# The Roundup on

# Glyphosate

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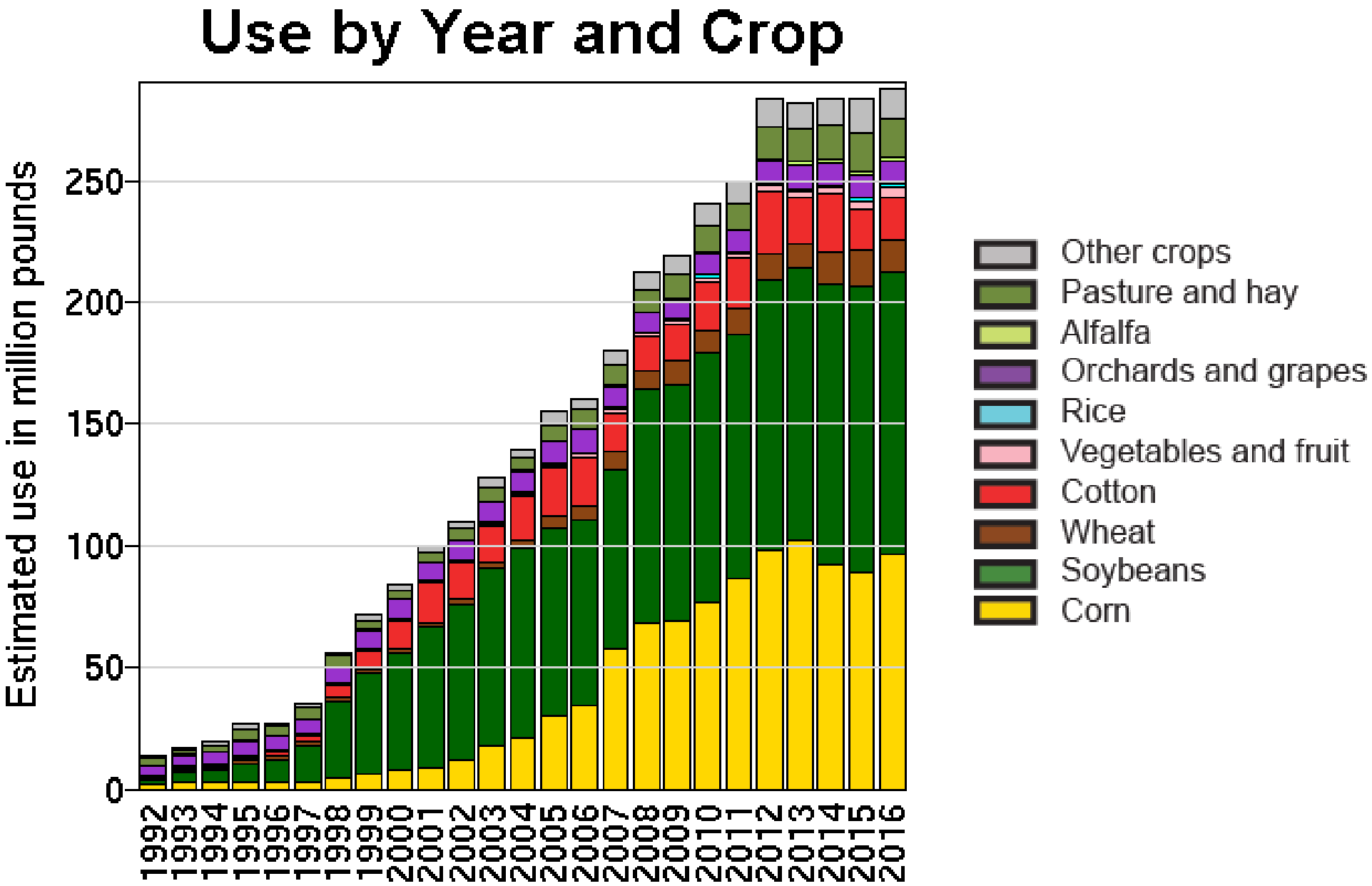
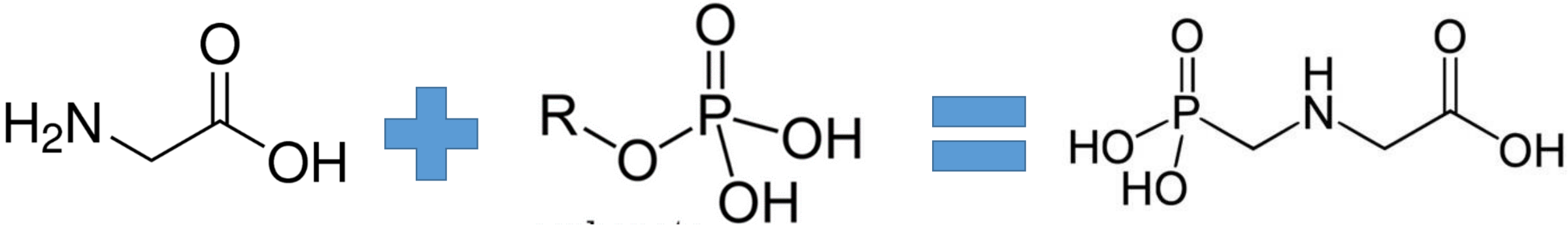
# History of Glyphosate

1950 – First synthesized by Swiss chemist Henry Martin but never published.
1964 – Patented by Stauffer Chemical as a chelator for binding and removing Ca, Mg, Mn, Cu, Zn (pipes, etc.)
1970 – Independently discovered at Monsanto and synthesized by chemist John Franz as an herbicide
1974 – Brought to the market as Roundup under patent
1991 – Initial patent expires but Monsanto retained exclusive US rights until auxiliary patent expired in 2000
1996-1997 – First Roundup Ready transgenic crops were introduced.


Use by Year and Crop
Estimated use in million pounds
0
50
100
150
200
250
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Other crops
Pasture and hay
Alfalfa
Orchards and grapes
Rice
Vegetables and fruit
Cotton
Wheat
Soybeans
Corn

# What Is Glyphosate and How Does It Work




Glycine

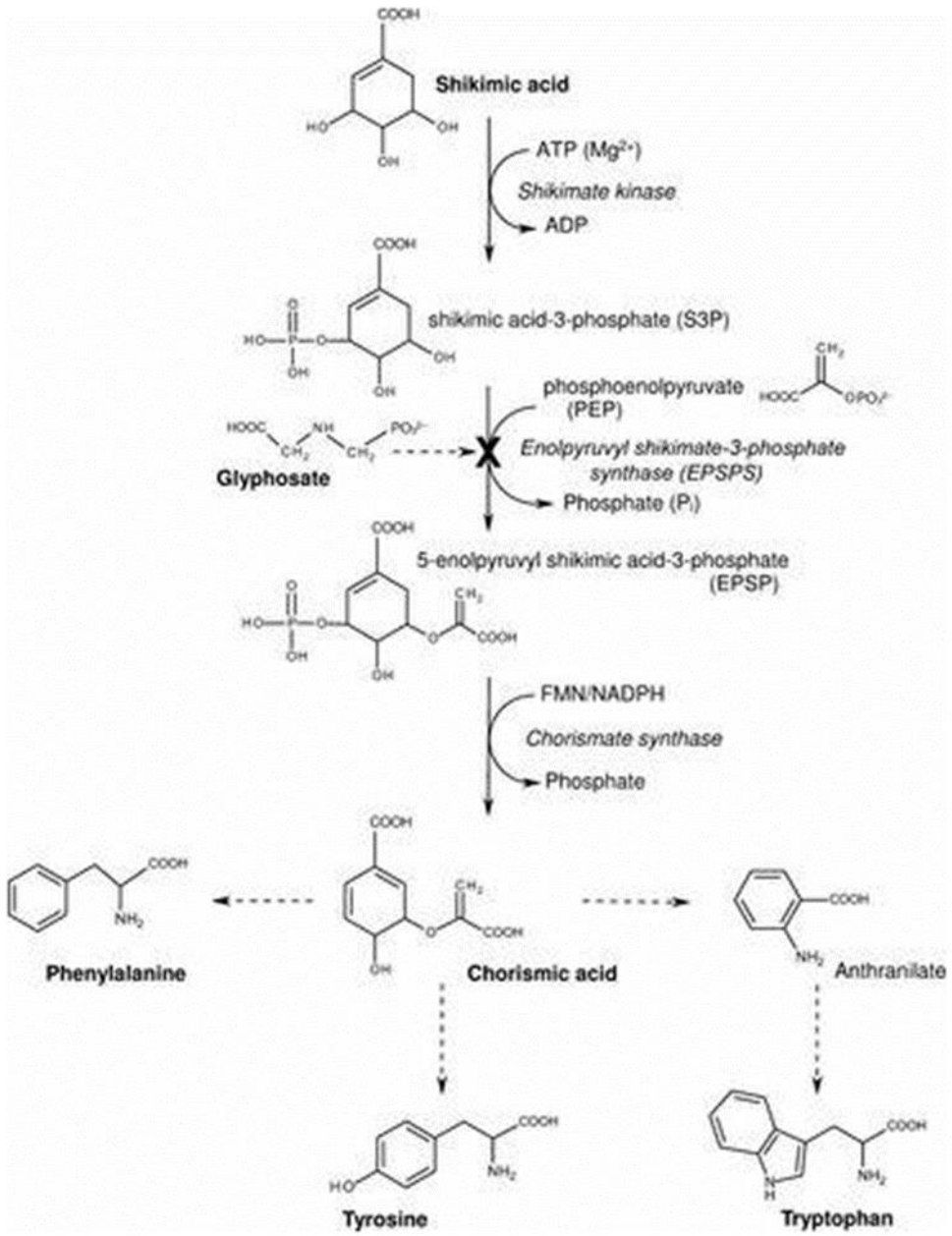
Phosphonate

Glyphosate

Glyphosate is an aminophosphonic analogue of the natural amino acid glycine.
The name is taken as a contraction of the compounds used in its synthesis - viz. glycine and a phosphonate.

# How Does It Work?

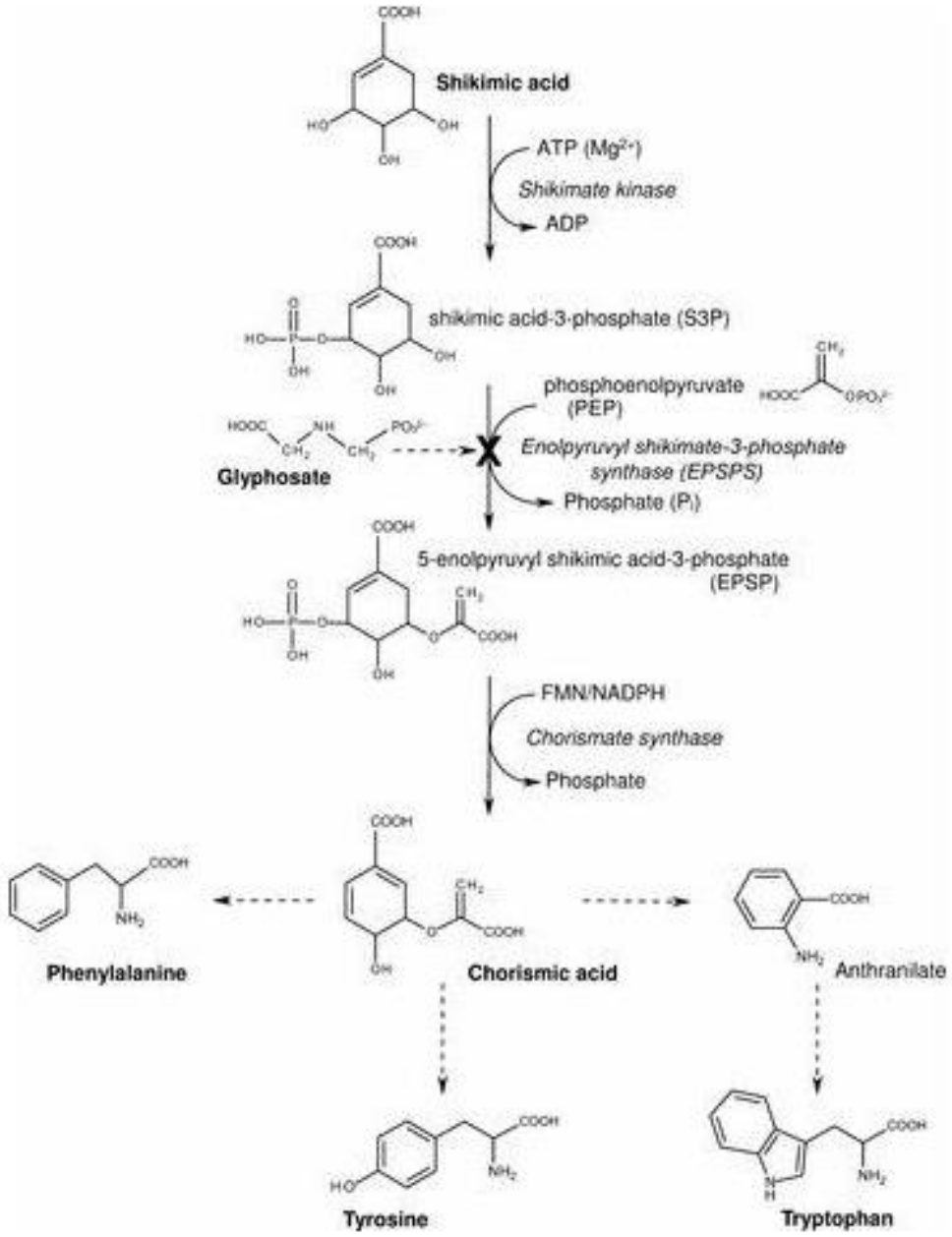
The **shikimic acid pathway** is a seven-step metabolic route used by bacteria, fungi, algae, parasites, and plants for the biosynthesis of aromatic amino acids (phenylalanine, tyrosine, and tryptophan).



# How does it work?

- Disrupts the shikimic acid pathway
- Inhibits EPSP synthase
- Plants cannot produce all of the proteins they need to survive.
- Plants take 4-20 days to die.

- EPSP synthase is not used by animals.
  - It is used by some micro-organisms.




Recent debate about the affect on gut microflora. Does affect microflora – so does anything that goes into the gut. Ongoing research on whether the affect is good, bad or benign.

# Glyphosate – Some Important Properties

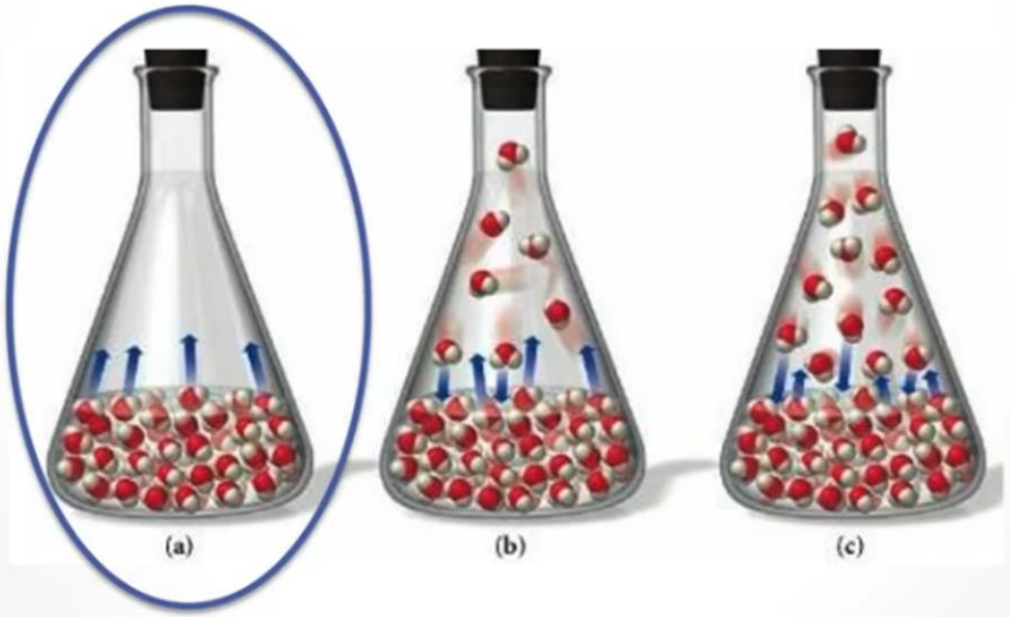
- Glyphosate binds very tightly to most soils and sediments in the environment – it's a dirt lover
- Glyphosate is generally not available for uptake by roots of nearby plants – some research has shown uptake in spinach and radish
- Glyphosate residues are not likely to leach into groundwater and only limited amounts of glyphosate are found in surface water as a result of runoff
- Glyphosate that reaches surface water is rapidly adsorbed to sediment and degraded to aminomethylphosphonic acid (AMPA) by microorganisms
- AMPA is further degraded to naturally-occurring substances such as carbon dioxide and phosphate by microorganisms
- Glyphosate does not volatilize (become vaporous)

Glyphosate sticks to soil strongly.

Many products registered for application to aquatic areas.

Does glyphosate become vaporous?

No.



# Glyphosate – Some Important Data

- In all the organisms tested, including earthworms, birds, mammals and arthropods, glyphosate exhibited only low toxicity at typical application rates.
- Honeybees were not affected by a glyphosate based-formulation even when they were fed high concentrations or exposed in semi-field studies when vegetation adjacent to beehives was over-sprayed.
- These results are also supported by a recently completed bee brood study conducted to meet current EU testing requirements for the ongoing glyphosate renewal process.
- Potential risks for most aquatic organisms are mild or negligible if glyphosate is used according to label instructions - fish, frogs and aquatic invertebrates are not affected by typical glyphosate usage.
- Glyphosate does not bioaccumulate in fish or other animals (doesn’t accumulate over time).
- Because of this relatively favorable safety profile, glyphosate products have even been used in protected habitats such as the Galapagos Islands and the Florida Everglades to protect the native flora from invasive weed species.
- Based on laboratory and field research the exposure risk from glyphosate and the primary soil metabolite aminomethylphosphonic acid (AMPA) on representative species of earthworms, springtails, and predatory soil mites and the effects on nitrogen-transformation processes by soil microorganisms with worst-case soil concentrations expected for glyphosate and AMPA for annual applications at the highest annual rate of indicate very low likelihood of adverse effects on soil biota.

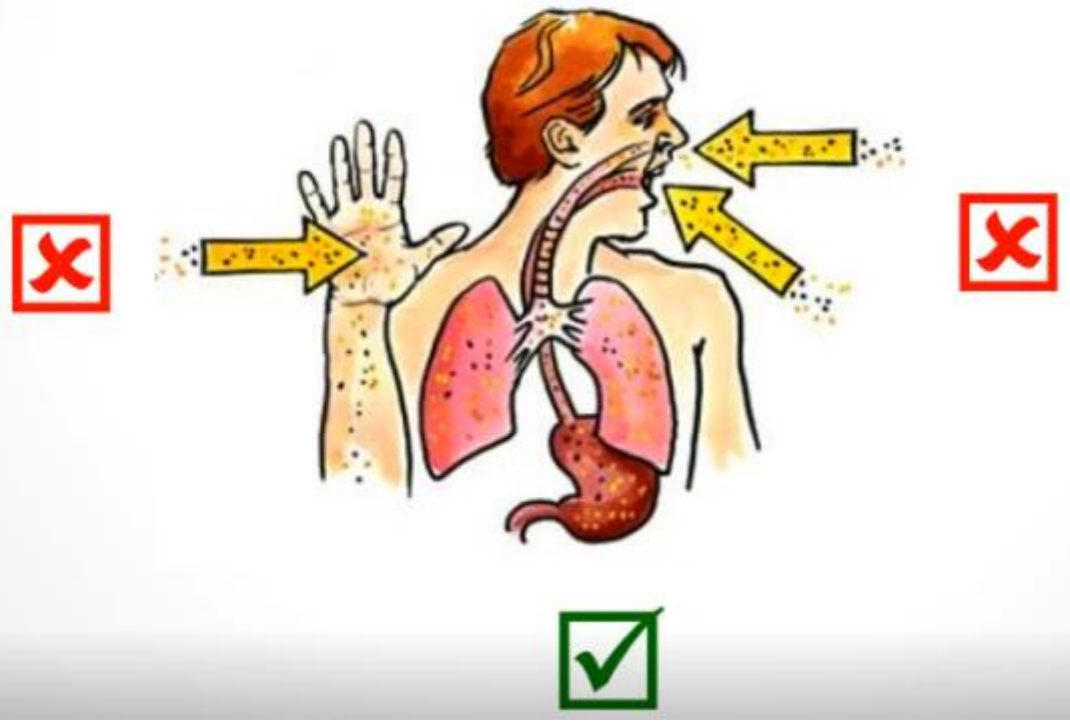
## TOXICITY CLASSIFICATION - GLYPHOSATE

| | High Toxicity | Moderate Toxicity | Low Toxicity | Very Low Toxicity |
|---|---|---|---|---|
| **Acute Oral $LD_{50}$** | Up to and including 50 mg/kg (≤ 50 mg/kg) | Greater than 50 through 500 mg/kg (>50-500 mg/kg) | **Greater than 500 through 5000 mg/kg (>500-5000 mg/kg)** | **Greater than 5000 mg/kg (>5000 mg/kg)** |
| **Inhalation $LC_{50}$** | Up to and including 0.05 mg/L (≤0.05 mg/L) | Greater than 0.05 through 0.5 mg/L (>0.05-0.5 mg/L) | **Greater than 0.5 through 2.0 mg/L (>0.5-2.0 mg/L)** | **Greater than 2.0 mg/L (>2.0 mg/L)** |
| **Dermal $LD_{50}$** | Up to and including 200 mg/kg (≤200 mg/kg) | Greater than 200 through 2000 mg/kg (>200-2000 mg/kg) | **Greater than 2000 through 5000 mg/kg (>2000-5000 mg/kg)** | Greater than 5000 mg/kg (>5000 mg/kg) |
| **Primary Eye Irritation** | Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days | Corneal involvement or other eye irritation clearing in 8 - 21 days | **Corneal involvement or other eye irritation clearing in 7 days or less** | **Minimal effects clearing in less than 24 hours** |
| **Primary Skin Irritation** | Corrosive (tissue destruction into the dermis and/or scarring) | Severe irritation at 72 hours (severe erythema or edema) | Moderate irritation at 72 hours (moderate erythema) | **Mild or slight irritation at 72 hours (no irritation or erythema)** |

**The highlighted boxes reflect the values in the "Acute Toxicity" section of this fact sheet.**
Modeled after the U.S. Environmental Protection Agency, Office of Pesticide Programs, Label Review Manual, Chapter 7: Precautionary Labeling. http://www.epa.gov/oppfead1/labeling/lrm/chap-07.pdf

# Glyphosate Enter Routes to the Body?

- When swallowed, about 1/3 of glyphosate is absorbed.
- About 2% of glyphosate is absorbed through skin.



# What About Cancer?

- Animal studies have mixed results, but mostly negative.
- A long-term study with over 50,000 applicators found no association with overall cancer rates or most subtypes.
- Epidemiological data show a suggested association with Non-Hodgkin Lymphoma (NHL)

- IARC classification: “Probable carcinogen” March 2015
- EPA Classification: “Evidence of non-carcinogenicity” September 2016

Why such a difference of classification between the Environmental Protection Agency (EPA) and the International Agency for Research on Cancer (IARC)?

# IARC Conclusions After Examining Published Data

**Cancer in humans**

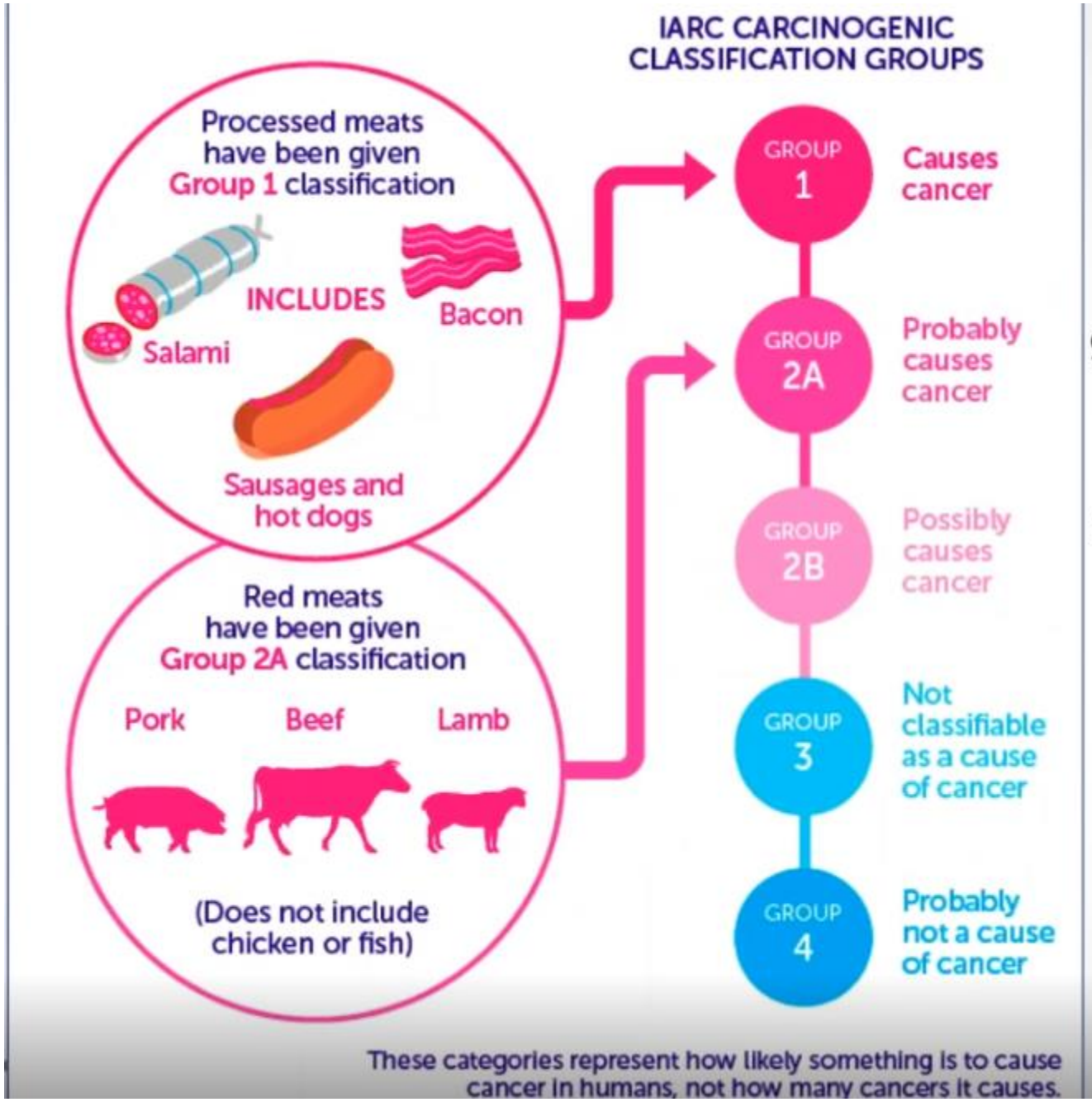
There is *limited evidence* in humans for the carcinogenicity of glyphosate. A positive association has been observed for non-Hodgkin lymphoma.

**Cancer in experimental animals**

There is *sufficient evidence* in experimental animals for the carcinogenicity of glyphosate.

**Overall evaluation**

Glyphosate is *probably carcinogenic* to humans (**Group 2A**)




Arsenic
Cigarette Smoke

glyphosate

2,4-D

# Why the Classification Difference?


IARC defers risk assessment and risk management to national and international bodies, restricting itself to provision of hazard identification as a scientific foundation to those subsequent steps. **IARC response to criticisms of the Monographs and the glyphosate evaluation - Prepared by the IARC Director, January 2018**

**Glyphosate Issue Paper:**
**Evaluation of Carcinogenic Potential**

**EPA's Office of Pesticide Programs**
**September 12, 2016**

For cancer descriptors, the available data and weight-of-evidence clearly do not support the descriptors "carcinogenic to humans", "likely to be carcinogenic to humans", or "inadequate information to assess carcinogenic potential". For the "suggestive evidence of carcinogenic potential" descriptor, considerations could be looked at in isolation; however, following a thorough integrative weight-of-evidence evaluation of the available data, the database would not support this cancer descriptor. The strongest support is for "not likely to be carcinogenic to humans" at doses relevant to human health risk assessment.

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http://bit.ly/glypho-cancer-2016

Food Safety News
*Breaking news for everyone's consumption*



# EFSA Finds Glyphosate 'Unlikely to Cause Cancer in Humans'

BY DAN FLYNN | NOVEMBER 13, 2015

Europe's gardeners and farmers probably won't have their Monsanto Roundup weed killer or other similar herbicides taken away from them now that the influential European Food Safety Authority (EFSA) has found that the ingredient glyphosate is unlikely to cause cancer in humans.

Glyphosate, which has been around since the 1970s, is used in herbicides around the world, including Monsanto's popular Roundup.

EFSA's research findings appear to trump the conclusion this past March by the International Agency for Research on Cancer (IARC), which listed glyphosate as "probably carcinogenic to humans."


EFSA's assessment will be used by the European Commission in deciding whether to keep glyphosate on the EU list of approved active substances. Currently, glyphosate is widely used in both Roundup and in generic brands of herbicides for home gardening and agriculture.

# Risk

**Toxicity X Exposure = Risk**

- Toxicology of the active ingredient
- Product signal word
- Does estimate
- Effects reported in the literature
- Onset, duration and resolution of symptoms

- Distance to application site
- Route of potential exposure
- Physical/chemical properties of active ingredient
- Duration/frequency of exposure
- Bioavailability by the route in question

# Benefits of Glyphosate Usage

**What are the benefits for farmers of glyphosate herbicide use?**

- Glyphosate herbicides provide simple, flexible and cost-effective weed control
- Glyphosate helps to remove perennial weeds for several years
- Glyphosate is effective on all weeds, providing broad spectrum control
- Pre-plant application of glyphosate has the potential to increase yields 30%-60% for many major crops
- Glyphosate reduces disease and insect incidence by removing weeds that might otherwise act as an intermediate host for parasites and disease vectors
- Its effectiveness as a broad-spectrum herbicide has reduced the use of plowing as a means of controlling weeds, which exposes fertile topsoil to water and wind erosion
- Studies have estimated that plowing control methods are approximately twice as costly and time consuming as chemical weed control

# Benefits of Glyphosate Usage

**Are there ecological benefits to use glyphosate?**

- By chemically controlling a broad spectrum of weeds and their entire root systems, glyphosate has eliminated or reduced the need for plowing. These reduced tillage practices allow farmers to plant crop seeds directly into stubble fields.
- A large proportion of cultivated land is prone to soil erosion, and minimal soil disturbance practices are sustainable alternatives that help to protect the soil from degradation and reduce greenhouse gas emissions and energy consumption.
- Several important crops worldwide, including corn and sugar beet, are predominantly managed with these practices in combination with glyphosate. This makes glyphosate a popular tool for many farmers that decide to pursue these soil conservation practices.

# Benefits of Glyphosate Usage

**Why is glyphosate so important for worldwide agriculture?**

- Several countries worldwide use glyphosate herbicides on roughly 50% of their total crop area.
- Recent case studies conducted by researchers in Germany and the UK predict that losing glyphosate would have a considerable effect on crop production costs and would also have an impact on international trade.
- Food prices would increase if glyphosate use was restricted.
- It is estimated that crop yields for farmers would be reduced by 5% to 40%, depending on the region and the crops if glyphosate was no longer available.
- A limitation in the availability of glyphosate is also predicted to have potential implications for land use, biodiversity, greenhouse gas emissions and water quality.
- By using glyphosate for weed control, farmers have been able to forgo or significantly reduce traditional plowing methods.
- Conventional plow tillage is an energy-intensive process that releases tons of carbon dioxide into the atmosphere from the soil.
- If farmers are forced to return to these weed-control methods, $CO_2$ emissions and fossil fuel consumption are predicted to more than double, while soil erosion could increase six times (6X).

# Glyphosate is Currently Undergoing Review of Registration – What and Why

Registration renewal is required of all registered pesticides approximately every 10 years. This is a standard, required, routine process.

The range of data required includes:

1) physical-chemical properties,
2) impact on human health following single, multiple or lifetime exposure, whether for workers, consumers or the general public, and includes consideration of neurotoxtic, mutagenic, carcinogenic and reproductive effects;
3) the nature and amounts of residual traces remaining in food; fate and behaviour in soil, surface, ground and drinking water and air;
4) impact on birds and mammals, aquatic species, earthworms and other soil borne organisms, bees and other invertebrate insects, micro-organisms and non-target plants. Furthermore, data on efficacy is requested and peer-reviewed publications have to be searched systematically for evidence of potentially adverse effects.

Based on currently available research-based data, use of glyphosate according to label directions and allowed use presents a very low risk of environmental, ecological, and human health injury.

LSU AgCenter

# Questions?

## Resources

- National Pesticide Information Center
  - http://npic.orst.edu 1-800-858-7378
- Glyphosate Technical Fact Sheet
  - http://npic.orst.edu/factsheets/archive/glyphotech.html
- Glyphosate General Fact Sheet
  - http://npic.orst.edu/factsheets/glyphogen.html
- PlainLanguage.gov
  - http://www.plainlanguage.gov/
- Debunking Handbook
  - https://www.skepticalscience.com/docs/Debunking_Handbook.pdf
- Book: Risk Communication: A Handbook for Communicating Environmental, Safety, & Health Risks by Regina Lundgren & Andrea McMakin

You could eat **450 BOXES**

of cereal every

# 24 HOURS

for the rest of your life and still be at a level of glyphosate exposure considered safe by the EFSA

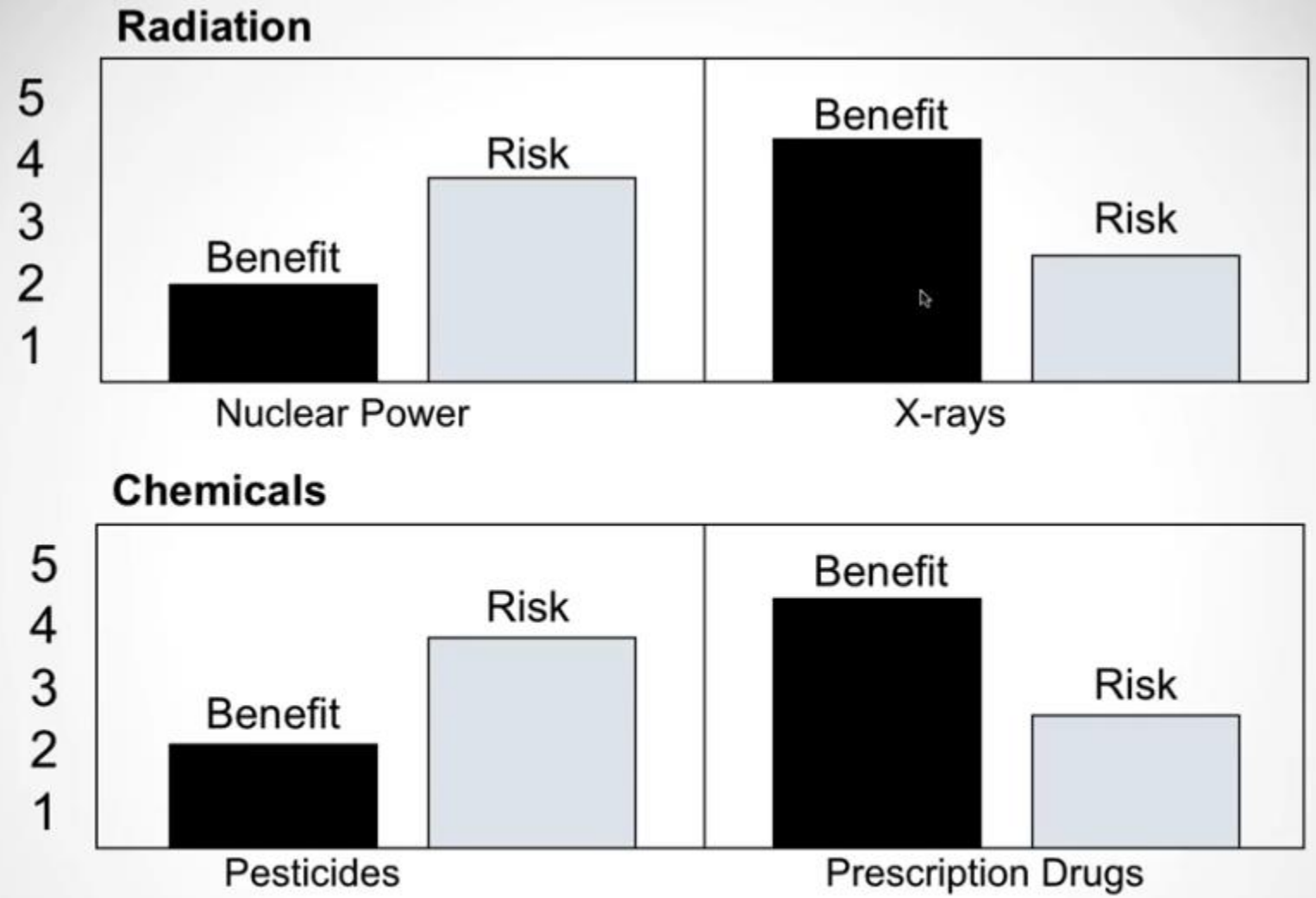
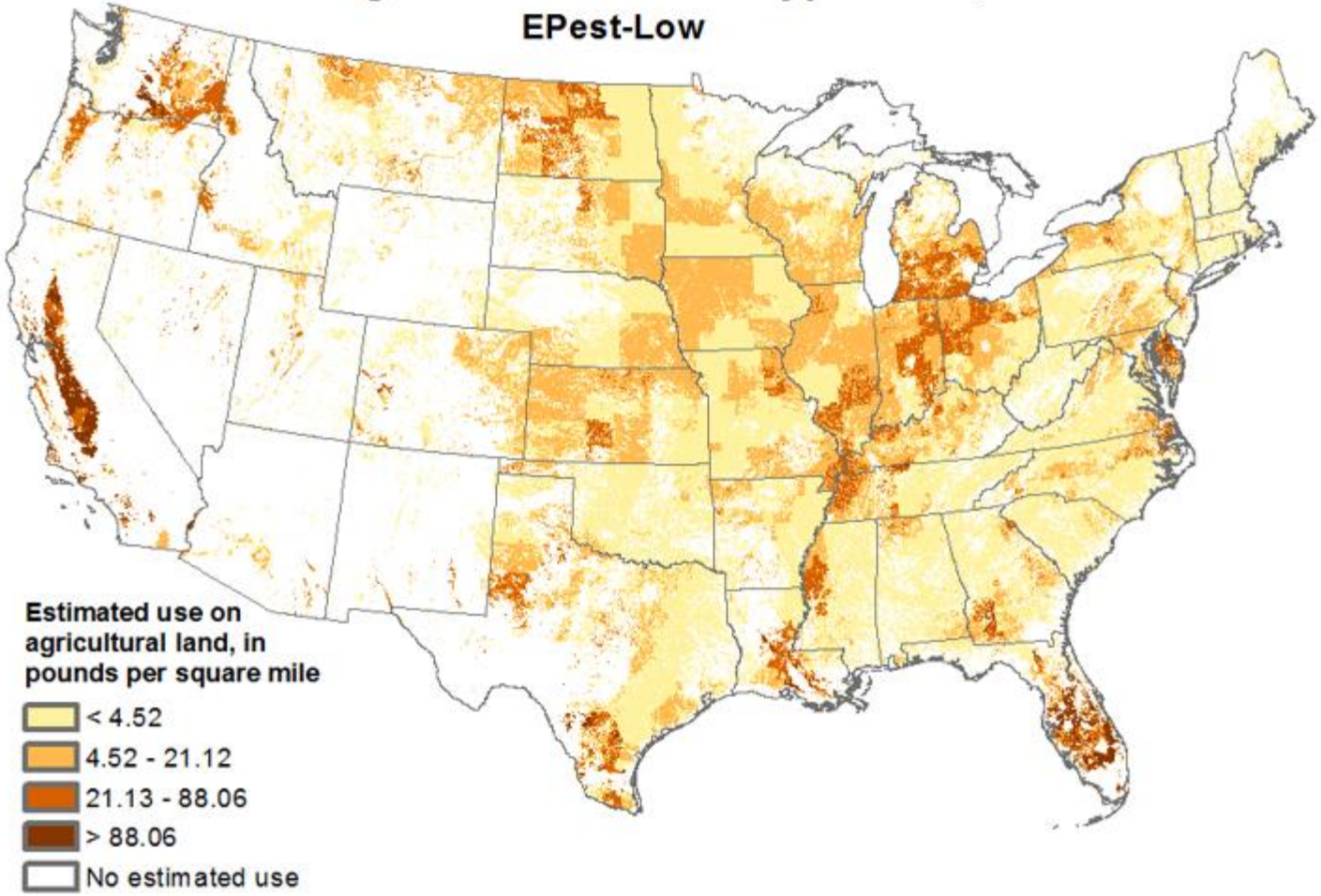



Figure 3. Mean perceived risk and perceived benefit for medical and nonmedical sources of exposure to radiation and chemicals. Each item was rated on a scale of perceived risk ranging from 1 (very low risk) to 7 (very high risk) and a scale of perceived benefit ranging from 1 (very low benefit) to 7 (very high benefit). Data are from a national survey in Canada by Slovic et al., 1991.

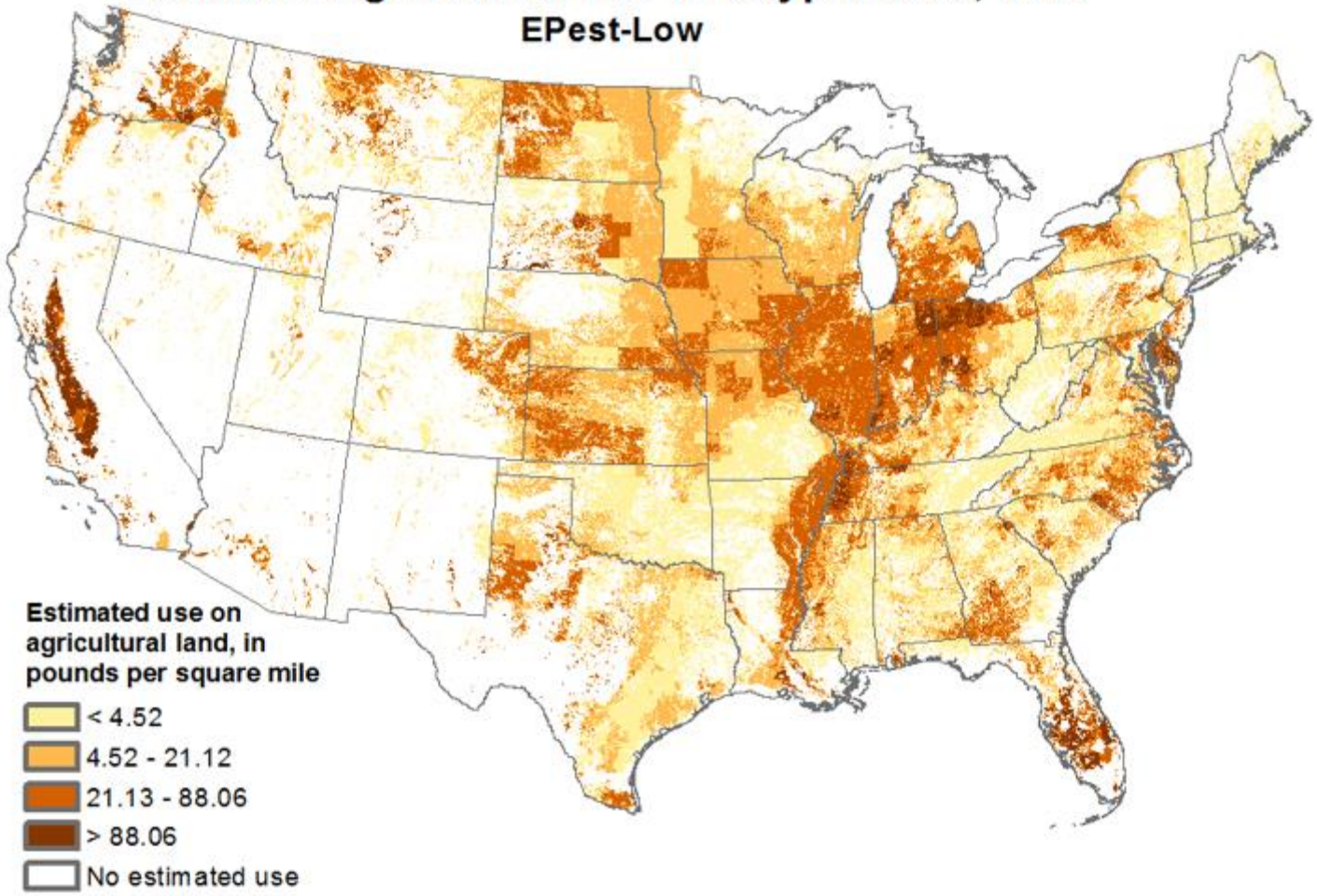
# Estimated Agricultural Use for Glyphosate , 1992

## EPest-Low



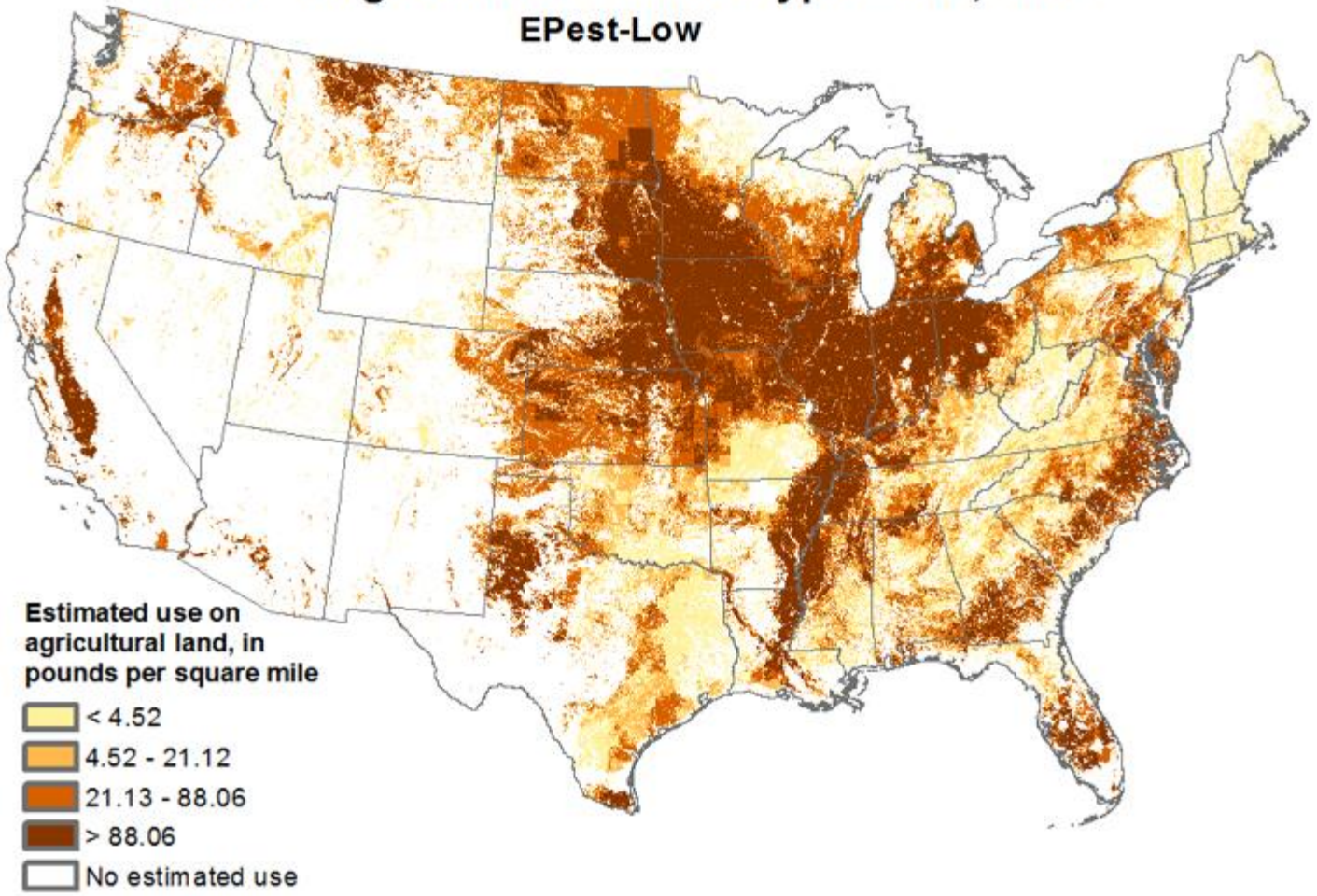
# Estimated Agricultural Use for Glyphosate , 1996

## EPest-Low



# Estimated Agricultural Use for Glyphosate , 2002

## EPest-Low



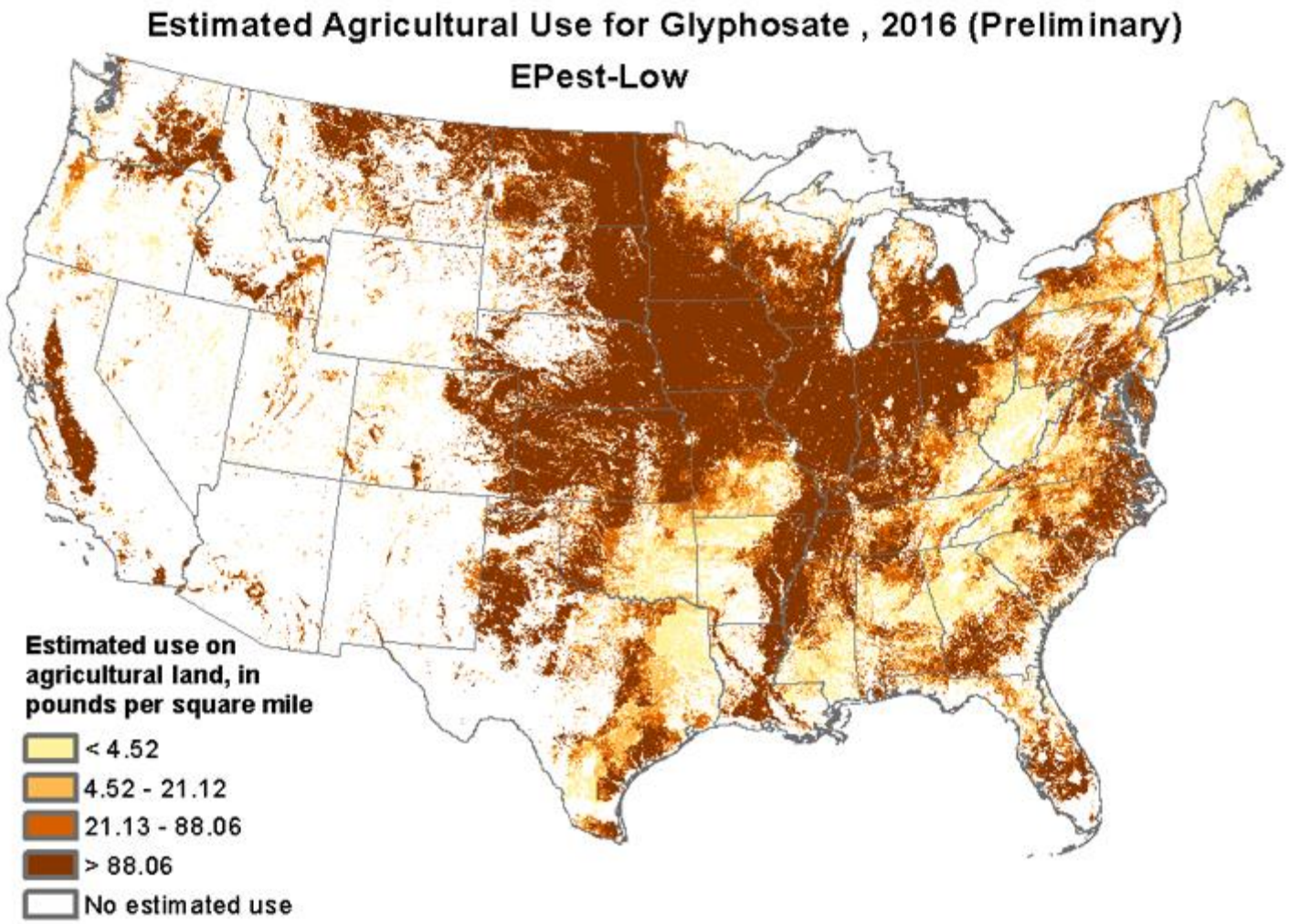

Estimated Agricultural Use for Glyphosate , 2016 (Preliminary)
EPest-Low
Estimated use on agricultural land, in pounds per square mile
< 4.52
4.52 - 21.12
21.13 - 88.06
> 88.06
No estimated use

Table 4. 1981 Bio/dynamics 26-month glyphosate feeding study [17]: incidence of pancreatic islet cell tumours in male Sprague Dawley rats.

| Glyphosate dose /mg $kg^{-1}$ $day^{-1}$ | 0 | 3 | 10 | 30 |
|---|---|---|---|---|
| Adenomas | 0/50 (0%) | 5/49 (10%) | 2/50 (4%) | 2/50 (4%) |
| Carcinomas | 0/50 (0%) | 0/49 (0%) | 0/50 (0%) | 1/50 (2%) |
| Adenomas and carcinomas | 0/50 (0%) | 5/49 (10%) | 2/50 (4%) | 3/50 (6%) |
| Hyperplasias | 3/50 (6%) | 2/49 (4%) | 1/50 (2%) | 0/50 (0%) |

Glyphosate, pathways to modern diseases IV: cancer and related pathologies by Anthony Samsel and Stephanie Seneff in *Journal of Biological Physics and Chemistry 15 (2015) 121–159*