# Preliminary Screening Information on Three Possible Pesticide Classes

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Presentation to the Scientific Guidance Panel
July 28, 2016

OEHHA

BIOMONITORING CALIFORNIA

# Purpose of agenda item

- Follow up on pesticides previously reviewed by SGP:
  - Glufosinate-ammonium
  - Glyphosate
  - Imidacloprid
  - Propanil
- Discuss three possible pesticide classes for possible future consideration:
  - Organophosphorus pesticides
  - Neonicotinoid pesticides
  - Anilide pesticides
- Obtain Panel and public input on next steps

# Why classes?

- Evaluating chemical classes, rather than individual chemicals:
  - Is resource efficient for SGP chemical selection
  - Allows the Program to quickly respond to shifts in chemical use and target emerging chemicals of concern
  - Facilitates development of broad lab panels for related chemicals
  - Allows for non-targeted screening within a class of chemicals

# Pesticide topic areas researched

Based on SGP and public input, we researched:

- Agricultural pesticides applied near schools
- Pet pesticides
- Cholinesterase-inhibiting pesticides

➢ Pesticide classes that encompass the four previously screened pesticides

# Background: Criteria for recommending designated chemicals

- ***Exposure or potential exposure*** to the public or specific subgroups
- The ***known or suspected health effects*** resulting from some level of exposure based on peer reviewed scientific studies
- The ***need to assess the efficacy of public health actions*** to reduce exposure to a chemical
- The ***availability of a biomonitoring analytical method*** with adequate accuracy, precision, sensitivity, specificity, and speed
- The ***availability of adequate biospecimen samples***
- The ***incremental analytical cost*** to perform the biomonitoring analysis for the chemical

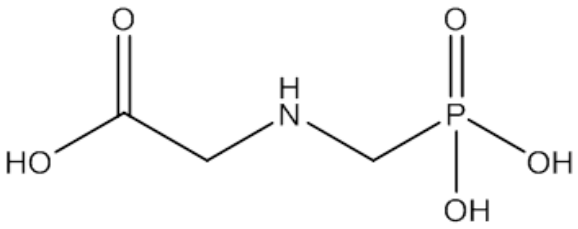
# Preliminary research on classes

- Class considerations
  - Function (pesticides)
  - Structure
  - Mechanism of action
- Toxicity concerns associated with members of the class
- Agricultural use trends in CA
- Availability of biomonitoring methods

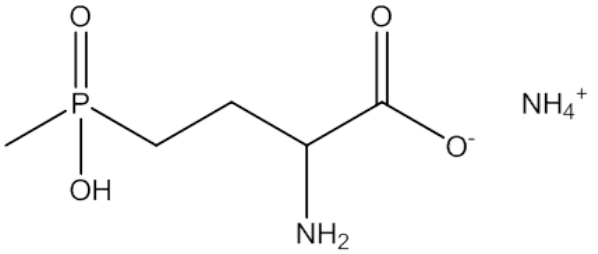
# Organophosphorus pesticides

- Phosphorus-containing organic compounds used as pesticides
- Potential toxicity concerns associated with pesticides in this broad group include:
  - Neurotoxicity
  - Carcinogenicity
  - Developmental effects
  - Endocrine effects

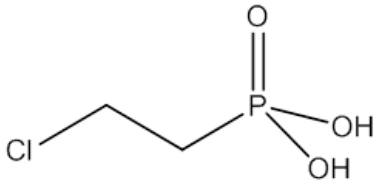
# Example organophosphorus pesticides



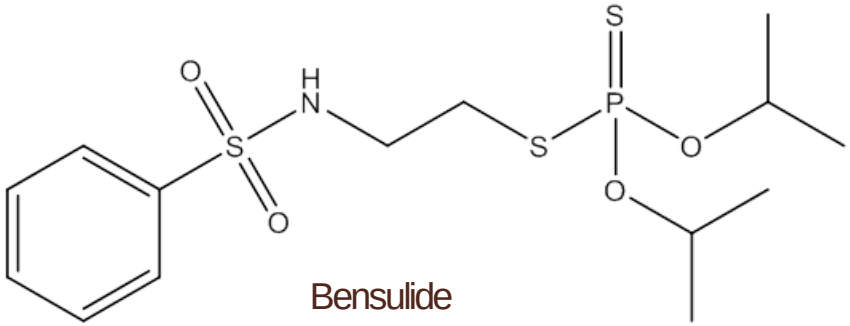

Glyphosate



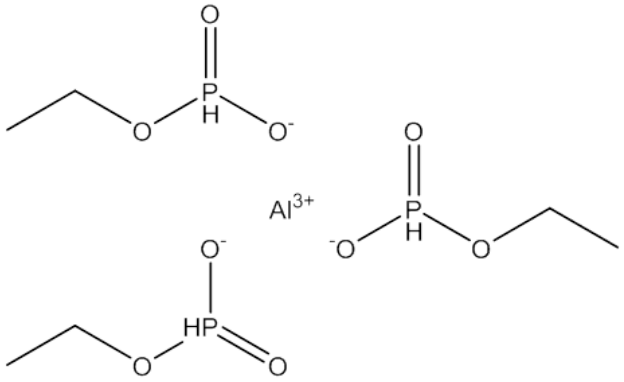

Glufosinate-ammonium




Ethephon



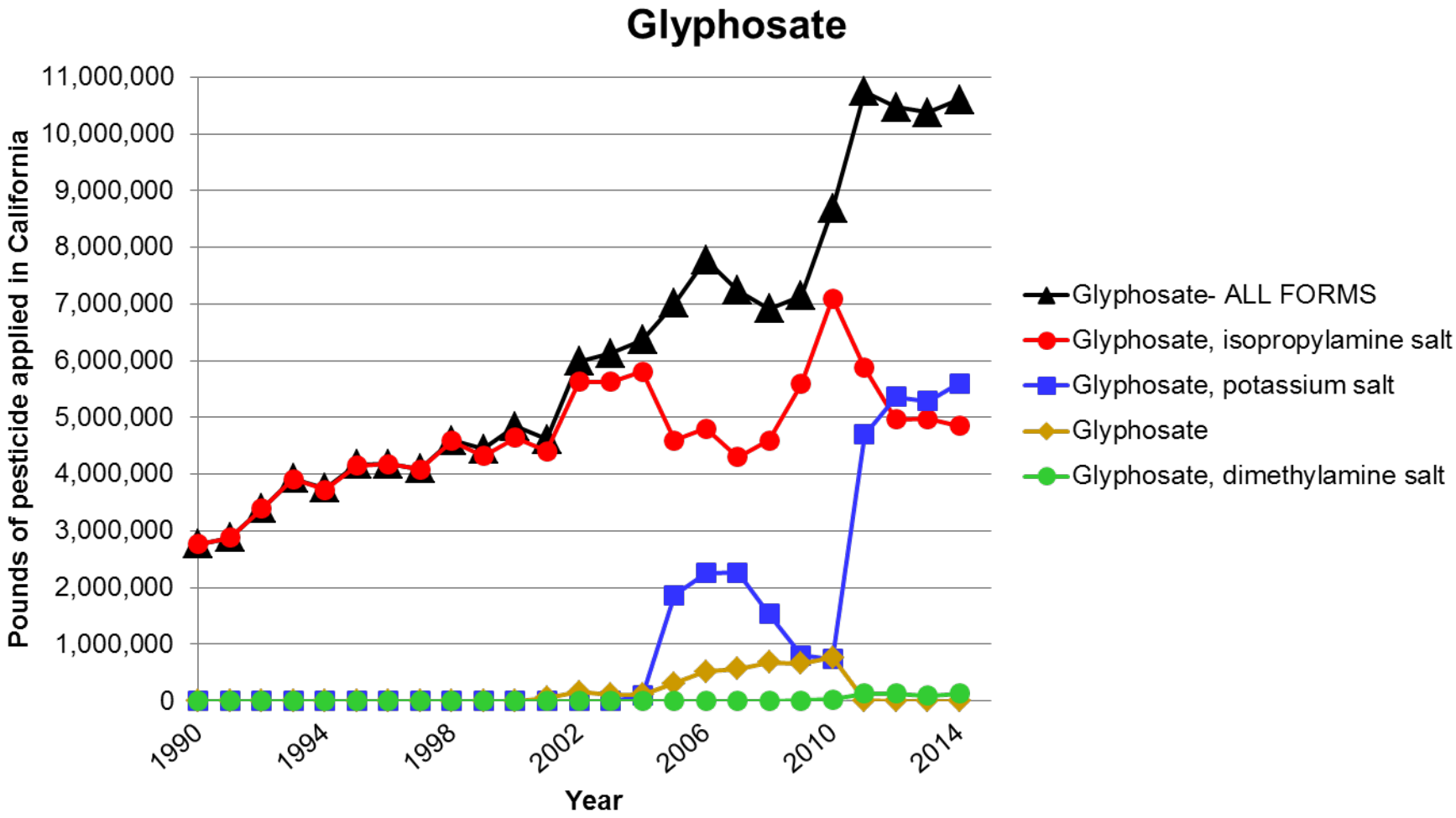

Bensulide




Fosetyl-aluminum

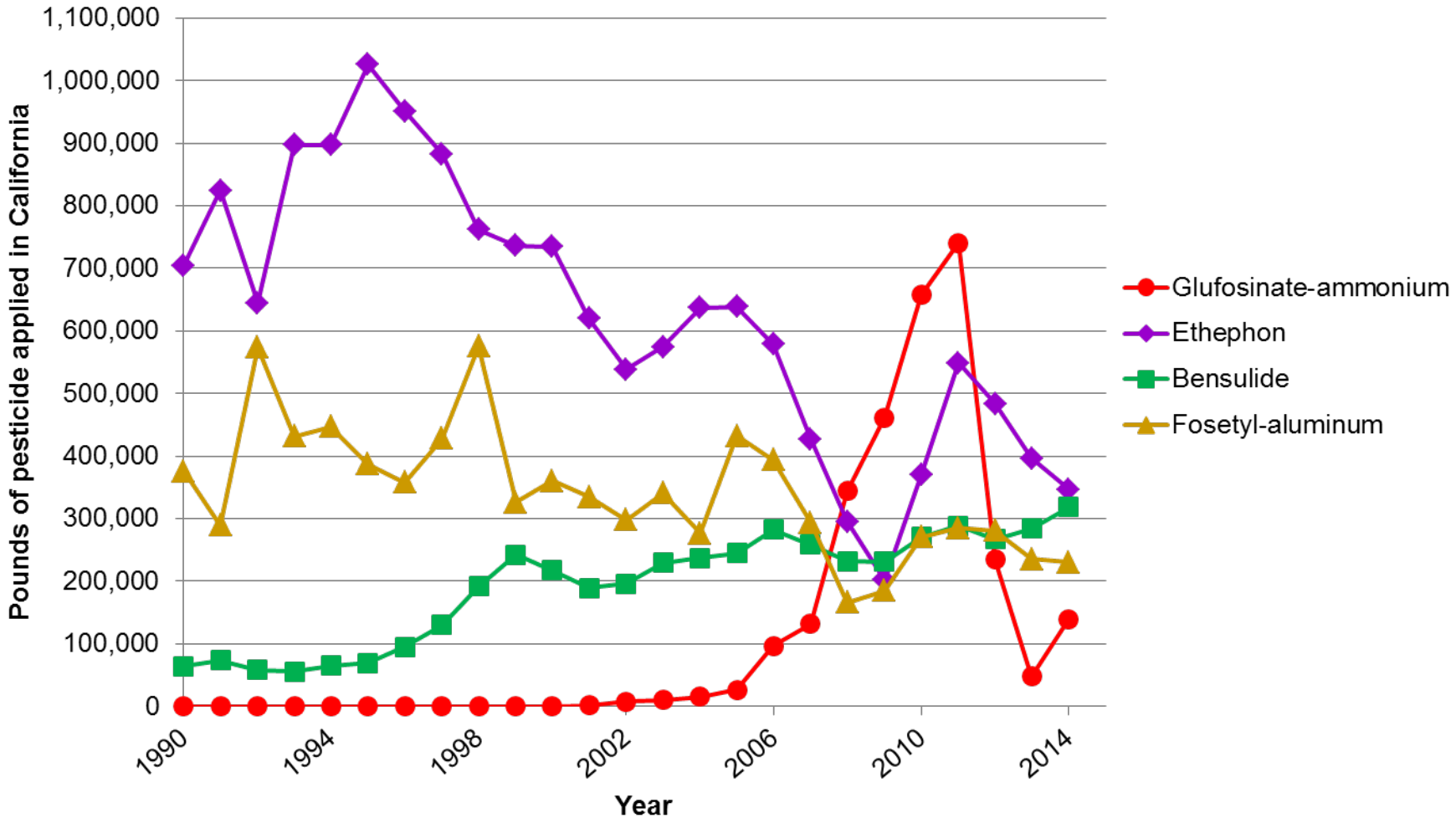
# Organophosphorus pesticides

## Agricultural pesticide use in California



# Organophosphorus pesticides

## Agricultural pesticide use in California



# Biomonitoring:
## Glufosinate-ammonium and glyphosate

| | Measured in serum | Measured in urine | Selected references |
|---|---|---|---|
| **Glufosinate-ammonium** | ✓ | ✓ | Adams et al., 2016; Hoppe, 2013; Jensen et al., 2016; Krüger et al., 2014; Watanabe et al., 2014 |
| **Glyphosate** | | ✓ | |
| **Aminomethylphosphonic acid (AMPA)** | | ✓ | |

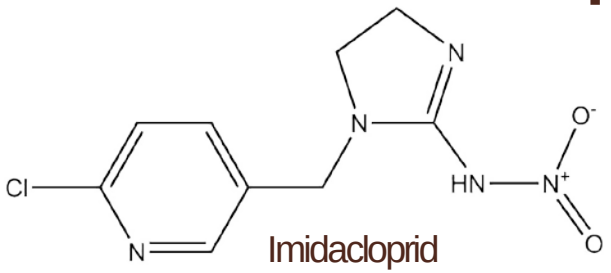
*Biomonitoring California lab capability - currently organophosphates only:*

- *Non-specific dialkyl phosphates (DAPs)*
- *Specific metabolites for chlorpyrifos and diazinon*

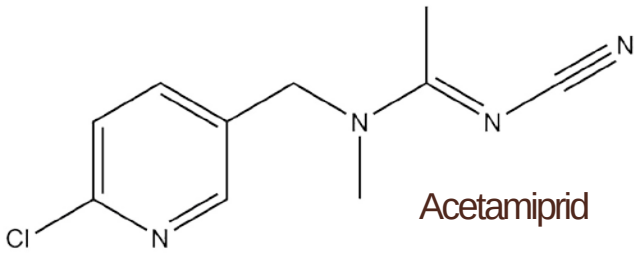
# Neonicotinoid pesticides

- Bind to and activate the nicotinic acetylcholine receptor
- Potential toxicity concerns associated with pesticides in this class include:
  - Immunotoxicity
  - Developmental neurotoxicity

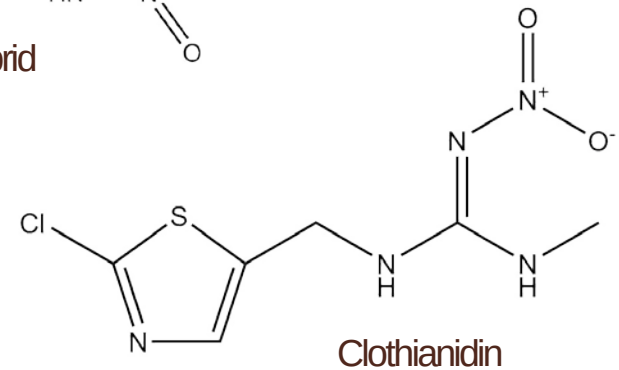
# Example neonicotinoid pesticides



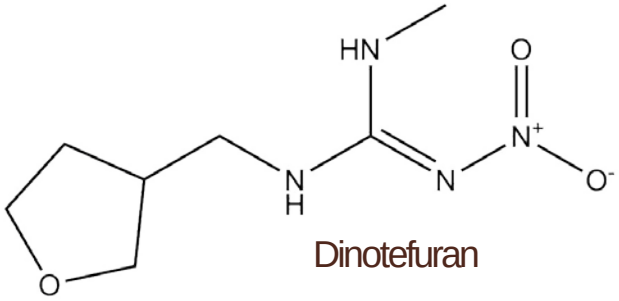

Imidacloprid



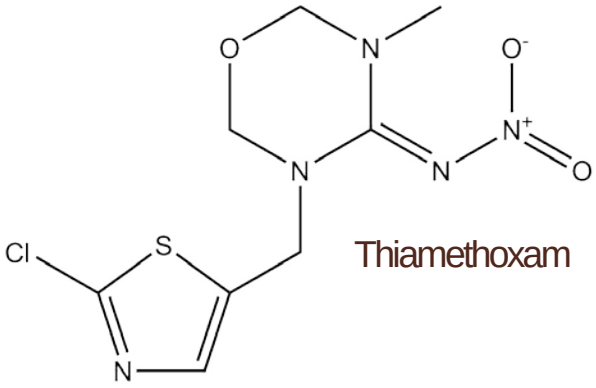

Acetamiprid




Clothianidin



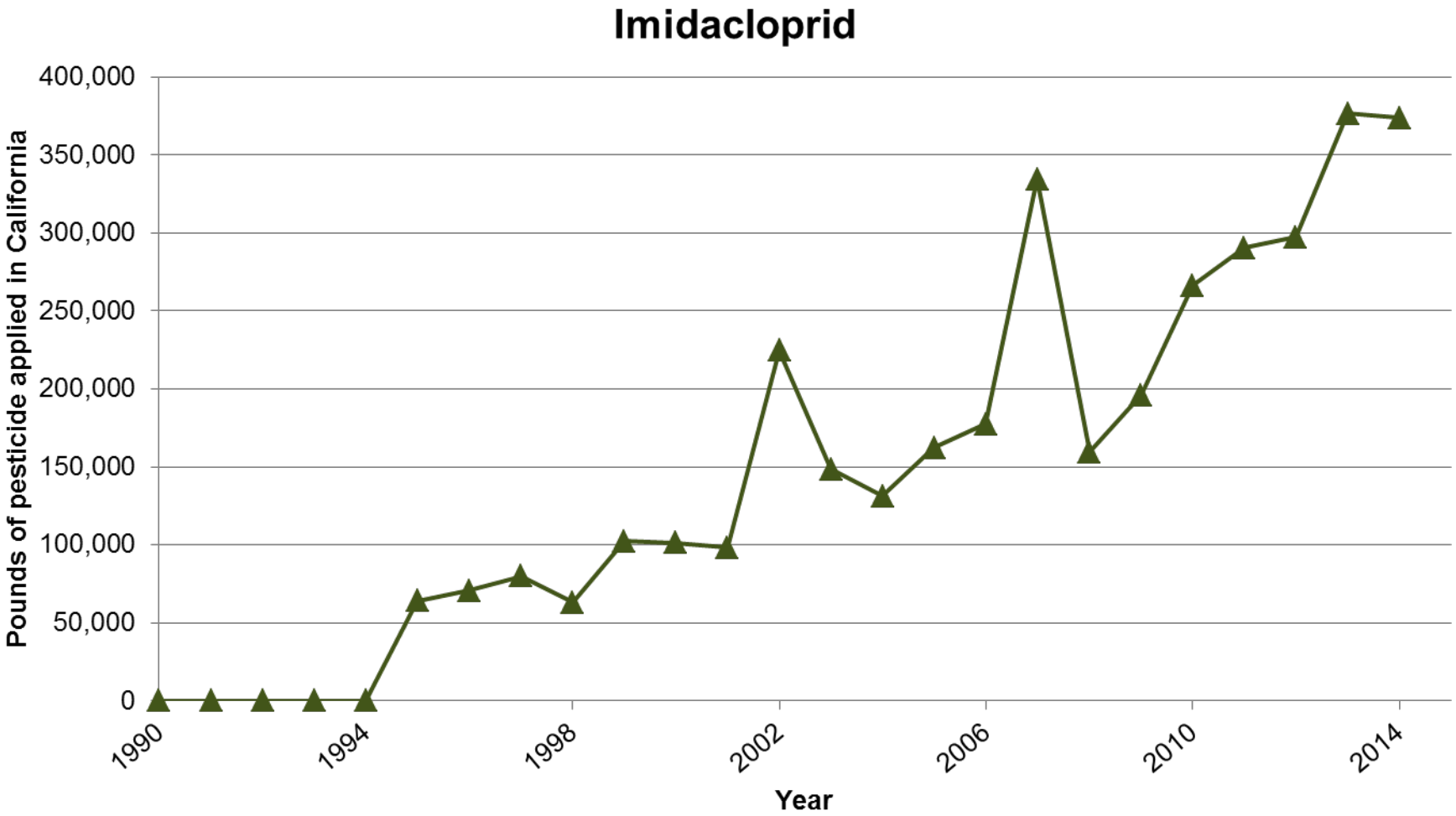

Dinotefuran




Thiamethoxam

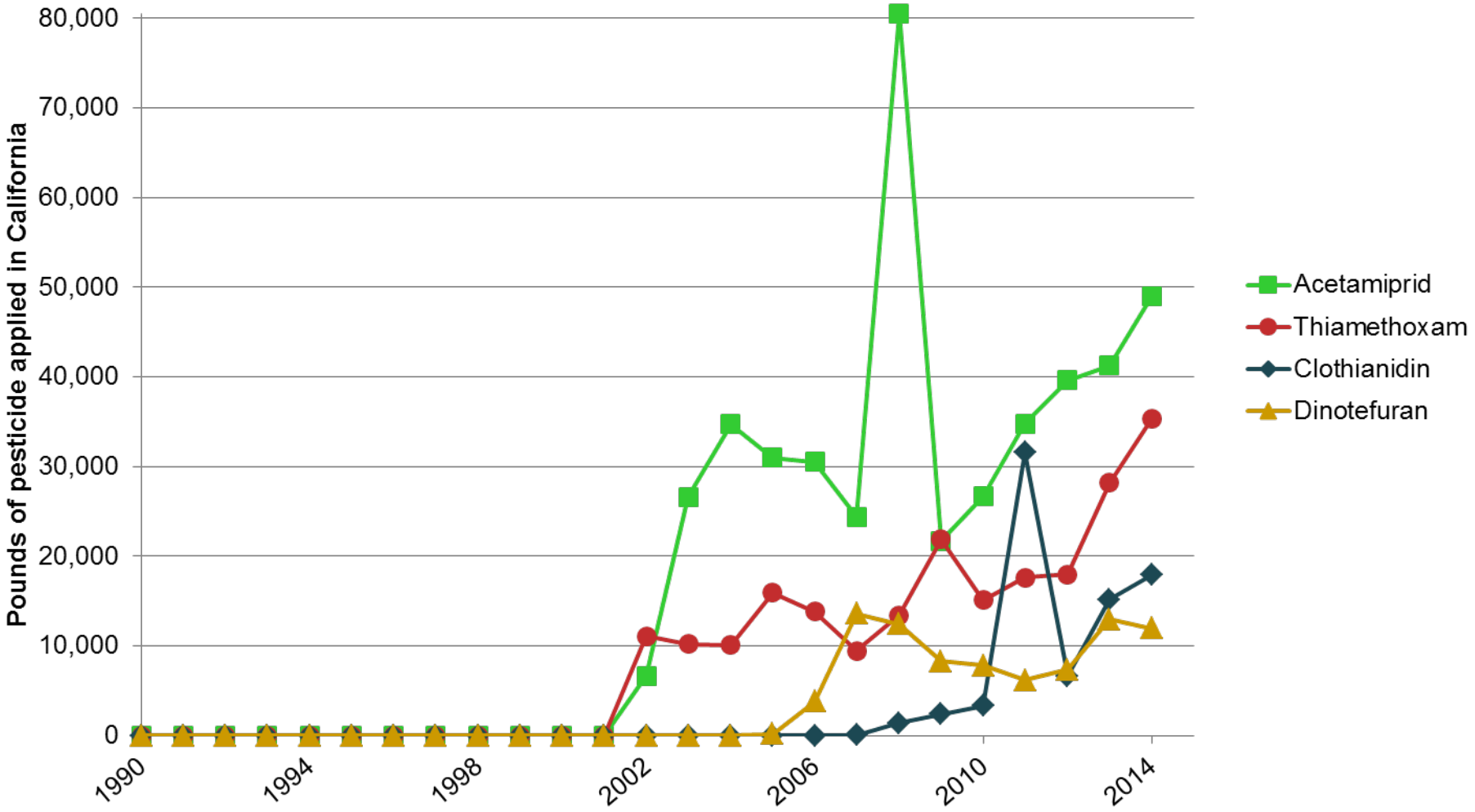
# Neonicotinoid pesticides

## Agricultural pesticide use in California



# Neonicotinoid pesticides

## Agricultural pesticide use in California



# Biomonitoring: Neonicotinoid pesticides

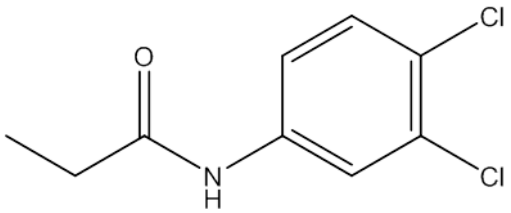
| | Measured in serum | Measured in urine | Selected references |
|---|---|---|---|
| **Imidacloprid** | ✓ | ✓ | Harada et al., 2016; Marfo et al., 2015; Osaka et al., 2016; Ueyama et al., 2014; 2015; Yamamuro et al., 2014 |
| **Acetamiprid** | ✓ | ✓ | |
| **5-(N-Acetylaminomethyl)-2-chloropyridine (5-AAM-2-CP)** | ✓ | ✓ | |
| **5-(N-Acetyl-N-methylaminomethyl)-2-chloropyridine (5-AMAM-2-CP)** | ✓ | ✓ | |
| ***N*-Desmethyl-acetamiprid** | ✓ | ✓ | |
| **Clothianidin** | ✓ | ✓ | |
| **Dinotefuran** | ✓ | ✓ | |
| **Flonicamid** | ✓ | ✓ | |
| **Nitenpyram** | ✓ | ✓ | |
| **Thiacloprid** | ✓ | ✓ | |
| **Thiamethoxam** | ✓ | ✓ | |

*Biomonitoring California lab capability: No current capability*

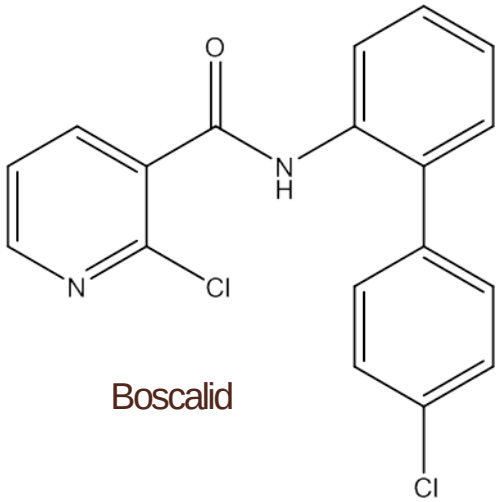
# Anilide pesticides

- Contain an amide group (-$CONH_2$) in which one hydrogen is replaced by a phenyl group
- Potential toxicity concerns associated with pesticides in this broad group include:
  - Immunotoxicity
  - Carcinogenicity
  - Developmental effects

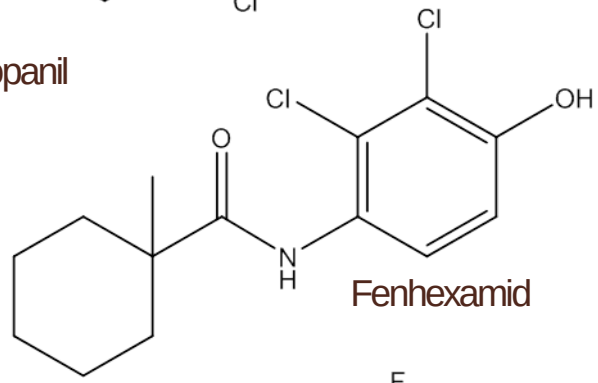
# Example anilide pesticides



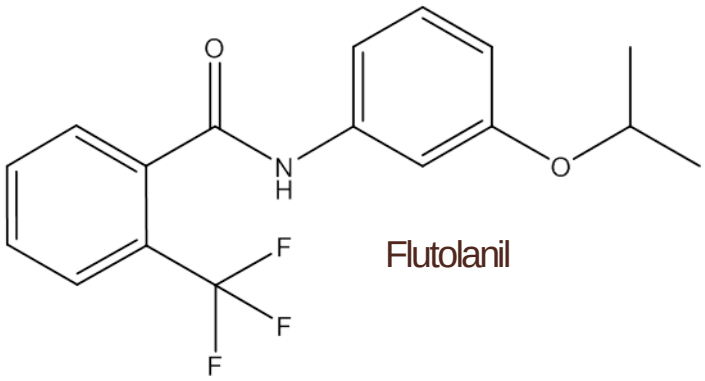

Propanil



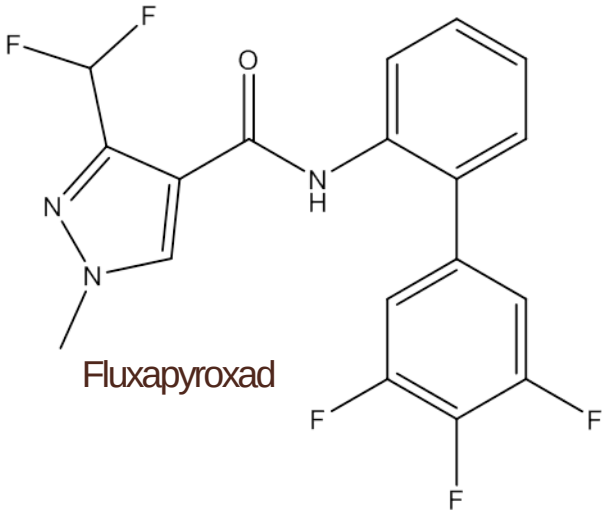

Boscalid




Fenhexamid



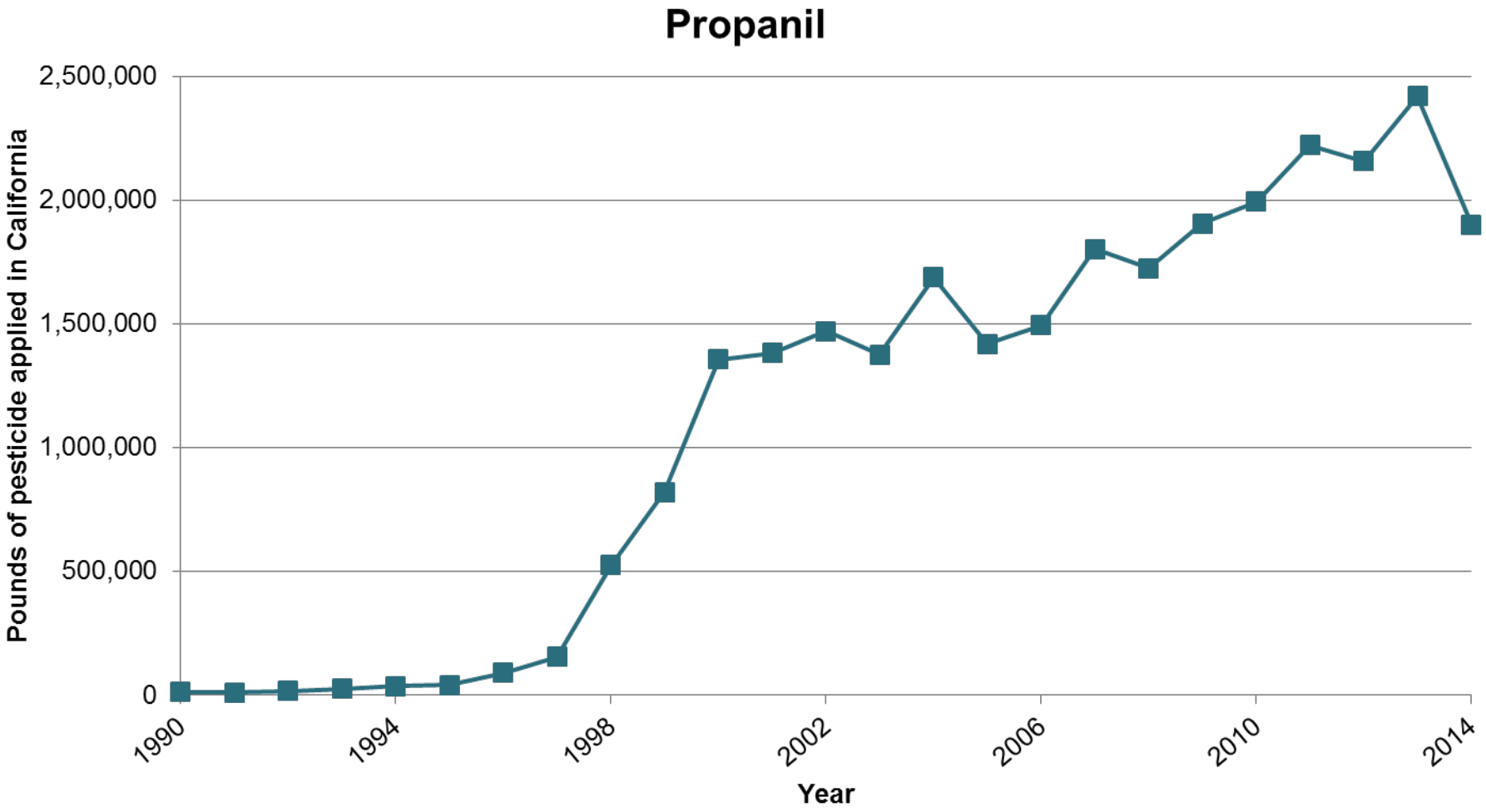

Flutolanil




Fluxapyroxad

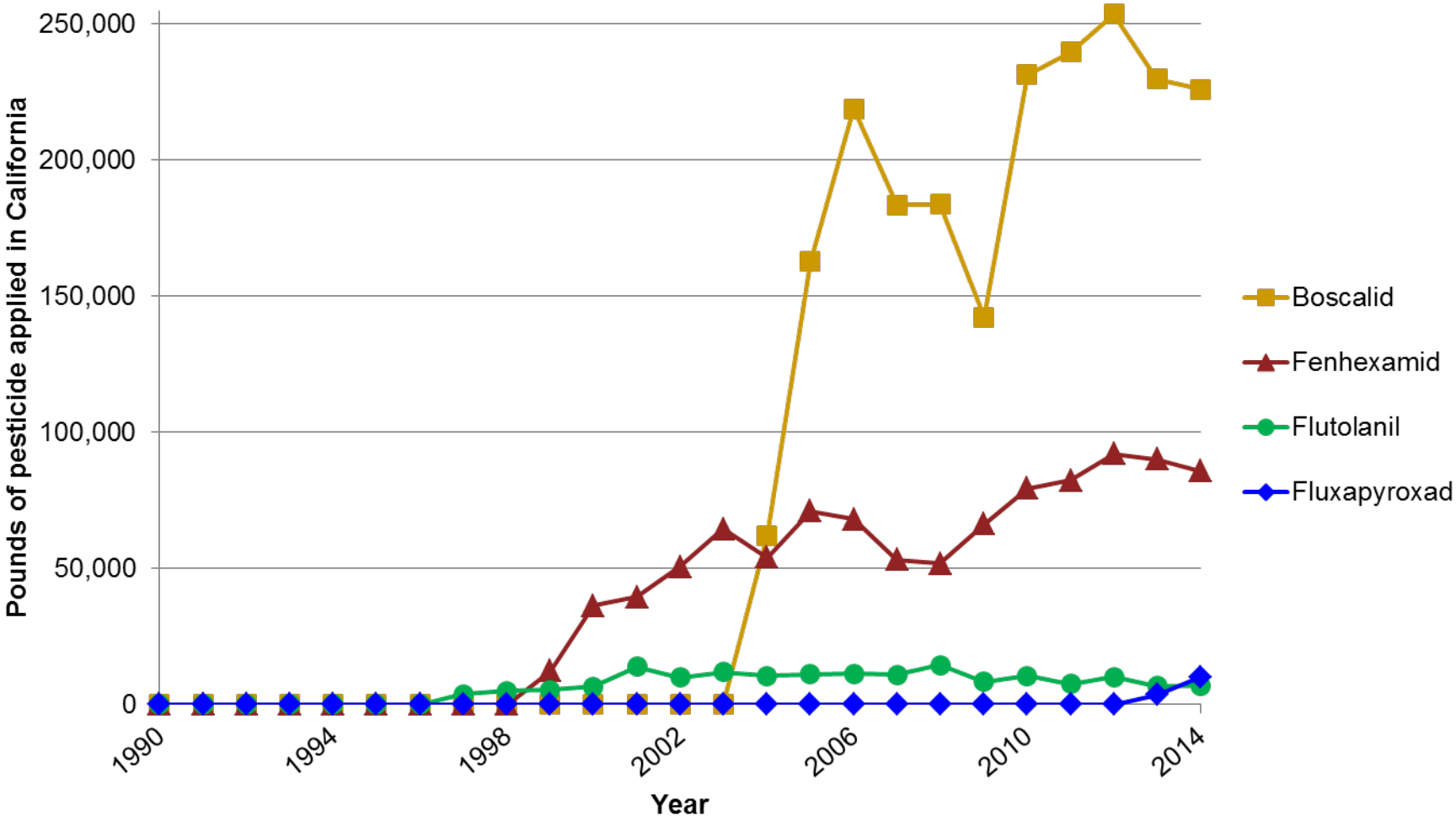
# Anilide pesticides

## Agricultural pesticide use in California



# Anilide pesticides

## Agricultural pesticide use in California



# Biomonitoring: 3,4-Dichloroaniline

*Shared metabolite of propanil and related pesticides*

| | Measured in serum | Measured in urine | Selected references |
|---|---|---|---|
| **3,4-Dichloroaniline (3,4-DCA)** | | ✓ | Rubino et al., 2012; Turci et al., 2006; Wittke et al., 2001 |

*Biomonitoring California lab capability: No current capability*

# Options for the Panel

The SGP could:

- Request that OEHHA prepare a potential designated chemical document on one of these pesticide classes for consideration in 2017
  - Additional classes could be considered later
- Propose further screening or continued tracking of one or more of these pesticide classes
- Advise no further action on any of these classes
- Suggest other pesticide classes for possible consideration

# Biomonitoring References

## Organophosphorus pesticides

Adams A, Friesen M, Olson A, Gerona R (2016). Biomonitoring of glyphosate across the United States in urine and tap water using high-fidelity LC-MS/MS method. Available to download here: http://detoxproject.org/1321-2/ (scroll down to UCSF presentation).

Hoppe H (2013). Determination of glyphosate residues in human urine samples from 18 European countries. Available at: http://www.gmoevidence.com/wp-content/uploads/2013/06/glyphosate_studyresults_june12.pdf

Jensen P, Wujcik C, McGuire M, McGuire M (2016). Validation of reliable and selective methods for direct determination of glyphosate and aminomethylphosphonic acid in milk and urine using LC-MS/MS. J Environ Sci Health B 51:254-9.

Krüger M, Schledorn P, Schrödl W, Hoppe H, et al. (2014). Detection of glyphosate residues in animals and humans. J Environ Anal Toxicol 4:1-5.

Watanabe D, Ohta H, Yamamuro T (2014). Solid-phase extraction of phosphorous-containg amino acid herbicides from biological specimens with a zirconia-coated silica cartridge. J Chromatogr B Analyt Technol Biomed Life Sci 969:69-76.

## Neonicotinoid pesticides

Harada K, Tanaka K, Sakamoto H, Imanaka M, et al. (2016). Biological monitoring of human exposure to neonicotinoids using urine samples, and neonicotinoid excretion kinetics. PLoS One 11:e0146335.

Marfo J, Fujioka K, Ikenaka Y, Nakayama S, et al. (2015). Relationship between urinary N-desmethyl-acetamiprid and typical symptoms including neurological findings: A prevalence case-control study. PLoS One 11:e0142172.

Osaka A, Ueyama J, Kondo T, Nomura H, et al. (2016). Exposure characterization of three major insecticide lines in urine of young children in Japan- neonicotinoids, organophosphates, and pyrethroids. Environ Res 147:89-96.

Ueyama J, Nomura H, Kondo T, Saito I, et al. (2014). Biological monitoring method for urinary neonicotinoid insecticides using LC-MS/MS and its application to Japanese adults. J Occup Health 56:461-8.

Ueyama J, Harada K, Koizumi A, Sugiura Y, et al. (2015). Temporal levels of urinary neonicotinoid and dialkylphosphate concentrations in Japanese women between 1994 and 2011. Environ Sci Technol 49:14522-8.

Yamamuro T, Ohta H, Aoyama M, Watanabe D (2014). Simultaneous determination of neonicotinoid insecticides in human serum and urine using diatomaceous earth-assisted extraction and liquid chromatography-tandem mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci 969:85-94.

## Anilide pesticides

Rubino F, Mandic-Rajcevic S, Ariano E, Alegakis A, et al. (2012). Farmers' exposure to herbicides in North Italy: assessment under real-life conditions in small-size rice and corn farms. Toxicol Lett 210:189-97.

Turci R, Barisano A, Balducci C, Colosio C, et al. (2006). Determination of dichloroanilines in human urine by gas chromatography/mass spectrometry: validation protocol and establishment of reference values in a population group living in central Italy. Rapid Commun Mass Spectrom 20:2621-5.

Wittke K, Hajimiragha H, Dunemann L, Begerow J (2001). Determination of dichloroanilines in human urine by GC-MS, GC-MS-MS, and GC-ECD as markers of low-level pesticide exposure. J Chromatogr B Biomed Sci Appl 755:215-28.