

Substantially Equivalent or not?

- *The important discussion on comparators*



Thomas Bøhn PhD
GenØk - Centre for Biosafety
Professor of Gene Ecology
UIT The University of Tromsø



GenØk

– Centre for Biosafety

“Safer use of biotechnology!”
“Safer use (bio)technology”

- *Independent research* on modern biotechnologies



GenØk, Tromsø



GenØk, Tromsø





Where do we meet the “Substantial Equivalence Principle”?

1. Testing by the product owner

- Measurements of **compositional elements**
 - Nutrients
 - Amino acids
 - Protein
 - Carbohydrates
 - Fibre
 - Oil
 - Testing the transgenic product by itself

2. Used to conclude on product safety



Example of use (NK603)

- These comparisons, together with the history of the safe use of corn as a common component of animal feed and human food, support the conclusion that Roundup Ready corn event NK603 is compositionally equivalent to, and as safe and nutritious as, conventional corn hybrids grown commercially today.

From
Ridley et al. 2002 J. Agric. Food Chem.
(Product Safety Center, Monsanto)



History of Roundup Ready GM soy testing (40-3-2 event)

- 1995-1999
 - Compositional analysis from unsprayed plants(!)
- 1999
 - “Must spray herbicide tolerant GM plants before testing” (Millstone 1999, *Nature*)



Quick response

- The analytical results from these studies demonstrate that the **GTS soybeans treated with glyphosate were comparable to the parental soybean cultivar, A5403, and other conventional soybean varieties.** (Tailor et al. 1999)

From
Tailor et al. 1999 J. Agric. Food Chem.
(Product Safety Center, Monsanto)



Feeding tests with herbicide tolerant (Roundup Ready) GM plants

- 2000-2013
 - 13 out of 16 feeding studies with herbicide tolerant GM crops did not spray the plant

(From Viljoen 2013 *Food and Chemical Toxicology*)

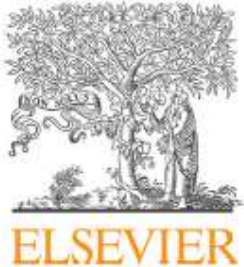


Food for thought

1. Tested Herbicide Tolerant GM plants are typically not sprayed!
2. Residues of herbicides have not been considered relevant as a compositional element, even in *Herbicide Tolerant GM plants*
3. Residues of herbicides have not been systematically monitored in food and feed



Our testing of RR GM soybeans



Contents lists available at [ScienceDirect](#)

Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem

Compositional differences in soybeans on the market: Glyphosate accumulates in Roundup Ready GM soybeans[☆]

T. Bøhn^{a,b,*}, M. Cuhra^{a,b}, T. Traavik^{a,b}, M. Sanden^c, J. Fagan^d, R. Primicerio^b

^a GenØk, Centre for Biosafety, P.O. Box 6418, 9294 Tromsø, Norway

^b Faculty of Health Sciences, UIT The Arctic University of Norway, 9019 Tromsø, Norway

^c National Institute of Nutrition and Seafood Research, NIFES, P.O. Box 2029, 5817 Bergen, Norway

^d Earth Open Source, 2nd Floor 145-157, St. John Street, London EC1V 4PY, United Kingdom



Soy material for testing

Iowa farmers
(n=31)

- GM (n=10)
- Conv. (n=10)
- Organic (n=11)



Production system description

	New genes	Herbicides	Pesticides
RR GM soy	X	X	X
Conventional			X(X)
Organic			

Interactions?



Impacts of Genetically Engineered Crops on Pesticide Use in the United States: The First Thirteen Years

by Charles Benbrook

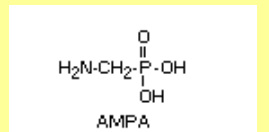
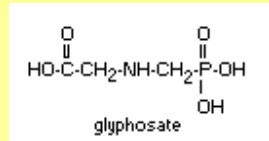
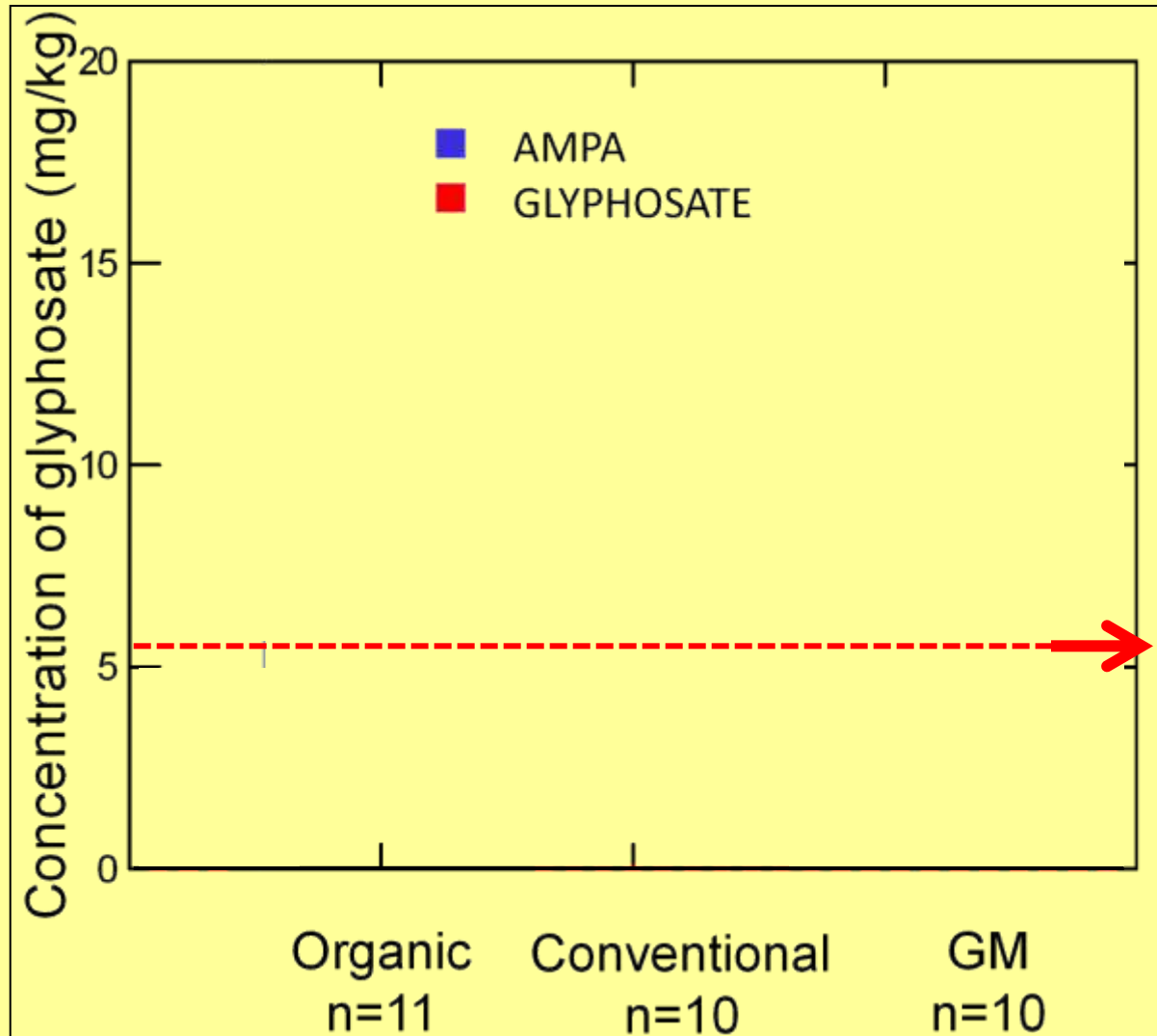
November 2009

Pesticides used

Type of soy	Variety	Seed treatment	Preplant	Postplant	Insecticide	Fungicide
RR GM	Latham 2158			Touchdown	Warhawk, Silencer	
RR GM	PB 2217VNRR			Roundup Power Max	Warrior, Lorsban	
RR GM	PB 2421			Roundup Power Max	Warrior	
RR GM	Pioneer 92M76	Cruiser Maxx		Touchdown	Cobalt	
RR GM	Stine		Trifluralin	Roundup		Apron Max
RR GM	Stine 2032	Cruiser Extreme		Roundup		
RR GM	Stine 2032			Roundup		
RR GM	Stine 2062-4			Touchdown	Warhawk, Silencer	Headline
RR GM	Stine 2538-4	Warden		Roundup (original Max), Durango	Leverage	Domark
RR GM	Stine 2602-4	Warden		Roundup (original Max), Durango	Leverage	Domark
Conventional	Asgrow 2869			Pursuit plus, Select, Flexstar	Lorsban, Warrior	Headline
Conventional	Asgrow 2869	Cruiser Maxx	Trust	Select, Flexstar, First Rate	Lorsban	
Conventional	Legend 2200			Pursuit plus, Select, Flexstar	Lorsban, Warrior	Headline
Conventional	Legend 2375	Cruiser Maxx	Treflan	Pursuit plus, Flexstar, First Rate	Cobalt	
Conventional	Legend 2375	Cruiser Maxx	Trust	Flexstar, Fusion, First Rate	Lorsban	
Conventional	Legend 2375	Cruiser Maxx	Prowl, Python	Pursuit plus	Cobalt	Headline
Conventional	Legend 2932	Cruiser Maxx	Prowl	Pursuit, Flexstar, Fusion	Lorsban	
Conventional	Legend 2932	Cruiser Maxx	Trust	Select, Flexstar, First Rate	Lorsban	
Conventional	Legend 2932	Cruiser Maxx	Trust	Flexstar, Fusion, First Rate	Lorsban	
Conventional	Legend 2932	Cruiser Maxx	Prowl, Python	Pursuit plus	Cobalt	Headline
Organic	ED 4315					
Organic	ED 4315					
Organic	Legend 2375					
Organic	Mark 0427					
Organic	Mark 0431					
Organic	PB291N					
Organic	Pioneer 9305					
Organic	Pioneer 9305					
Organic	Pioneer 93M52					
Organic	Stine 2686					
Organic	US Soy 20333					

(not allowed)

Glyphosate and AMPA in soybeans



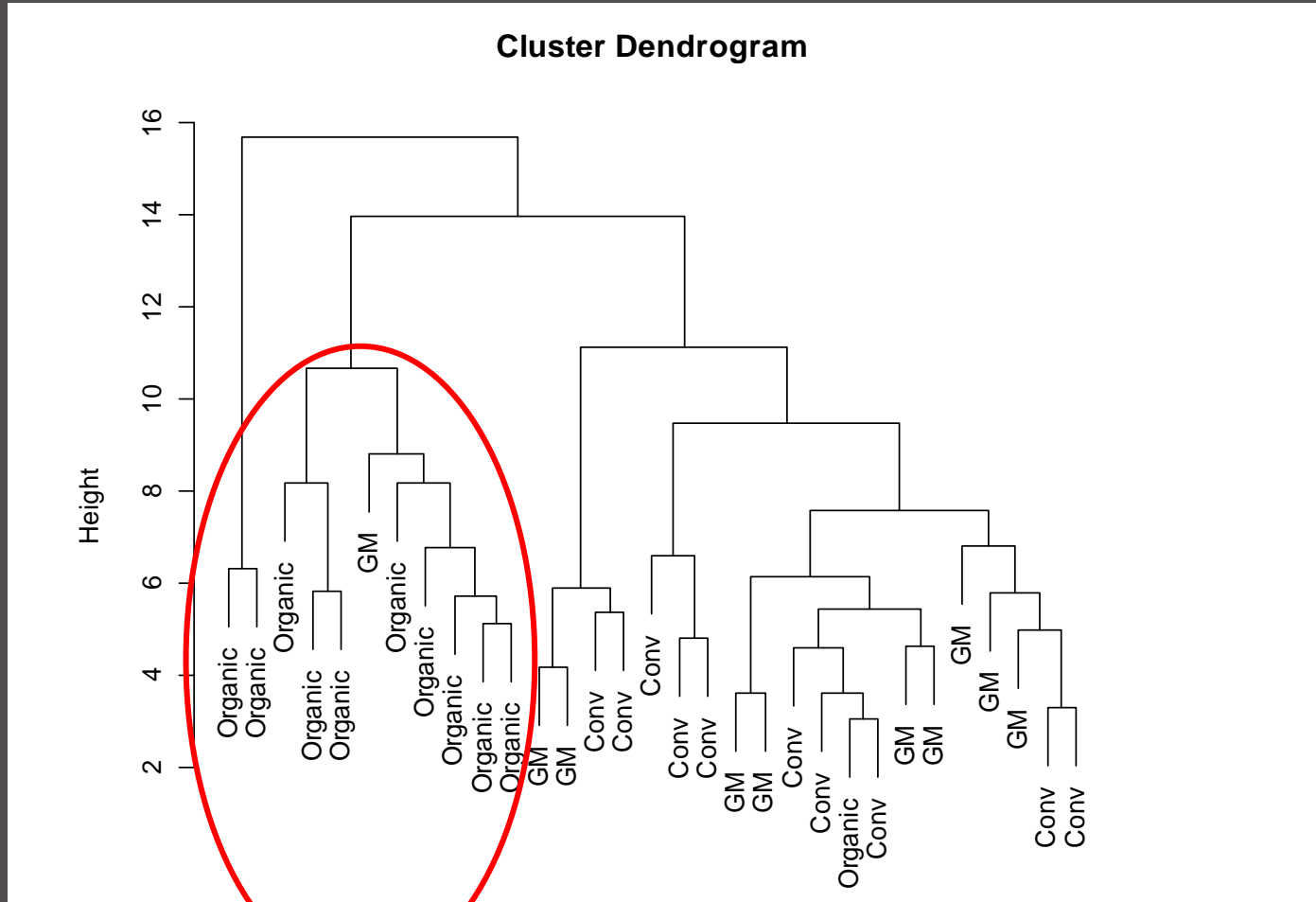
“Extreme levels and far higher than those typically found”
(Monsanto 2011)

Elemental composition

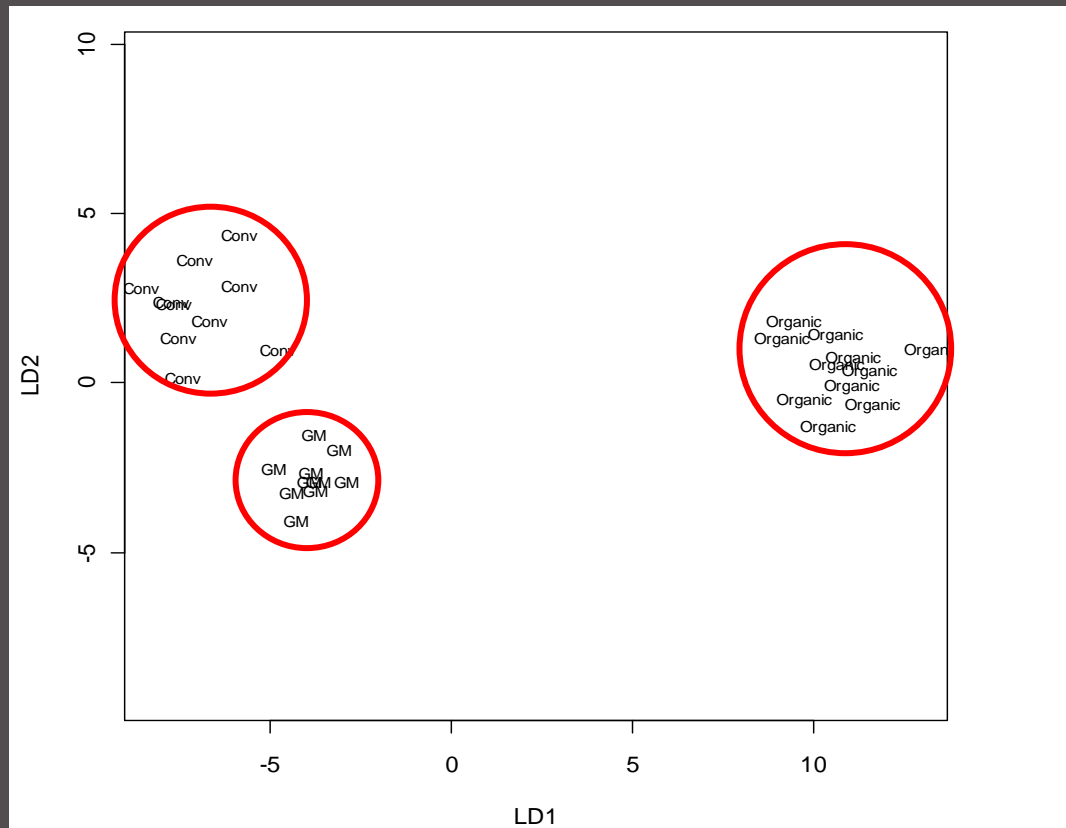
	GM	SD	Conv.	SD	Organic	SD	Anova
Proximate composition							
Dry matter (%)	89.4	1.4	88.1	2.0	88.2	2.6	ns
Protein (%)	34.6 ^b	1.3	34.3 ^b	1.5	36.3 ^a	1.1	p=0.003
Fat (%)	19.0	0.8	19.1	1.3	18.3	0.9	ns
Ash (%)	4.6 ^{ab}	0.2	4.5 ^b	0.2	4.7 ^a	0.2	p=0.005
Amino acids (mg/g)							
Methionine	4.2	0.3	4.0	0.3	4.0	0.4	ns
Lysine	22.1 ^b	1.5	22.2 ^b	1.3	24.2 ^a	0.9	p=0.002
Histidine	8.9	0.3	8.9	0.4	9.0	0.6	ns
Isoleucine	15.2	0.7	15.0	0.7	15.6	0.5	ns
Leucine	26.3 ^{ab}	0.9	26.2 ^b	1.1	27.4 ^a	1.0	p=0.02
Phenylalanine	18.0	0.6	17.7	0.7	18.0	1.2	ns
Threonine	13.8	0.4	13.8	0.5	14.3	0.6	ns
Valine	15.9	0.7	15.7	0.7	16.3	0.6	ns
Arginine	24.0 ^{ab}	0.9	23.4 ^b	1.1	24.9 ^a	1.8	p=0.04
Sum of IAAs ¹	142.3	5.4	140.8	5.2	147.1	5.8	p=0.037
Vitamins (mg/kg)							
Vitamin B6	15.7	1.5	14.9	1.2	14.9	1.4	ns
Fatty acids (mg/g)							
16:0 (palmitic acid)	22.6 ^a	1.2	21.1 ^{ab}	1.1	21.0 ^b	1.9	p=0.046
Sum Saturated	33.0 ^a	1.4	31.0 ^{ab}	1.6	29.7 ^b	2.3	p=0.001
18:1n-9 (oleic acid)	41.1	3.0	38.5	2.9	38.5	4.3	ns
Sum Monounsaturated	44.4	3.2	41.5	3.1	41.5	4.5	ns
18:2n-6 (linoleic acid)	115.7 ^{ab}	5.2	117.8 ^a	5.8	108.4 ^b	9.3	p=0.01
18:3n-3 (linolenic acid)	19.1	4.4	19.6	0.8	18.0	1.6	ns
Elements mg/kg							
Barium (Ba)	6.4 ^b	2.2	6.2 ^b	1.7	11.0 ^a	3.3	p=0.0005
Copper (Cu)	10.4	1.1	10.8	1.1	11.3	1.7	ns
Iron (Fe)	86.8	7.2	84.4	8.7	84.7	11.3	ns
Manganese (Mn)	24.1	2.8	22.8	1.7	24.5	2.3	ns
Molybdenum (Mo)	1.9	1.0	4.5	4.0	2.1	1.1	ns
Selenium (Se)	0.7 ^b	0.1	0.8 ^a	0.2	0.2 ^b	0.2	p=0.0003
Zinc (Zn)	30.4 ^b	2.4	31.7 ^b	2.8	37.0 ^a	3.4	p=0.0002

¹ IAAs Indispensible amino acids (except tryptophan).

Clustering of samples



Substantially different!



Discriminant analysis for GM, conventional and organic soy samples based on 35 variables (Glyphosate/AMPA residues are not included)



Feeding study in *Daphnia magna*



Aquaculture Nutrition



Aquaculture Nutrition 2014

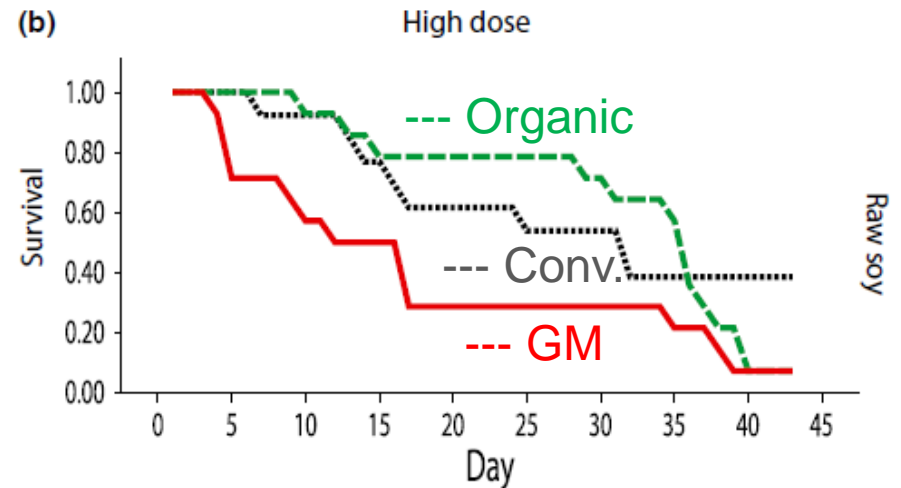
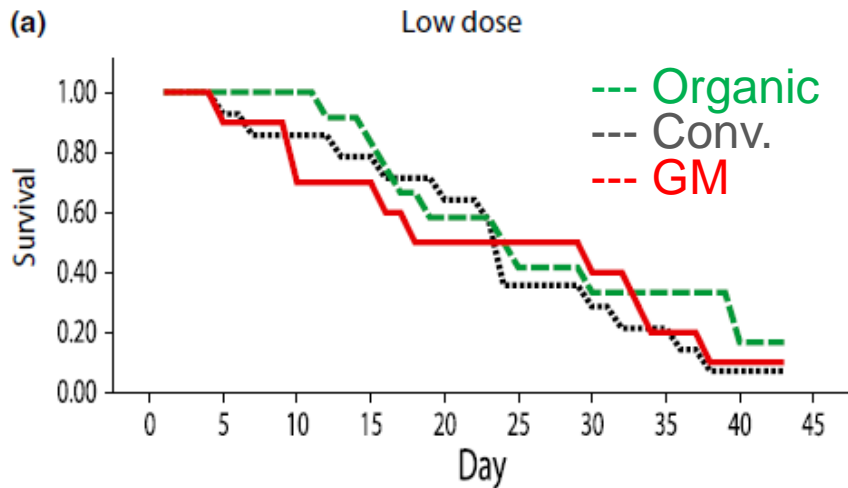
doi: 10.1111/anu.12199

Life cycle fitness differences in *Daphnia magna* fed Roundup-Ready soybean or conventional soybean or organic soybean

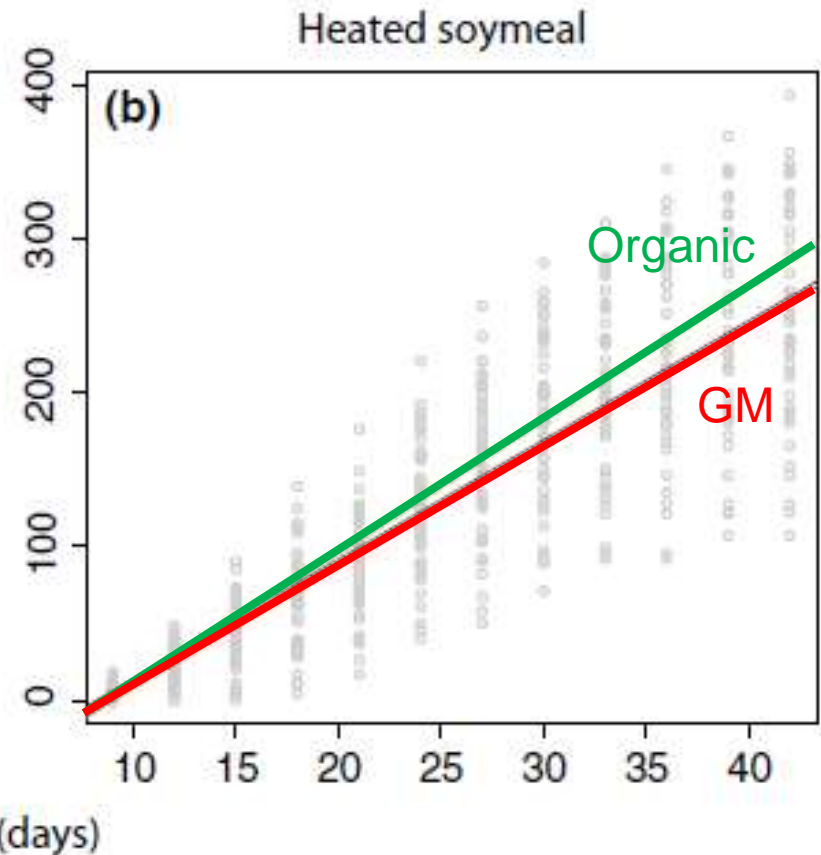
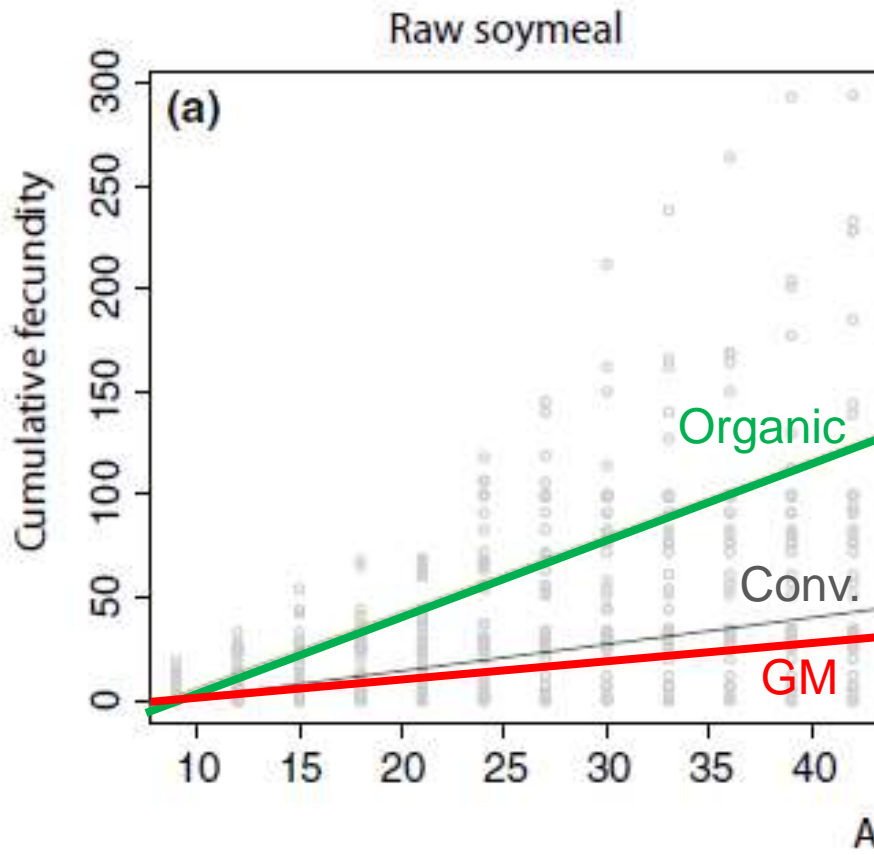
M. CUHRA^{1,2}, T. TRAAVIK^{1,2} & T. BØHN^{1,2}

¹ GenØk – Centre for Biosafety, The Science Park, Tromsø, Norway; ² Faculty of Health Sciences UiT, Arctic University of Norway, Tromsø, Norway

Differences in survival (raw soy)

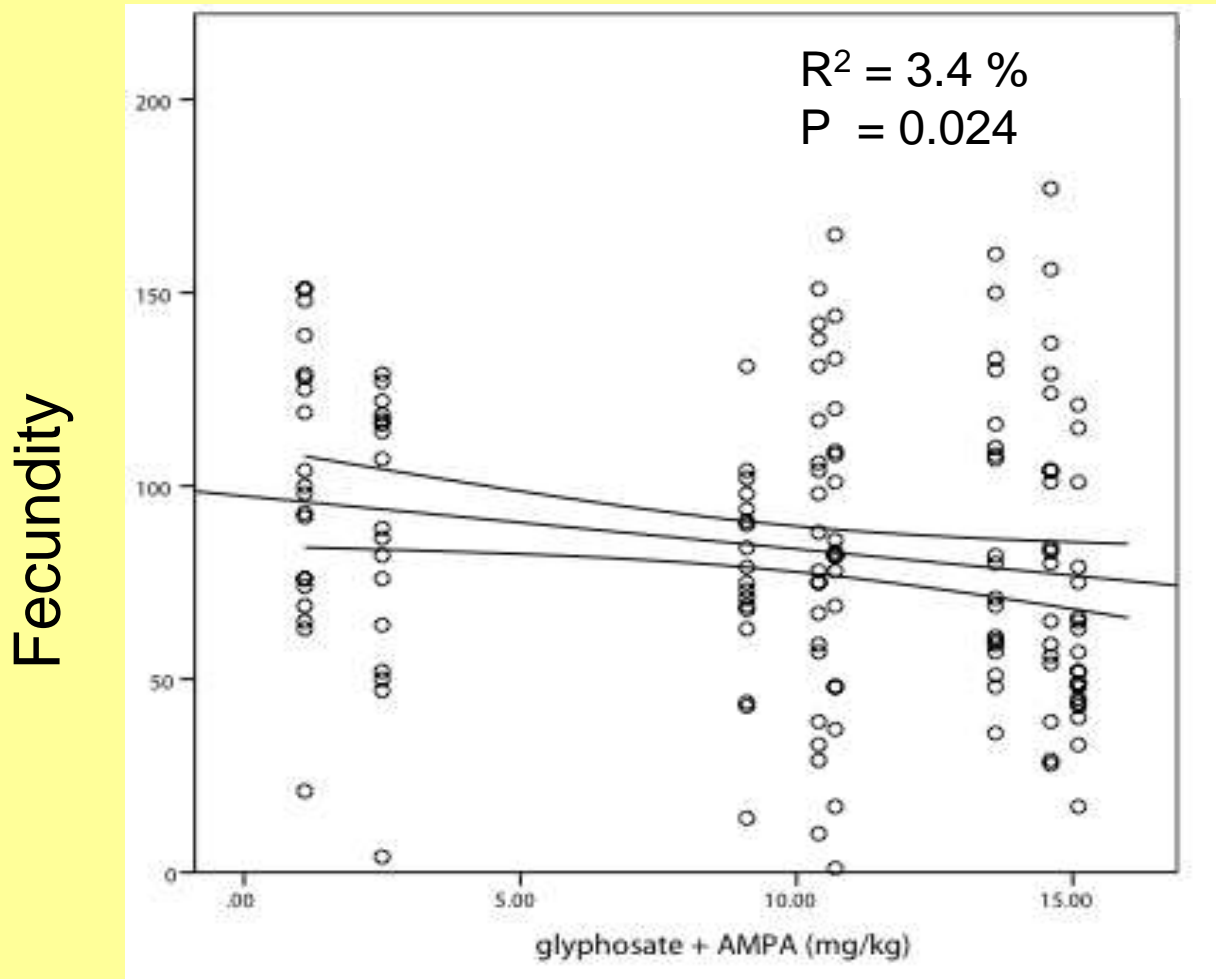


Much higher fecundity for animals fed (raw) organic soy



Testing only HT GM soybeans

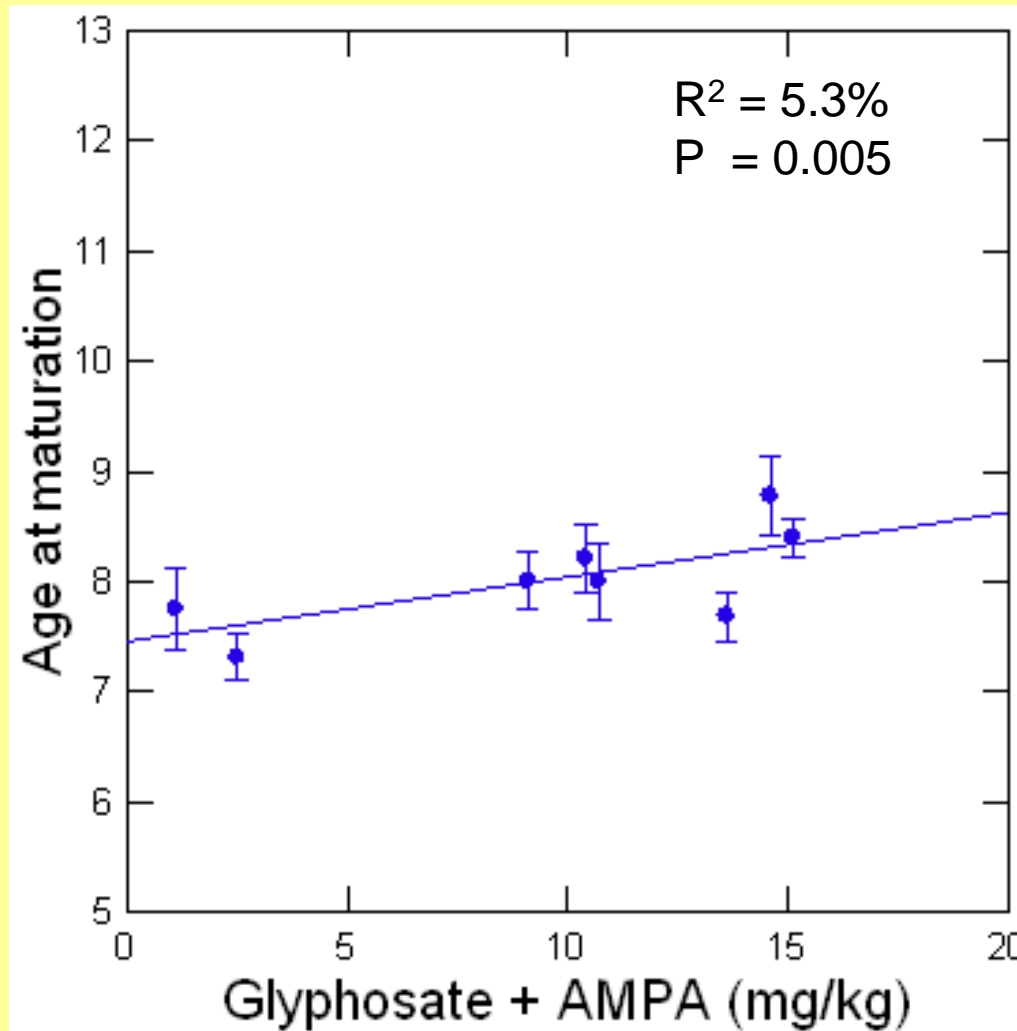
More glyphosate in soybeans - reduced fecundity



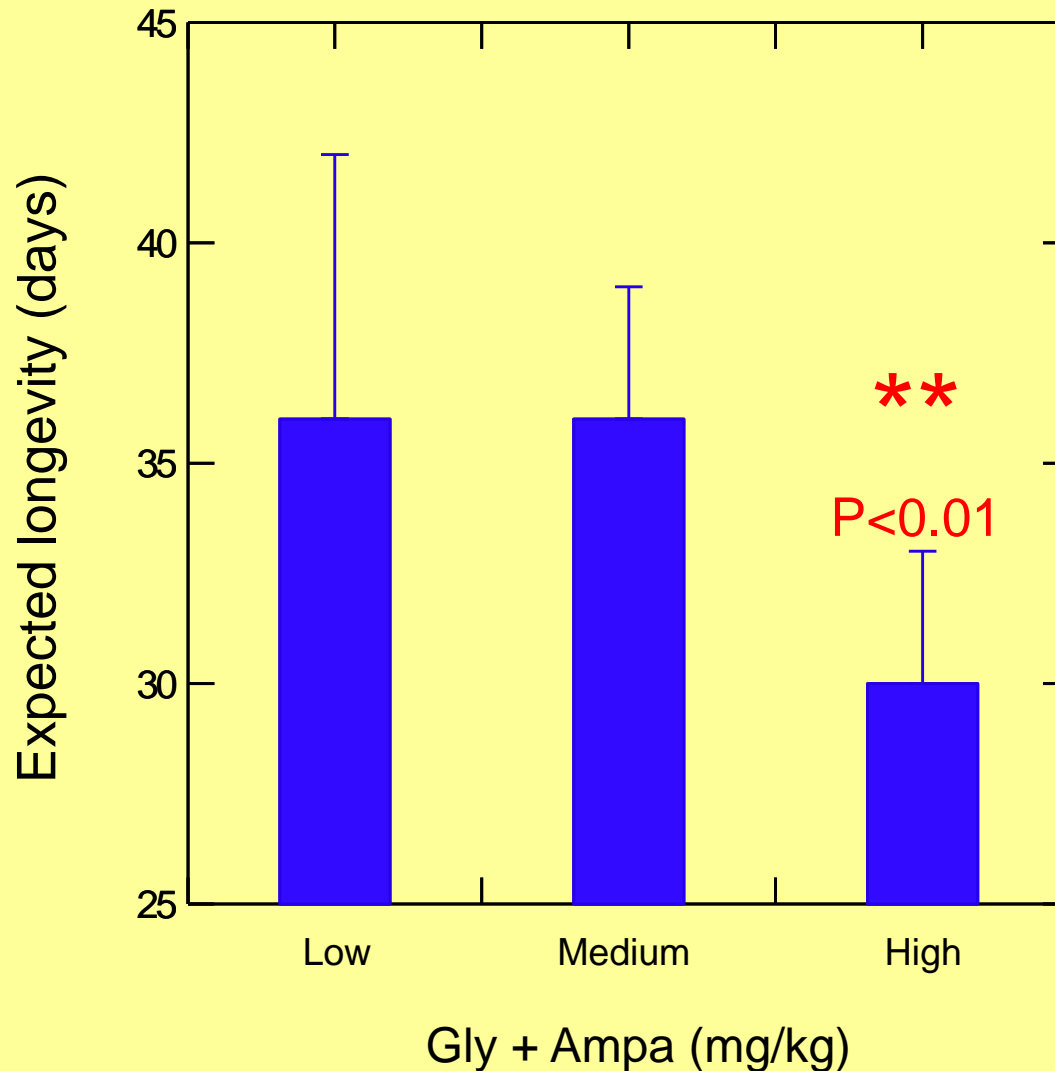
Glyphosate in feed (mg/kg)

(Cuhra et al. in prep)

More glyphosate in soybeans – delayed reproduction



High glyphosate in soybeans – reduced life span



Conclusions

- Herbicide tolerant GM crops:
 - Leads to **increased use of herbicides**
 - ...due to resistance evolution in weeds

 - **GM plants accumulate herbicides**
 - ...for food and feed products
- **Organic soy quality superior** in *Daphnia magna* feeding tests
- HT **GM soy inferior as feed** to organic and conventional soy
- Proof of concept that **high levels of herbicide residues in soy reduces feed quality**



Conclusions

- “The Substantial Equivalence Principle” – a superficial and crude first comparison:
 - Misses key elements like pesticide residues
 - Assumes no interaction between inserted gene(s) and receiving genome/plant/environment
 - Misses (potential) changes in gene expression /changes in proteome
 - Needs to be followed up by long-term feeding studies
 - For the future, comparative approach using near-isogenic comparators may be lost



Thank you for
your attention!



As you can see:
This pile is substantially
equivalent to six people

