Evidence for Continued Use of Hexazinone in California

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DuPont Crop Protection
May 9, 2011

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Key Considerations for PREC

- Hexazinone detections in groundwater
  - Frequency of detection
  - Concentrations
  - Projected pattern of detection
- Determination of level that avoids adverse human health effects with margin of safety
- Decision on whether hexazinone has polluted groundwater
- Decision on whether hexazinone threatens to pollute groundwater
- Economic impact on agriculture from restrictions on use or cancellation

Speakers

- Aldos Barefoot, Environmental Science
- Michael Battalora, Toxicology
- Dan Putnam, UC Davis Extension Agronomist
- Mick Canevari, UCCE Advisor Emeritus

Agricultural Use

- Weed control in alfalfa
- Control of weeds toxic to livestock
  - Only option for control of groundsel post-emergence
  - Groundsel – widespread across San Joaquin and Sacramento Valleys in alfalfa fields
- Label Use rates
  - 0.5 to 1.5 lb ai/ac
  - Dependent on soil
- Most applications during winter

Hexazinone Use Restrictions

- Environmental Hazard Statement
  - Warning on leaching potential
- Application rate restrictions
  - Max. 1.5 lb ai/ac/year
    - Clays and loams
    - High organic matter - >5% OM
  - Coarse soils: max rate 0.7 lb ai/ac
- Use prohibited on gravelly, rocky or sandy soils
- Use prohibited in CA on seed alfalfa where %OM<1
- Max rate 0.5 lb ai/ac in CA on seed alfalfa where soil is sandy loam or loamy sand with %OM 1-2%

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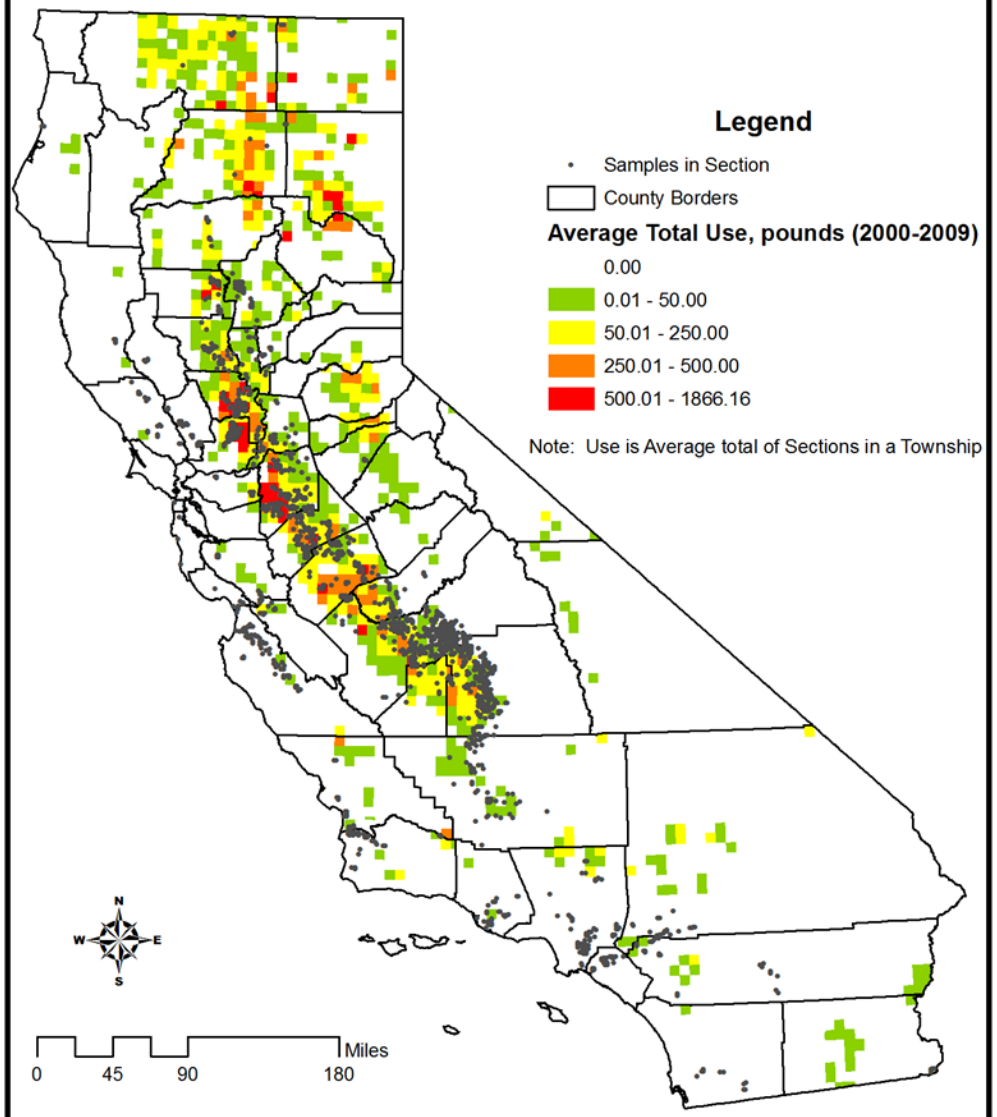
Hexazinone Detection in Groundwater

- DPR monitoring studies
  - 2344 wells sampled
    - Most in areas with hexazinone use
  - Low percentage of samples with hexazinone
    - 27 wells sampled between 1994 and 2010
    - Maximum concentration – 0.27 µg/l
- Legal Agricultural Use Determination
  - 5 wells that met DPR criteria
    - Fresno county, single section, 3 wells
    - San Joaquin county, two wells in adjacent sections

Groundwater Sampling and Average Use



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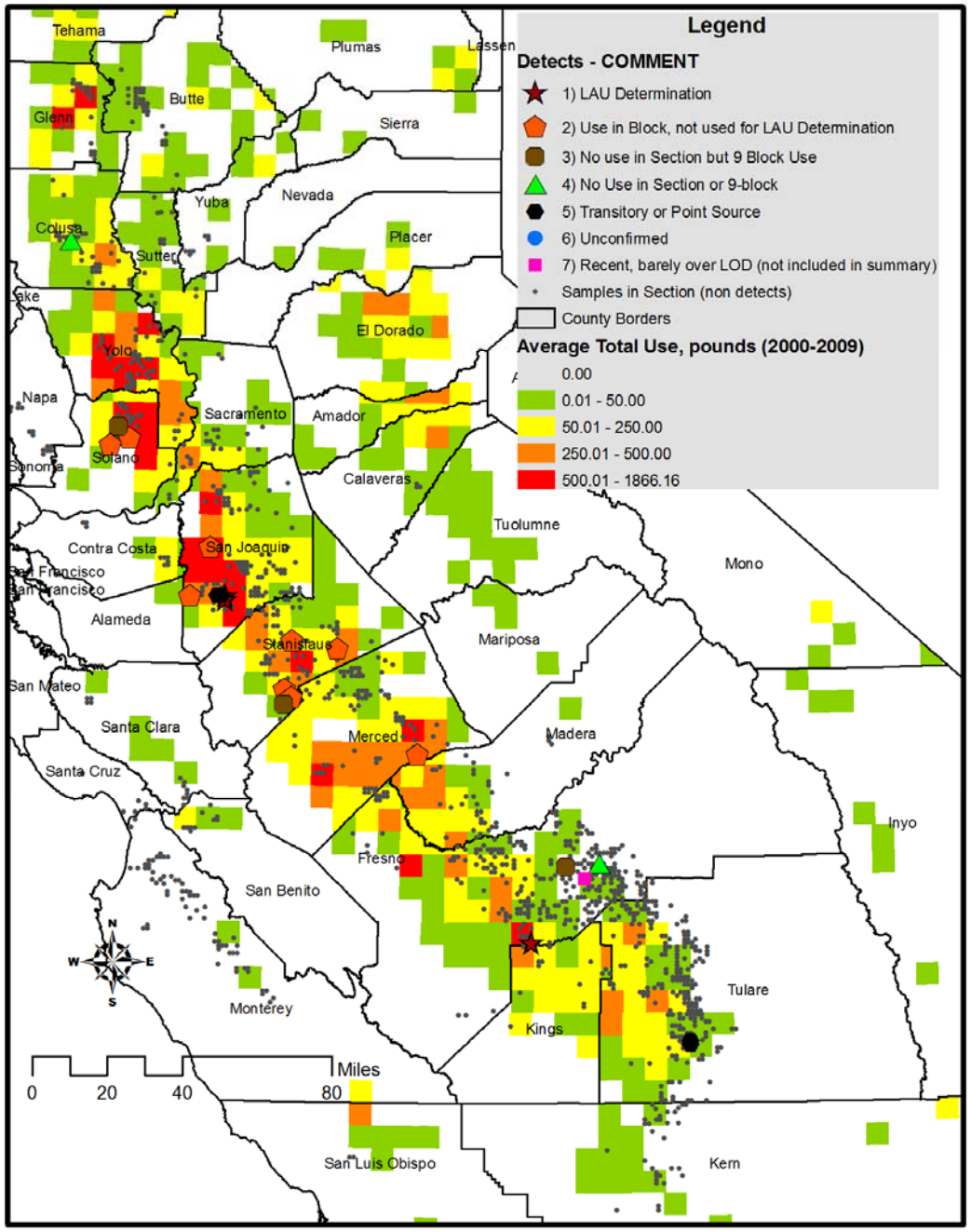
Groundwater Sampling and Average Use



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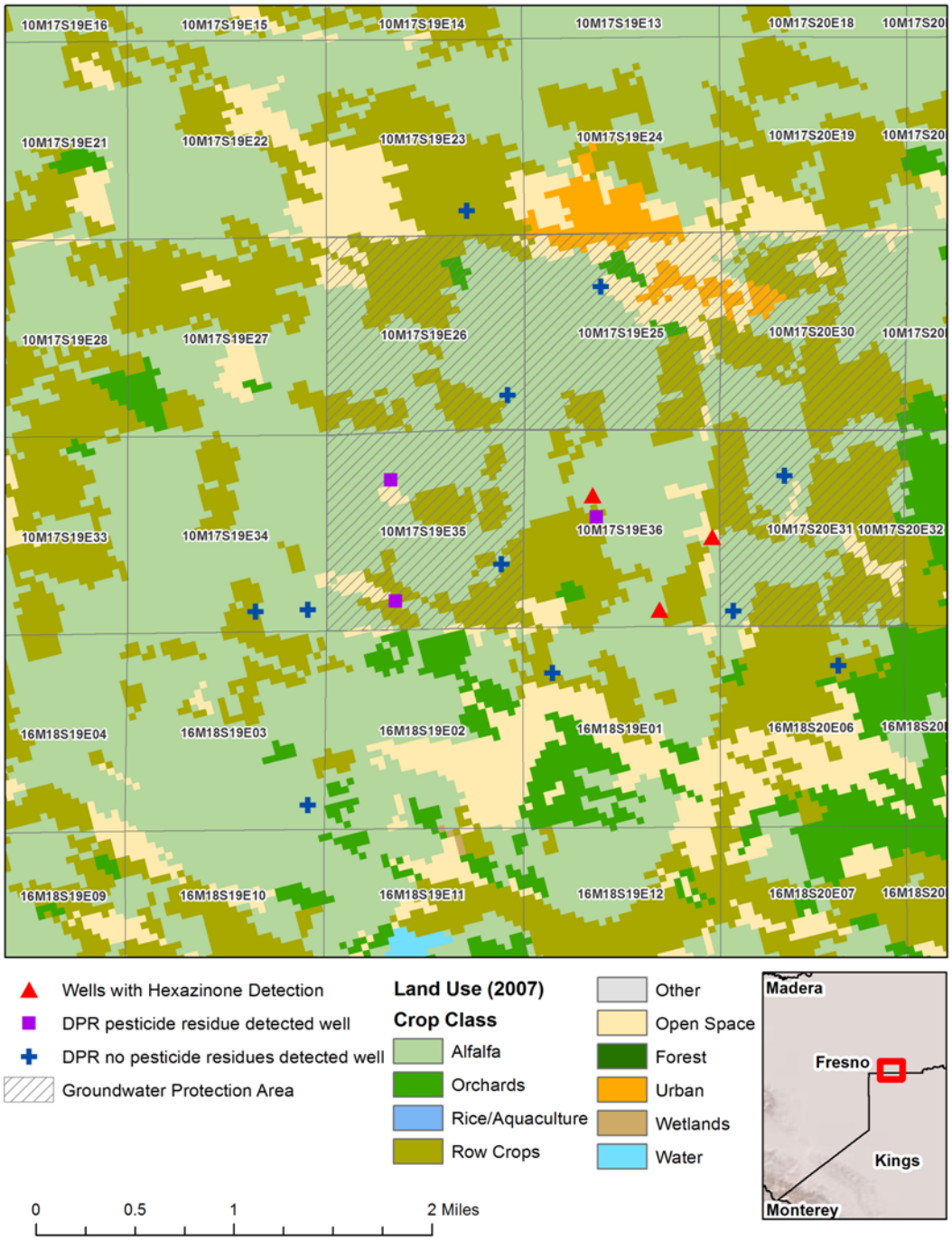
Land-use and Monitoring Locations around COMTRS 10M17S19E36



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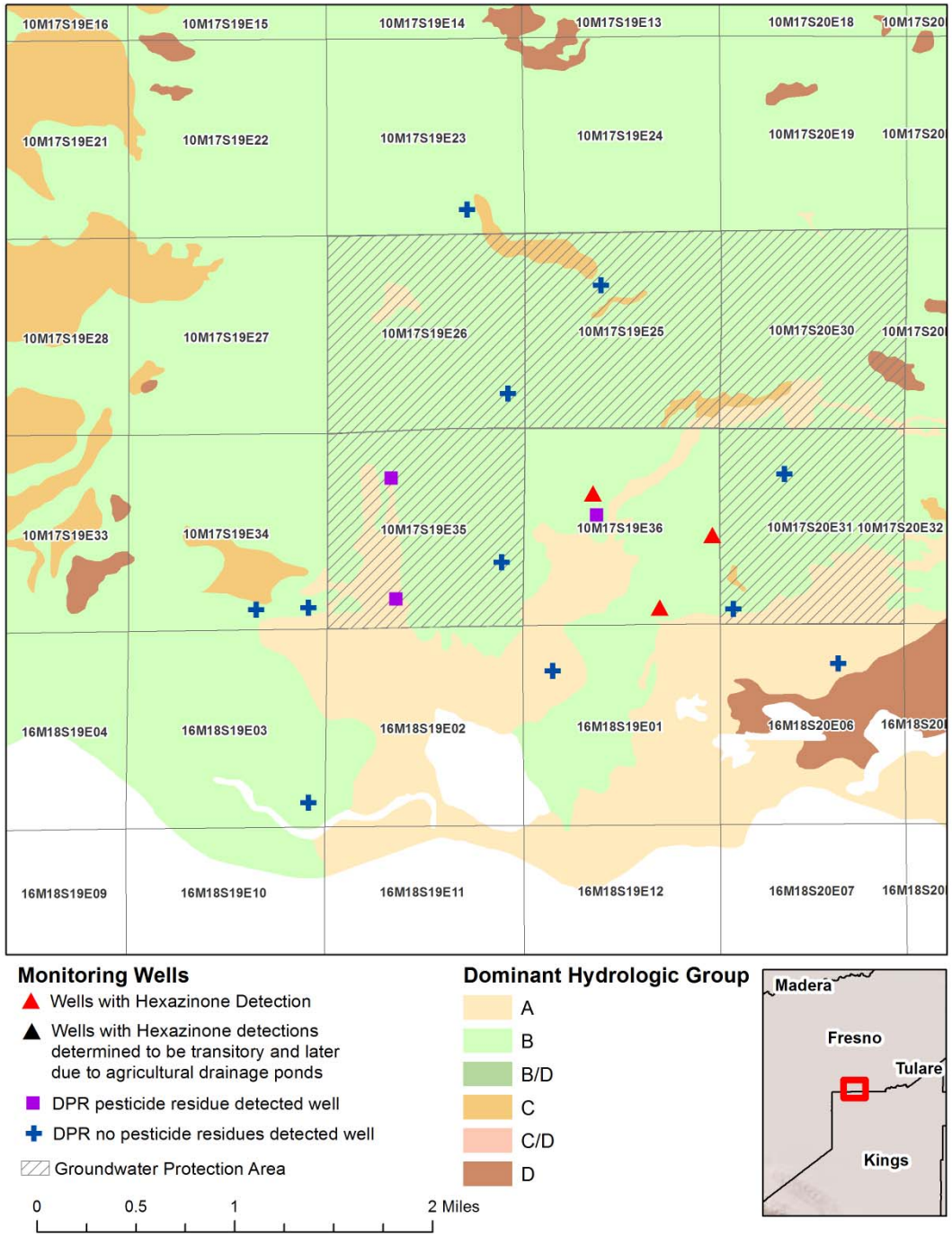
Hydrologic Soil Group and Monitoring Locations around COMTRS 10M17S19E36



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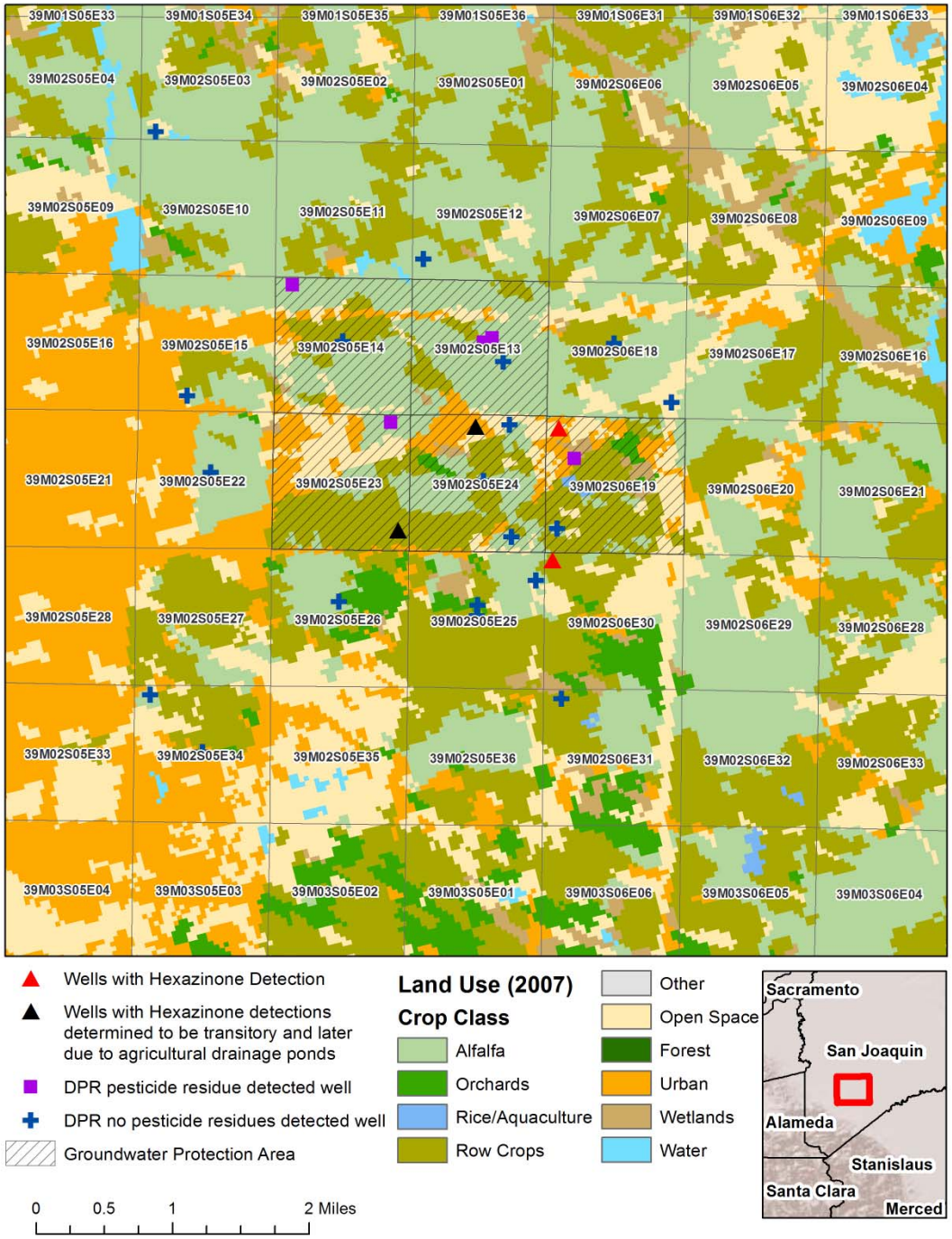
Land-use and Monitoring Locations around COMTRS 39M02S06E19 and 39M02S06E30



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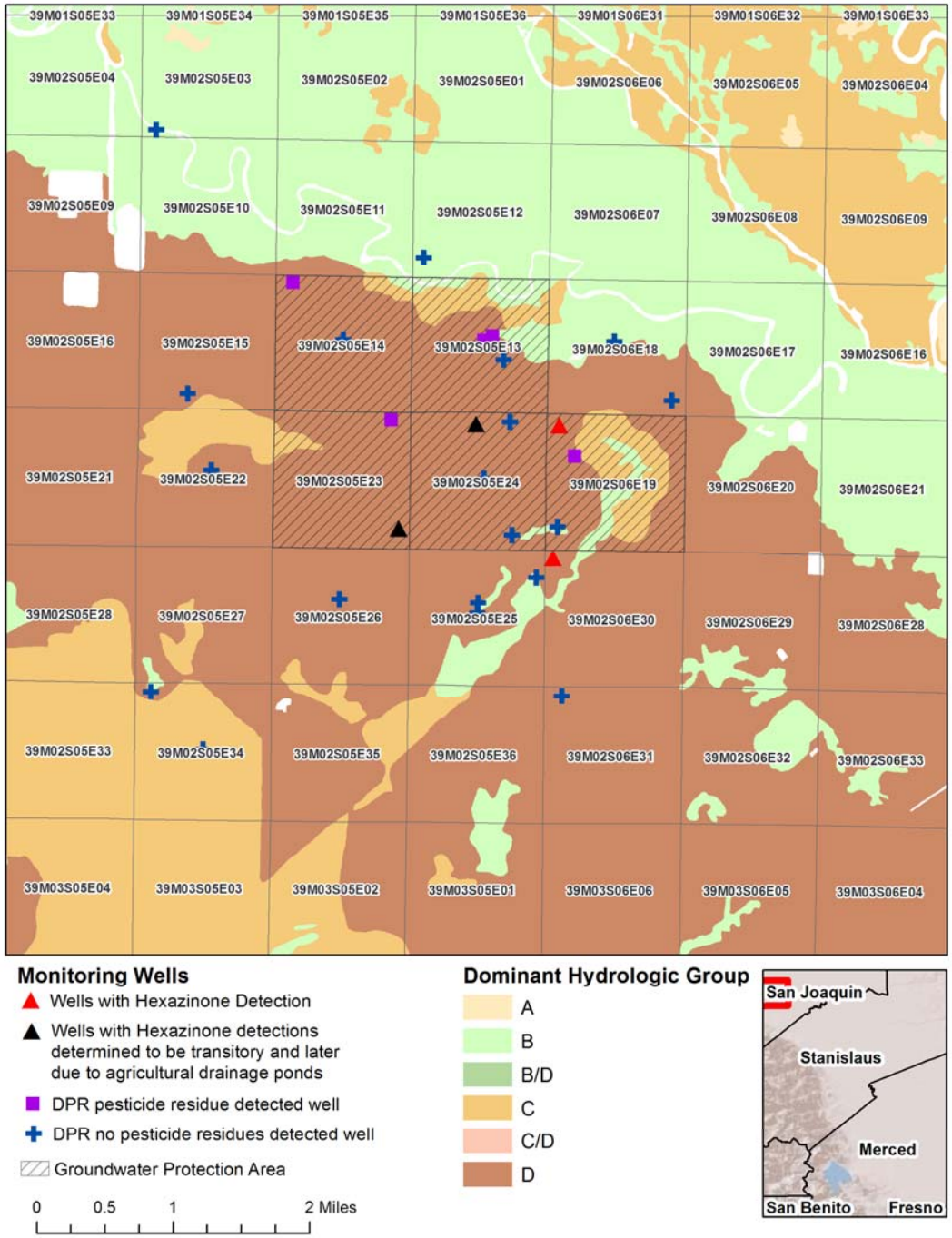
Hydrologic Soil Group and Monitoring Locations around COMTRS 39M02S06E19 and 39M02S06E30



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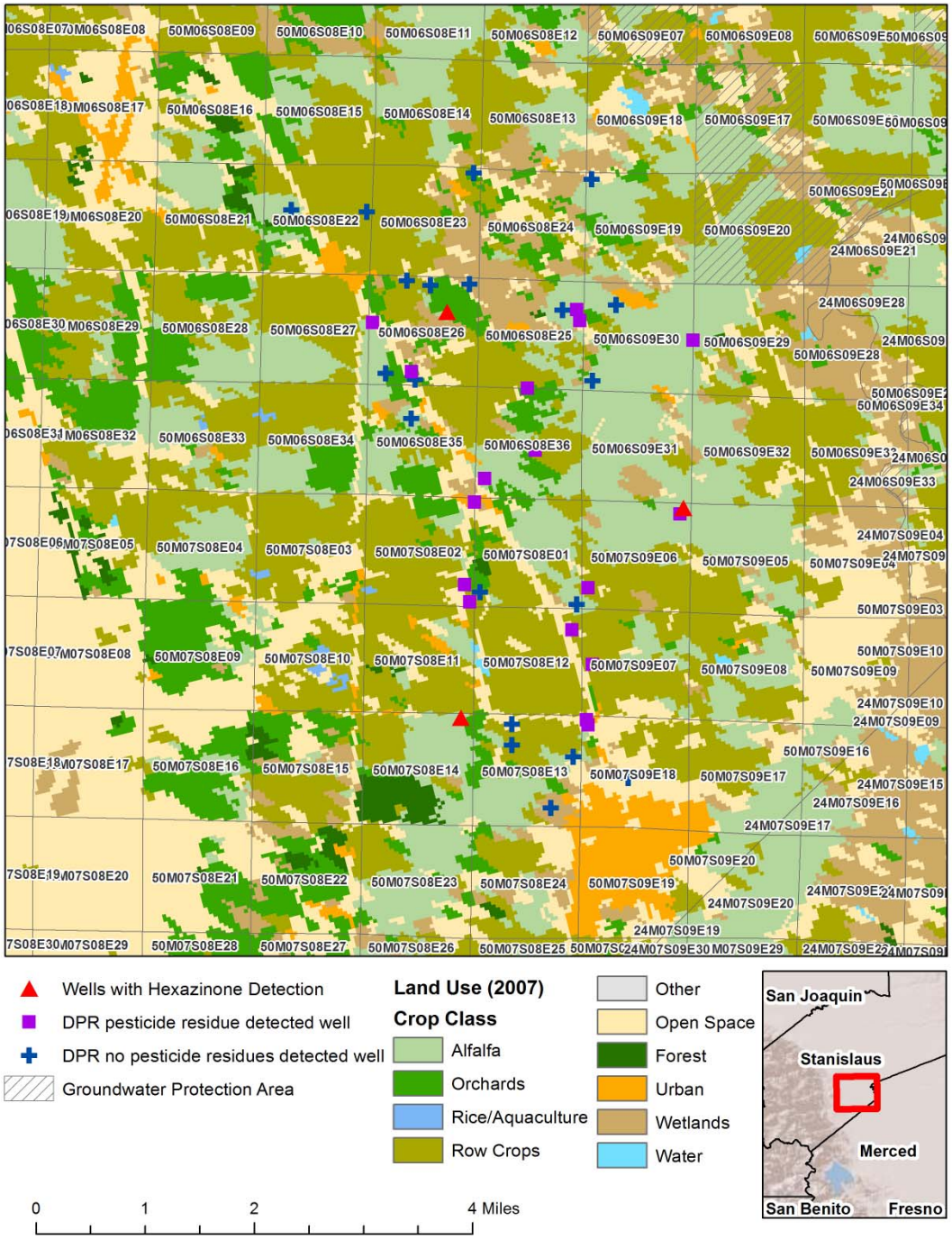
Land-use and Monitoring Locations around COMTRS 50M06S08E26, 50M07S09E06, and 50M07S08E14



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Prospective Groundwater Study

- US EPA study design
  - 8 well clusters (2 wells, 4 lysimeters in each)
- Site – alfalfa field, Merced County, CA
- Soil characterization –
  - Surface: loamy sand, sand
    - 0.8% OM
    - pH 7.5
  - Subsoils: sand, discontinuous layers of loam, silt loam, sandy clay loam
- Water table – 8-15 ft below ground surface
- Application rate – 0.75 lb ai/acre
- Flood irrigation – cumulative irrigation exceeded evapotranspiration

PGW Results

- Hexazinone dissipation half-life – 25 days
  - Metabolites observed
- First detection of hexazinone in groundwater at 336 days
- Maximum concentration
  - Western part of the site - detection in one well at 9.2 ppb
  - Eastern part of the site- <1 ppb
  - Difference attributed to slight difference in soil characteristics

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Conclusions

- Hexazinone has potential for leaching
- Soil characteristics have effect on leaching
- Use pattern, label restrictions reduce probability for detection
- Concentrations are low, maximum 0.27 µg/l
- Detections are sporadic
- Many wells with detectable hexazinone are isolated
  - No detections in wells in close proximity
- Observed low frequency of detection and low concentrations demonstrate the success of label restrictions and ag practice in mitigating the leaching potential

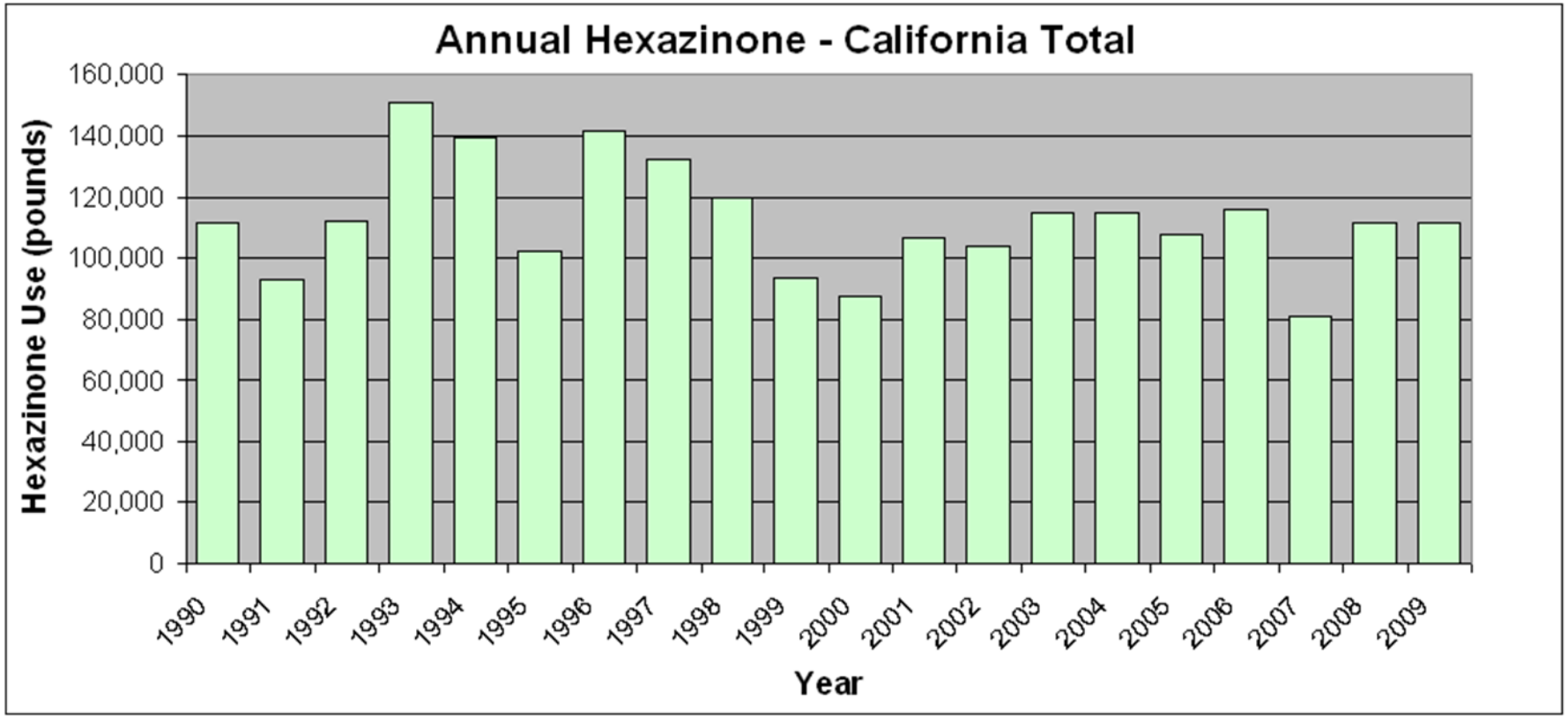
Potential for Pollution of Groundwater as Defined by Statute

- Health Effects endpoint
  - EPA Health Advisory Level, Lifetime exposure – 400 µg/l
- Maximum concentration observed in monitoring – 0.27 µg/l
- Margin of exposure – 1480
- Conclusion: hexazinone has not polluted groundwater

Potential to Threaten Pollution of Groundwater as Defined by Statute

- History of use
- Projections of detection in groundwater
  - Estimated concentrations
  - Estimated geographical range of detections
- Comparison of projected concentrations to Health Advisory Level

Hexazinone Use



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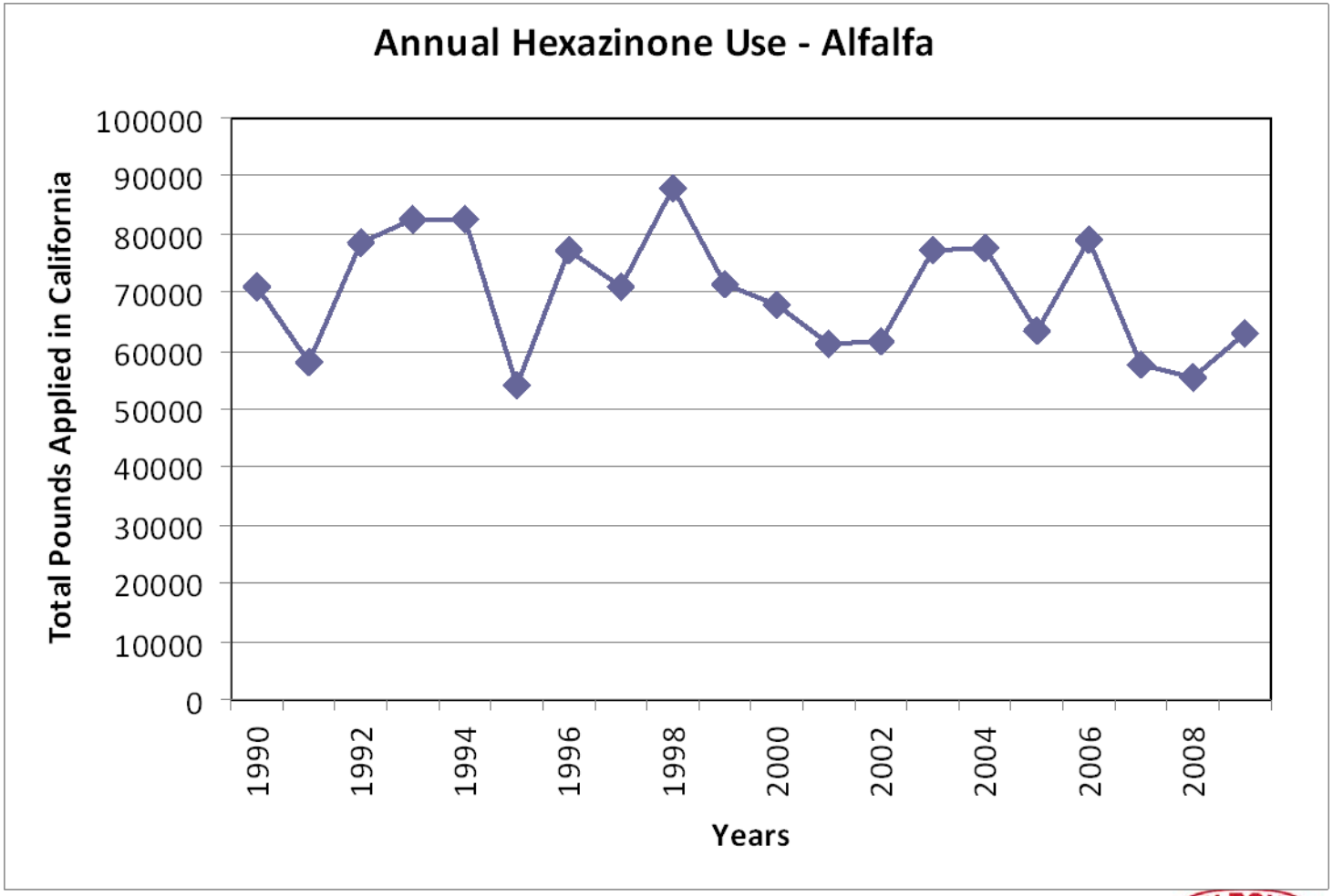
Hexazinone Use in Alfalfa



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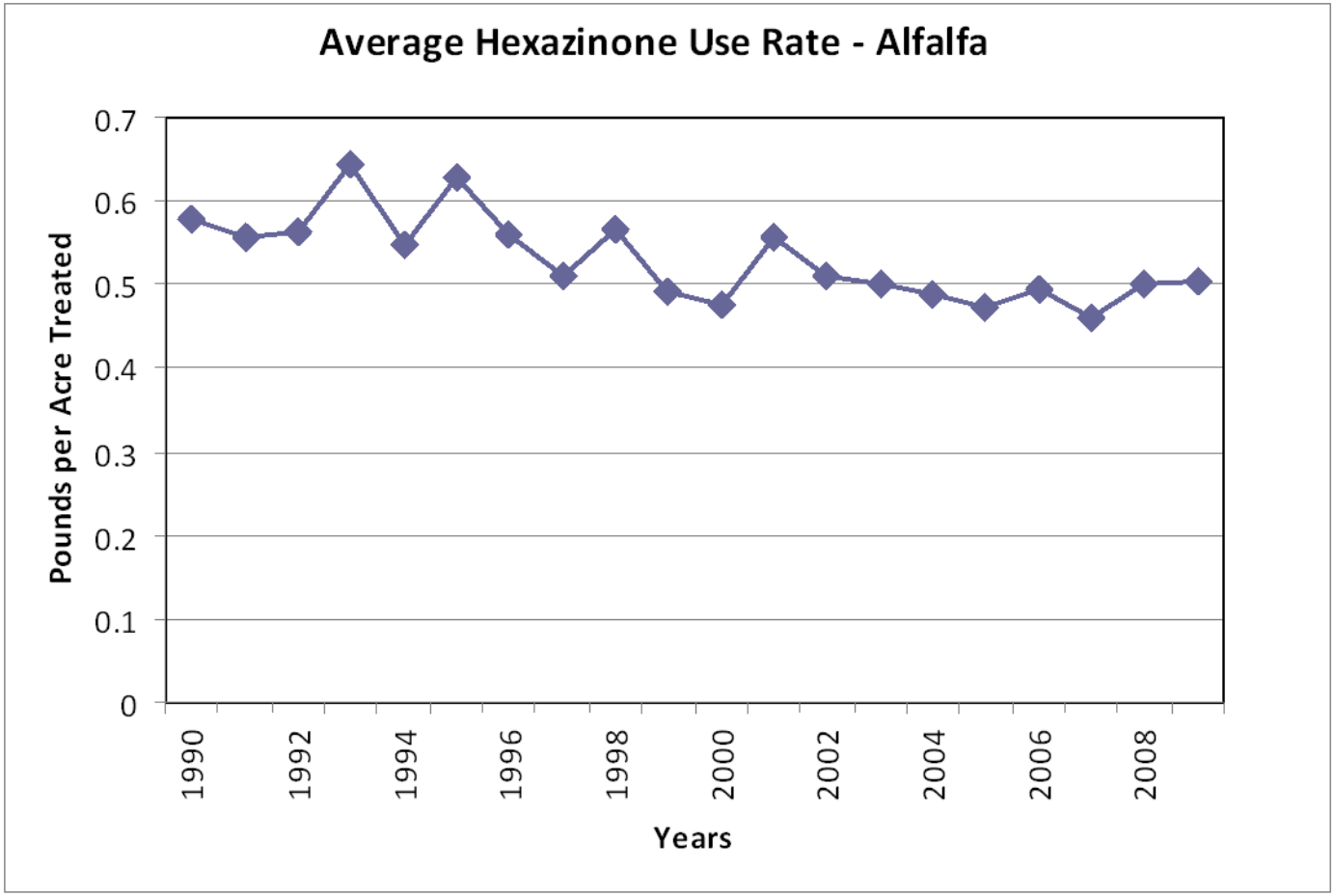
Hexazinone Use Rate in Alfalfa



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Projected Concentrations Using Modeling

- CDPR Modeling Tool
  - Calibrated to monitoring data
  - Single vulnerable site
  - Realistic and excessive irrigation inputs
  - 10 and 13 year travel times to wells
  - Probabilistic assessment using range of environmental properties
    - Soil sorption coefficient
    - Soil dissipation half-life
    - Decision point – 95th percentile concentration >0.05 µg/l
- Spatial Modeling using PRZM
  - Distribution of leaching throughout the Sacramento, San Joaquin watersheds
  - Use data from the PUR, 2000-2008
  - Soils from SSURGO
  - Maximum soil dissipation half-life, minimum soil sorption coefficient

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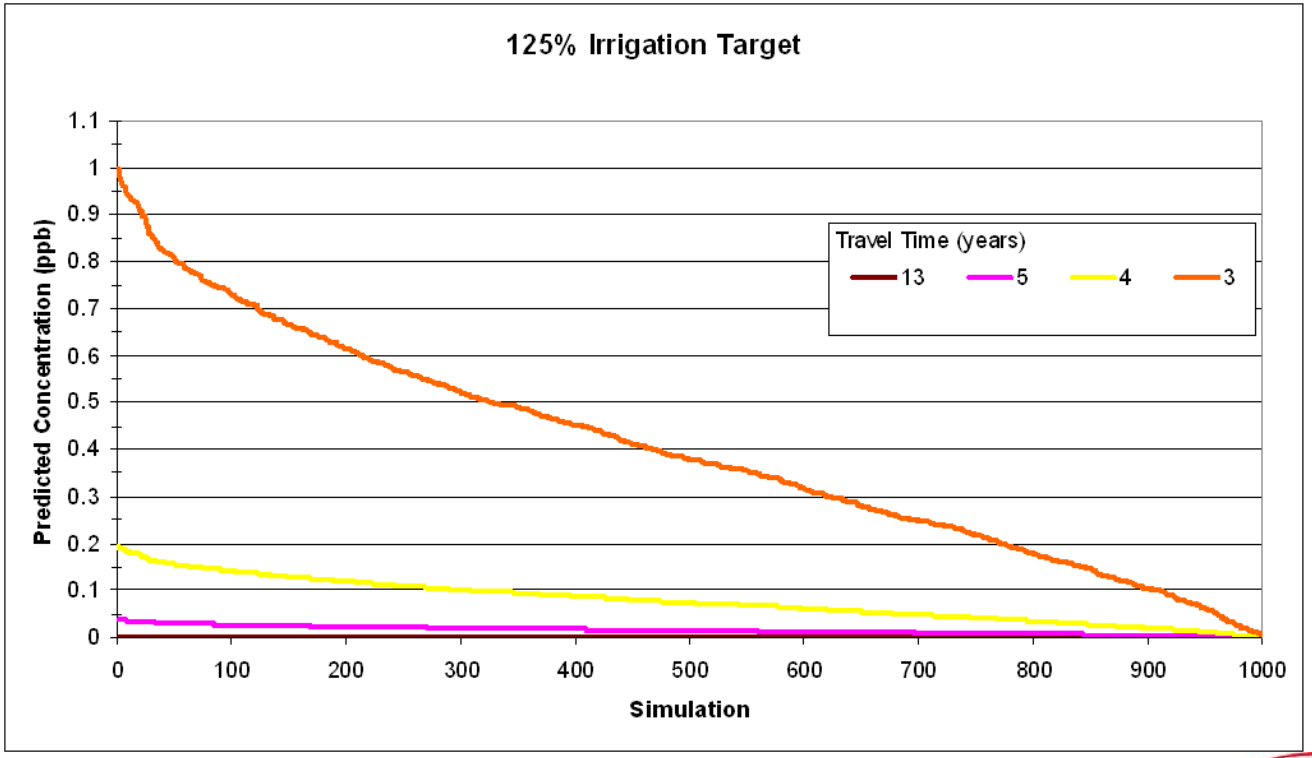
DPR Probabilistic Modeling Tool Results

Application rate	Irrigation amount	Aging time (years)	Longest half-life (days)	Cumulative percentile (µg/L)		
				50th	90th	95th
1.5 lb/acre	125%	13	154	0.00	0.00	0.00
1.5 lb/acre	125%	5	154	0.01	0.03	0.03
1.5 lb/acre	125%	4	154	**0.07**	**0.14**	**0.16**
1.5 lb/acre	125%	3	154	**0.38**	**0.73**	**0.80**



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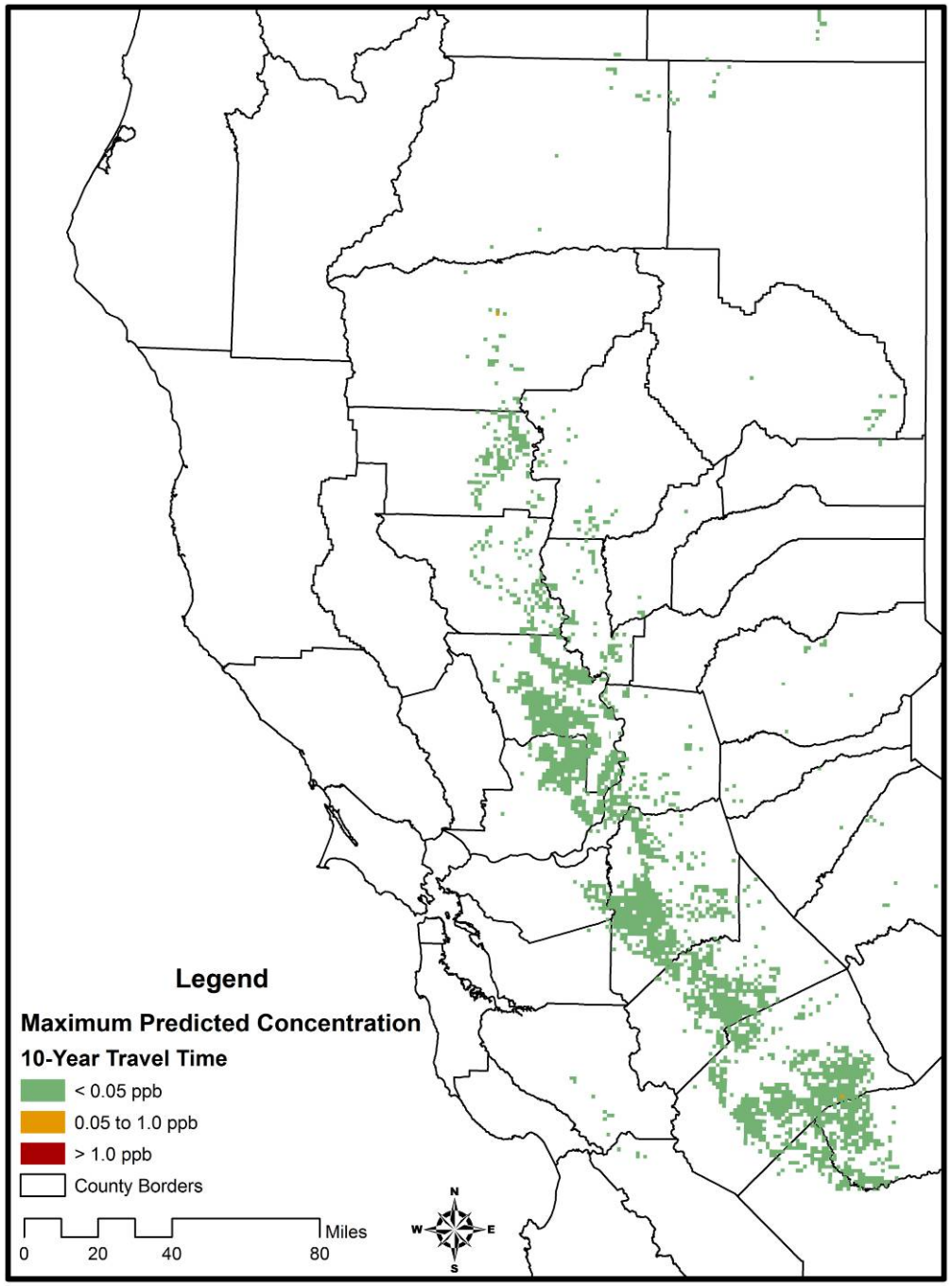
Spatial Modeling Maximum Predicted Well Concentration (10-Year Travel Time)



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Potential to Threaten Pollution of Groundwater as Defined by Statute

- Hexazinone use is not increasing
  - Average use rate has decreased to 0.5lb ai/a
- Estimated concentrations in groundwater are much less than the EPA HAL
  - DPR modeling tool – 95th percentile concentration <0.05 µg/l
  - Estimated geographical range of detections
    - <0.05 µg/l in all sections modeled
- Projected concentrations are << Health Advisory Level
- Conclusion: Hexazinone does not threaten to pollute groundwater

Hexazinone: Basis for EPA's Drinking Water Health Advisory

Michael Battalora, Ph.D.
Regulatory Toxicologist
DuPont Crop Protection

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Outline

- Overview of drinking water risk assessment
- Toxicity database of hexazinone
- Reference dose for Hexazinone
- Details of US EPA risk assessment for hexazinone in drinking water
- Conclusions

Drinking water risk assessment (US EPA)

- Doses with no effects in animal studies (NOAEL) are lowered by dividing with uncertainty factors* (usually 100**) yielding a reference dose (RfD)
- A chronic RfD is a level you can be exposed to for a lifetime without a risk of an adverse effect
- A health advisory life-time is only allots 20% of RfD to be from water exposure
- 0.27 µg hexazinone/L (maximum detect) found in well water samplings should not be of concern since it is well below the 400µg/L (0.4 mg/L) health advisory life-time

Level with findings
38 mg/kg bw/day

↓

No-Observed-Adverse-Effect Level (NOAEL)
5 mg/kg bw/day

↓

Human exposure limit i.e. reference dose
0.05 mg/kg/bw/day

↓

Health advisory life-time
(0.4 mg/L)

***Safety factors or adjustment factors**
****Interspecies (10) x Intraspecies (10) = 100**

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Toxicology Data for Hexazinone

- The most sensitive endpoint from multiple tests in multiple species is used for the human health risk assessment
  - Acute effects studies
  - Developmental toxicity
  - Reproductive toxicity
  - Repeated dose toxicity
  - Mutagenicity
  - Carcinogenicity
- US EPA chose the one year dog study to set the chronic Reference Dose (cRfD)
  - Body weight effects & liver effects at 38 mg/kg bw
  - NOAEL of 5 mg/kg bw
- cRfD: 5 mg/kg / 100* = 0.05 mg/kg bw

*Interspecies (10) x Intraspecies (10) = 100

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US EPA Drinking Water Risk Assessment - 1

- A Drinking Water Equivalent Level is derived first
- It is a lifetime exposure level protective from adverse health effects that assumes **all exposure to hexazinone comes from drinking water**; it is calculated as

DWEL

= (cRfD) x (mass of the person*) / water consumed per day

= (0.05 mg/kg/day) x (70 kg person) / 2 L

= 1.75 mg/L, rounded to 2 mg/L

*Reference human: 70 kg

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US EPA Drinking Water Risk Assessment - 2

- From a DWEL a **H**ealth **A**dvisory **L**ife-time (HAL) is derived*
- It is the concentration of a chemical that will not cause any adverse effects after a lifetime of exposure; it allots **only 20% of exposure to hexazinone** is via drinking water; it is calculated as

HAL

= DWEL x 0.2

= 2 mg/L x 0.2

= 0.4 mg/L (400 µg/L or 400 ppb)

*The full calculation without 1st calculating the DWEL is HAL = cRfD x body weight x exposure from water / 2 L water, i.e. 0.05 mg/kg bw x 70 kg x 0.20 / 2 L

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What is a µg/L?

It is like…

1 dollar in a billion
1 drop in 500 barrels of water
1 pinch of salt in 10 tons of potato chips
1 second in 32 years

US EPA Health Advisory Lifetime		California Maximum detect
400 µg/L	⟷	**0.27 µg/L**

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Conclusions

- According to California Food & Agric. Code Sect. 13142 (j), "Pollution" means the introduction into the groundwaters of the state of an active ingredient, other specified product, or degradation product of an active ingredient of a pesticide above a level, with an adequate margin of safety, that does not cause adverse health effects
- The maximum level of hexazinone found in California monitoring wells was 0.27 ppb (i.e. 0.27 µg/L)
- This is well below the health advisory life-time of 400 µg/L (0.4 mg/L) established by US EPA and should not be of concern from a human health standpoint (i.e. adequate margin)
- Given the levels of hexazinone detected in the monitoring wells, one can reasonably state that it has not polluted and does not threaten to pollute the groundwater of the state

Back-up slides

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US EPA's Assessments of Hexazinone

- A complete toxicology battery was evaluated by US EPA resulting in the RED of 1994
- Health Advisory Lifetime of 400 µg/L (1996)
- EPA re-evaluated the human health data in 2002 for a tolerance assessment
- Office of Water reaffirmed the Health Advisory in 2011

Hexazinone Reference Dose

- EPA used the 1-year dog study as the basis for the establishing a chronic reference dose (cRfD) with a NOEL of **5 mg/kg** body weight/day, based on clinical chemistry parameters, weight effects and histological findings in the liver at 37.6 mg/kg (details next slide)
- An uncertainty factor of 100 was applied to give a cRfD of **0.05 mg/kg body weight/day**

Critical Endpoint for Reference Dose Derivation - Extract from US EPA DER

1-year dog study:

- Dietary levels of 0, 200, 1500 or 6000 ppm; equivalent to dietary concentrations 0/0, 5.0/4.9, 41.2/37.6 and 161/167 mg/kg/bw
- At 1500 ppm liver vacuolation and balloning; thinness in one male; clinical chemistry changes suggestive of liver effects more pronounced at 6000 ppm; body weight decreases, food consumption down, especially in females; increased liver weights at 6000 ppm; liver inflammation and cytotoxicity in males and females at 6000 ppm; decreases in red cell parameters