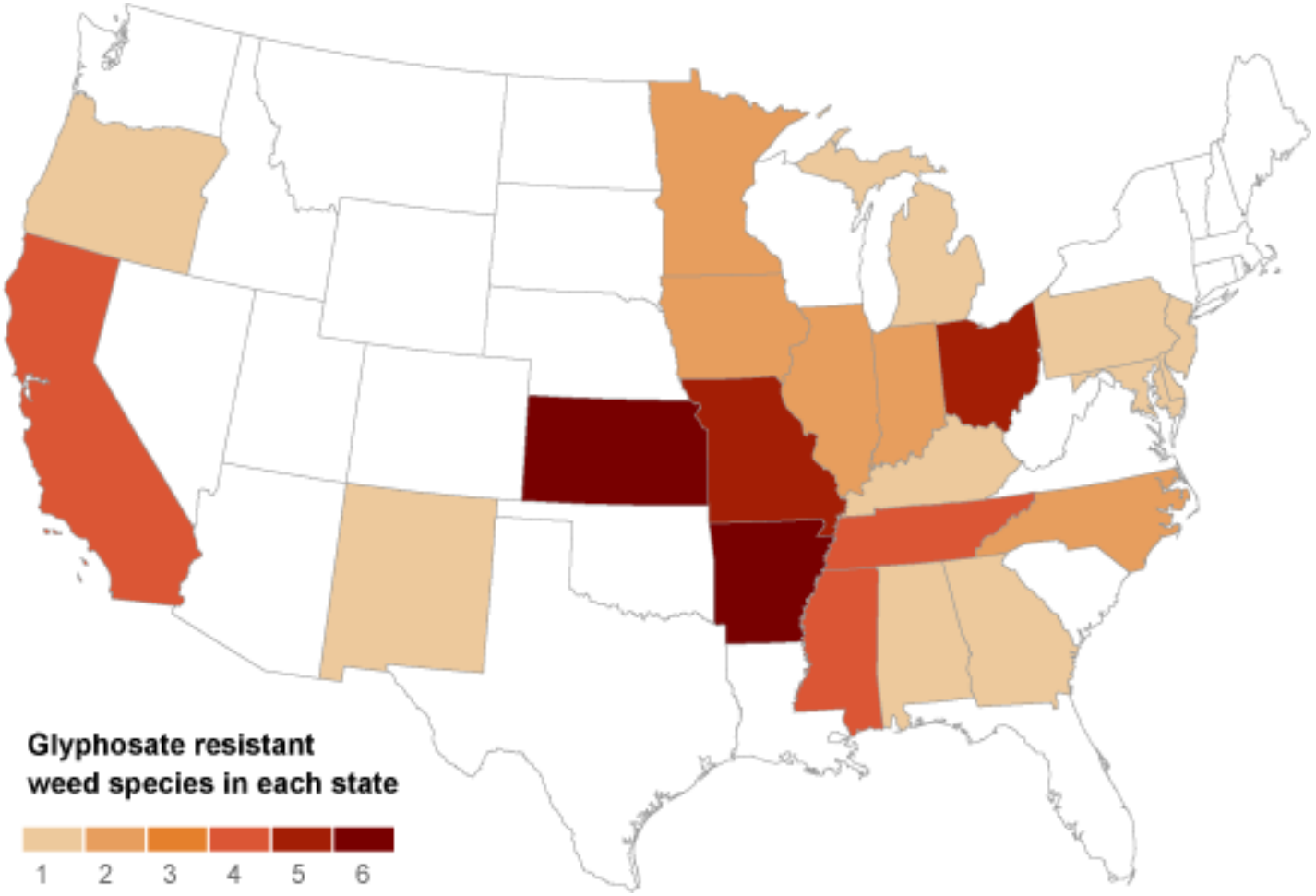
Amphibians - highly sensitive
toxicity to larvae at environmental concentrations (1-2 mg/L)

Endocrine disruption
effects on aromatase
effects on StAR protein

Toxicity to non target plant species

ROUNDUP/GLYPHOSATE - CONCERNS

- **Evolution of Glyphosate-resistant weeds**



- # Dependance of food production on GM seeds

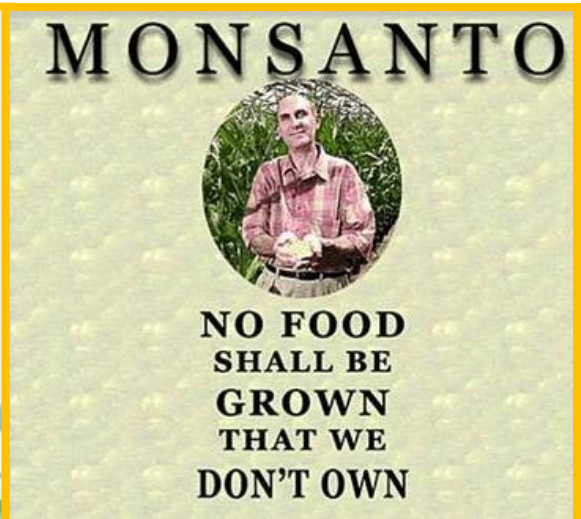
Table 1 **Differences between Roundup Ready and non-GM canola systems**

Factor	Non-GM canola (TT, CL & conventional)	Roundup Ready canola
Timing of decision to grow	Can delay until sowing.	Need to complete accreditation course and order seed early.
Cost of seed	Variable, depending on variety.	$3–25/kg (2009) depending on whether open-pollinated or hybrid.
Training and legal agreements to use seed	None.	Accreditation, Licence and Stewardship Agreement, Technology User Agreement. End-point royalty payable—$12.60/t in 2009. No "grower-saved seed" allowed.
Roundup Ready herbicide on crop	No.	Yes, before 6 leaf stage.
Spraying timetable	Moderately flexible.	Very tight.
Weed walk required	No, but desirable.	Yes, mandatory 14–28 days after spraying.
Yield	TT is generally less than non-TT types.	Similar to most non-TT canola types.
Delivery	Most receival sites. No extra fees unless to prove non-GM for CSO1-A.	Restricted receival sites (check storage and handler website).
Price	May gain premium over GM canola for small parcels in specific markets.	As for international pricing of GM canola.

Risk assessment for Roundup

Biofuel production
Food production

Greater use of RU
Economics of food production
Contamination of surface water
Health risks



Waterton National Park – Alberta, Canada