Challenges in biomonitoring exposure to diesel exhaust

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Outline

- Why are we concerned about diesel exposure?
  - Diesel as a Toxic Air Contaminant (TAC)
  - Diesel as part of ambient particulate matter (PM)
  - Exposures in California
- What is in diesel engine exhaust?
  - Composition changes
- What are the characteristics of a good biomarker?
- What are the complications inherent in trying to find a good biomarker for diesel engine exhaust exposure?

Very Brief History

- IARC 2A carcinogenicity: animals sufficient, humans limited (1989)
- HEI (1995), WHO (1996): epidemiological data consistent in showing weak association
- California identified diesel exhaust particulate (DEP) as TAC (1998) noting evidence consistent with causal association with lung cancer
- IARC Group 1: sufficient evidence for carcinogenicity in humans based on lung cancer (2012)

Health Effects of Diesel Exhaust

- Increased lung cancer risk observed in numerous studies of diesel exhaust-exposed workers (primary basis for listing as a Toxic Air Contaminant).
- Targets of toxicity include respiratory and immune systems.
- Enhanced allergic response in humans exposed to DEP directly.
- Pulmonary inflammatory changes and changes in cardiovascular measures observed after controlled exposures of human volunteers.
- Increased incidence of COPD in workers with long term exposure.

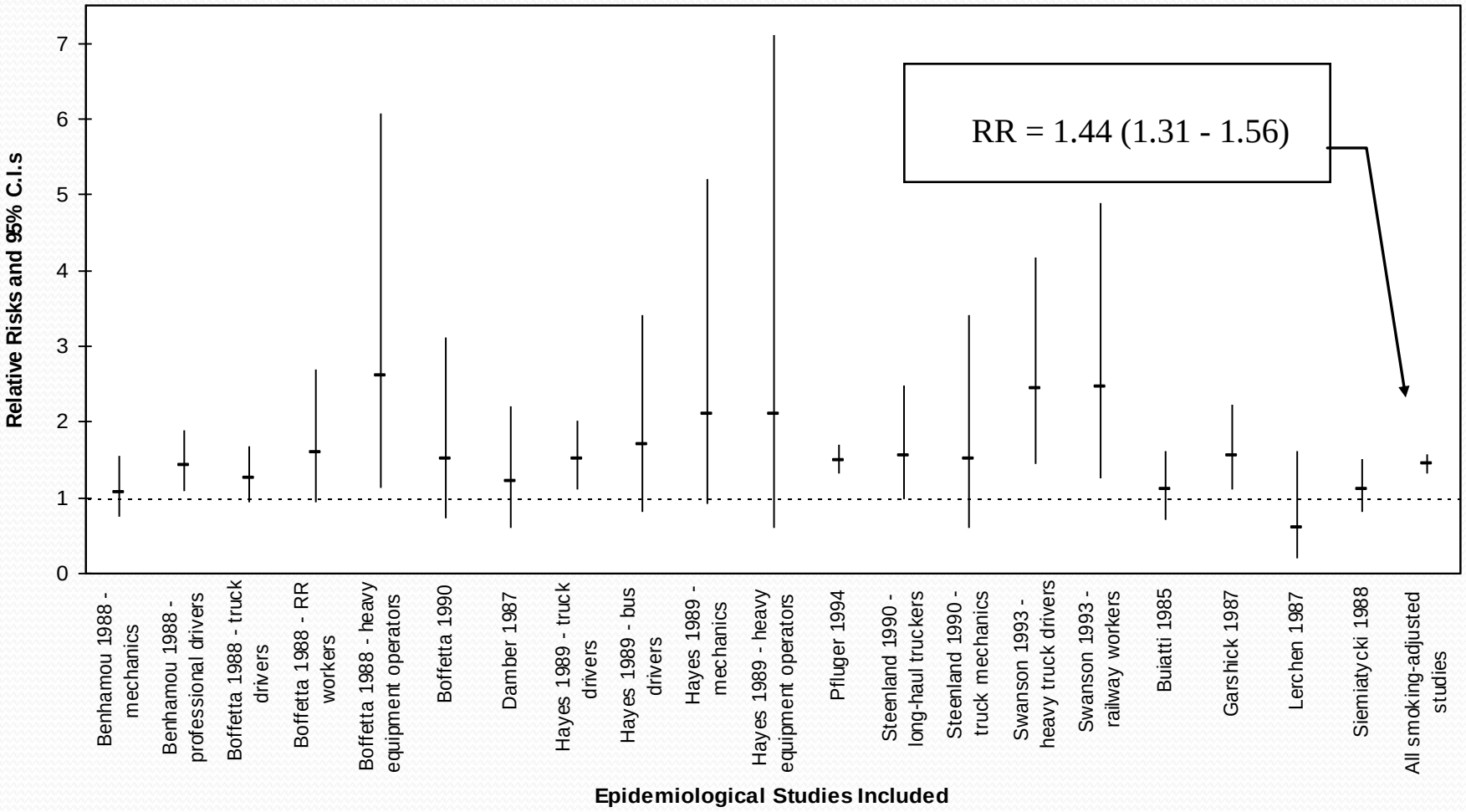
Diesel Exhaust Particulate is a Component of Ambient PM2.5

Consistent associations of ambient PM2.5 with:

- Daily and long-term cardiopulmonary mortality
- Hospital and emergency room visits for cardiac and respiratory illness
- Acute and chronic respiratory symptoms
- Lung function decrements and decreased lung function growth in children
- School absenteeism
- Medication use and symptoms in asthmatics

OEHHA's 1998 Meta-analysis – TAC program

Figure C-3: Estimates of Relative Risks for Smoking-Adjusted Studies of Diesel Exhaust Exposure and Lung Cancer



Select risk estimates from more recent studies

Study	Risk
Garshick et al (2004)	railroad workers lung cancer relative risk (RR) = 1.40 (95% CI = 1.30 – 1.51).
Laden et al (2006)	Railroad workers hired post-1945, lung cancer RR = 1.77 (95% CI = 1.50 – 2.09), dose–response relationship with exposure duration
Garchick et al (2008)	Long-haul truck drivers employed 20 yrs, smoking-adjusted lung cancer HR = 1.40 (95% CI = 0.88 – 2.24); pickup/delivery drivers employed 20 yrs, smoking-adjusted lung cancer HR = 2.21 (95% CI = 1.38 – 3.52).
Vermuellen et al (2014)	meta-analysis of 3 cohort studies - "approximately 6% of annual lung cancer deaths may be due to DEE exposure".
Laden et al (2006)	COPD OR = 1.61 (95% CI = 1.12–2.30) for engineers or conductors who had worked ≥ 16 years after 1959

Diesel Quantitative Cancer Risk Assessment for TAC Identification

- OEHHA staff included bracketing assumptions about historical exposures of railroad workers
- 95% UCL risks estimated ranged from 1.3 X 10^{-4} to 2.4 x 10^{-3} [per µg DEP/m^3]
- Subject to extensive public scrutiny and approved by State's Scientific Review Panel (SRP).
- Best value of 3 x 10^{-4} [per µg DEP/m^3] (SRP)

"Form" of the Listing as a TAC

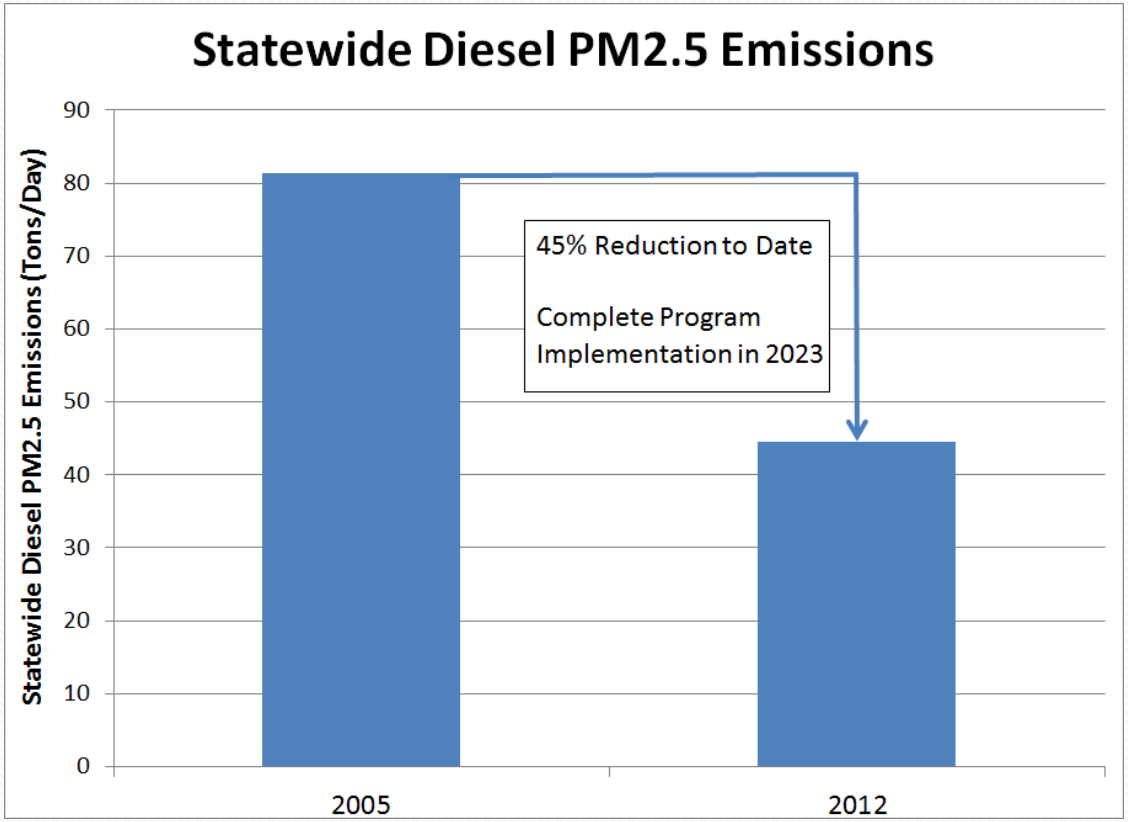
- Diesel exhaust is a complex mixture of gases, aerosolized liquids, and fine particles
- Particulate matter and vapor phase emissions most likely contribute to adverse health effects, including cancer
- CARB listed "particulate matter from diesel fueled engines" as a Toxic Air Contaminant, although the health effects assessment was based on exposure to the mixture.
  - Enabled a measurement of diesel emissions and ambient air concentrations to be made
  - Help to monitor results of diesel emissions reductions strategies

Ambient DEP Concentrations (1998)

Location	Concentration
Various U.S.	1 - 3 µg/m³
California	0.2 - 3.6 µg/m³
Austria	11 µg/m³
Urban hotspots	up to 15 µg/m³
Occupational	Several µg/m³ to >1 mg/m³

Source: CARB, 1998

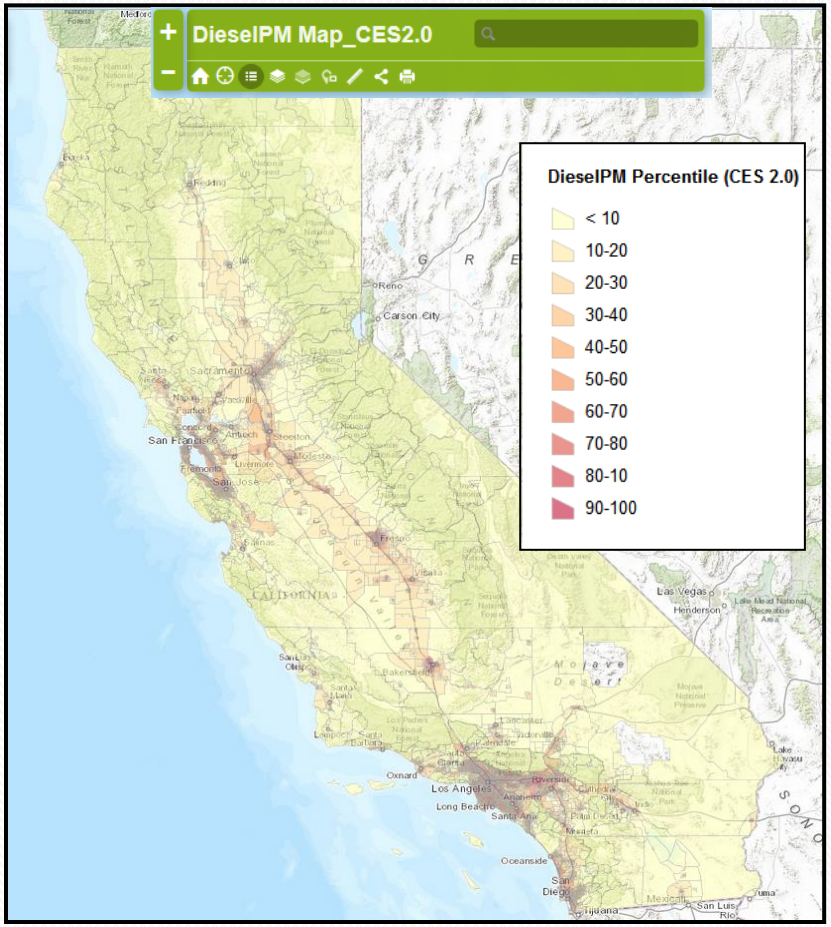
Statewide Diesel PM2.5 Emissions



Source: CARB, 2012

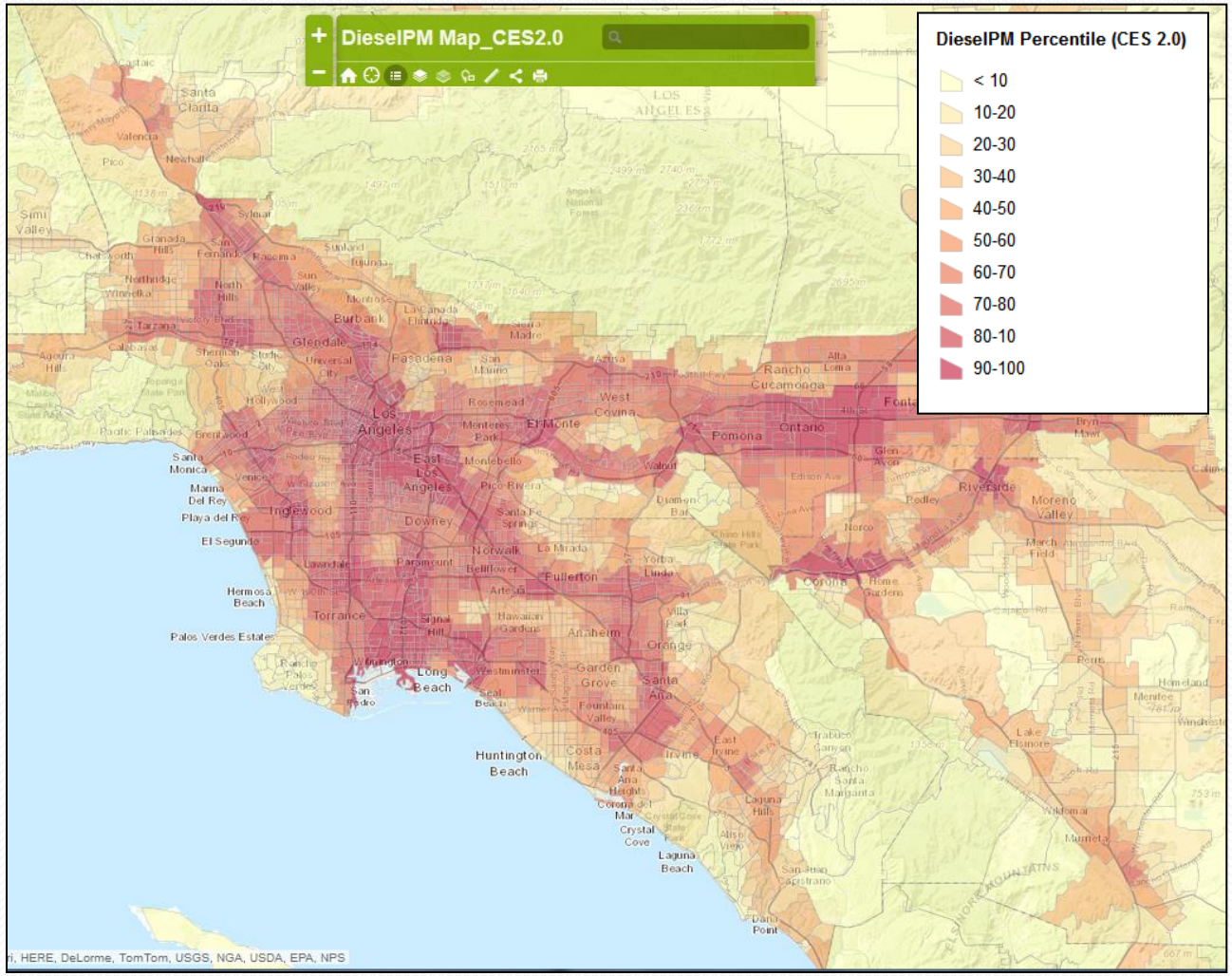
CalEnviroScreen2.0[1]
Exposure Indicator: Diesel Particulate Matter

- Diesel PM emissions (kg/day) from on-road and non-road sources for a 2010 summer day in July.[2]
- Emissions estimated for a 4km by 4km statewide grid which was then converted to census tracts.
- Raw data and calculated percentiles for individual indicators for individual census tracts available.[3]



1. CalEnviroScreen2.0 http://www.oehha.ca.gov/ej/ces2.html
2. Data source: California Air Resources Board
3. Data file: www.oehha.ca.gov/ej/pdf/CalEnviroScreen_v20FINAL_latlong_ecs.xlsx

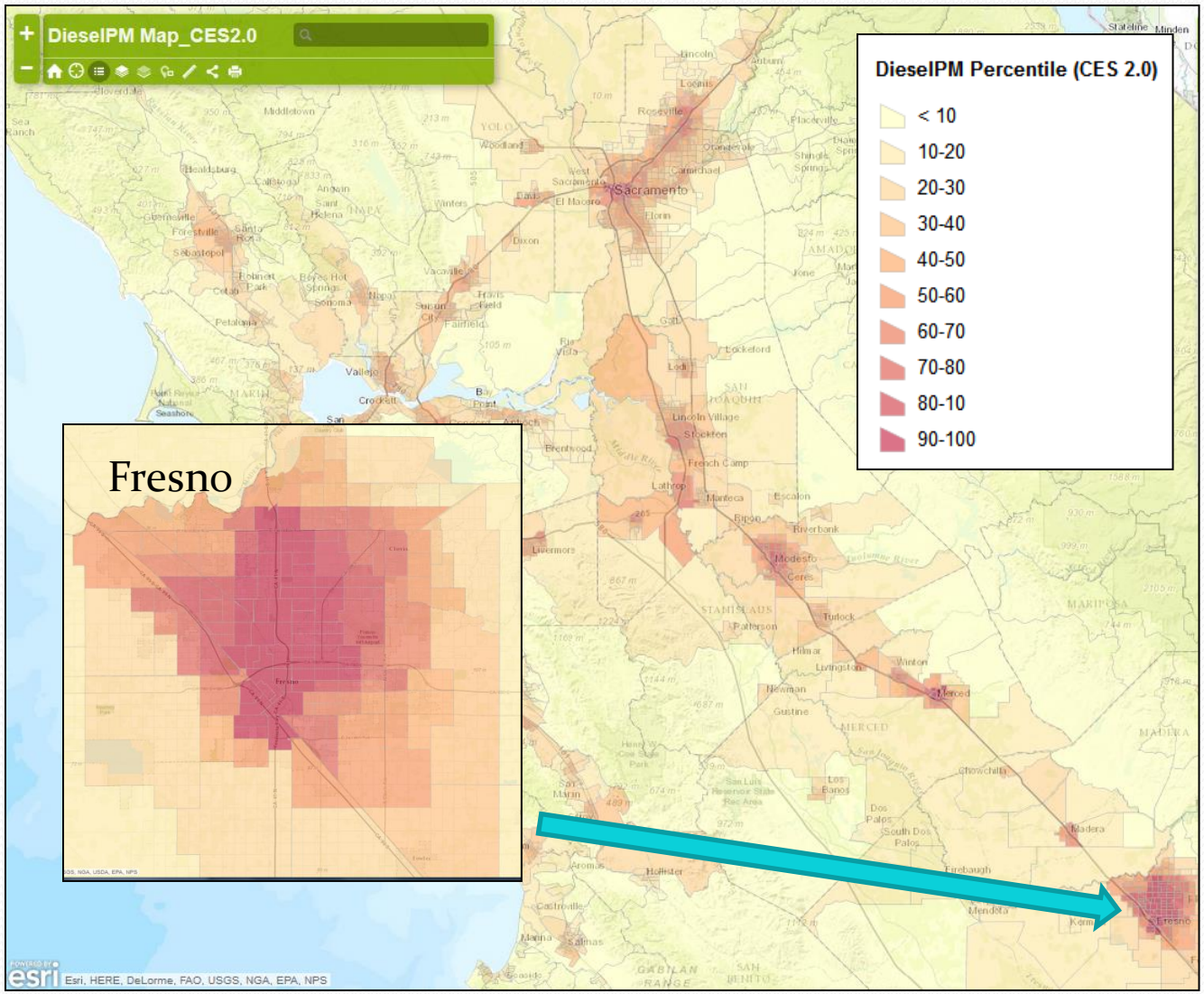
Southern California



Cities with census tracts in the top 10% for diesel pollution fall within the following **counties**--

- **Los Angeles County**/Long Beach, City of Los Angeles, San Pedro, Bell, Glendale, Inglewood, plus 17 other cities
- **Riverside County**/ Riverside, Corona, Mira Loma
- **Orange County**/Seal Beach, Los Alamitos
- **San Bernardino**/Ontario, Rancho Cucamonga, Fontana, Upland

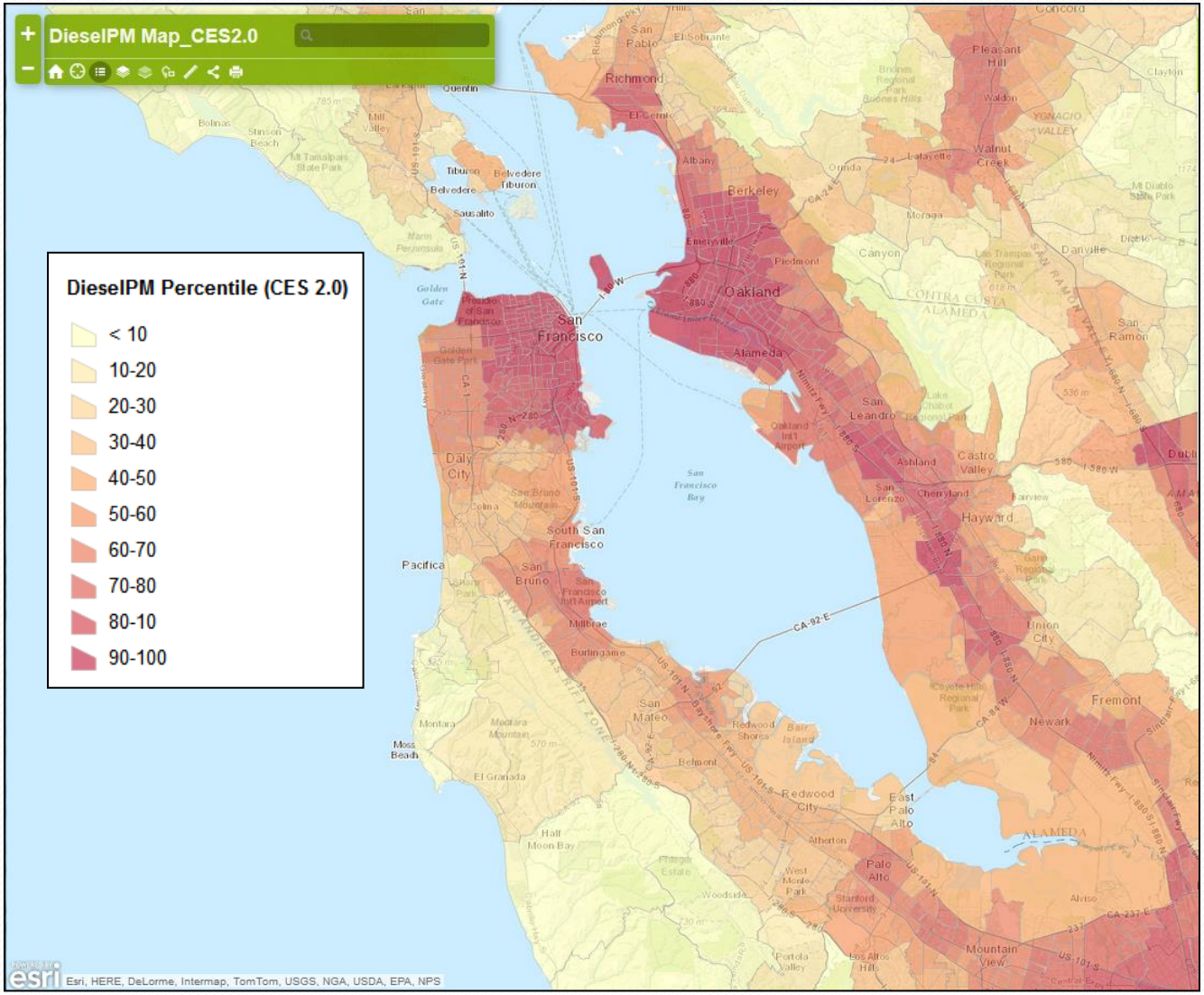
Central Valley



Cities with census tracts in the top 10% for diesel pollution fall within the following **counties**--

- **Fresno County**/Fresno
- **Kern County**/Bakersfield
- **Merced County**/Merced

San Francisco Bay Area



Cities with census tracts in the top 10% for diesel pollution fall within the following **counties**--

- **Alameda County**/ Alameda, Oakland, Emeryville, Hayward, Berkeley
- **San Francisco**/ San Francisco (downtown)

Diesel Exhaust Constituents

- Gases
  - CO, NOx, SOx, large number of VOCs (e.g., formaldehyde, 1,3-butadiene)
- Particles - >90% are <1 μ diameter
  - Inorganic - Elemental carbon, metals
  - Organic – Many thousands of semi-volatile compounds adsorb to particle surfaces (15 - 65% of particle mass); includes PAHs and PAH derivatives (e.g., nitro-, oxy-, keto-, quinones), other products of incomplete combustion (PICs)
- Which are the key to observed adverse health effects?

Good Biomarker

- Somewhat unique to the substance/mix being measured to avoid major confounding by other sources
- Consistent quantitative relationship with external exposure measures
- Reliably measurable with reasonable analytical methodology
- Useful at low levels of exposure (especially for community monitoring)
- Low inter-individual variability in pharmacokinetics

Many Risk Management Actions Taken by ARB to Address Diesel Exhaust Emissions

Off-Road

Cargo Handling Equipment at Ports and Intermodal Rail Yards

In-Use Off-Road Equipment

Locomotives

Transport Refrigeration Units (TRUs)

On-Road

On-Road Heavy-Duty Vehicle Program

Buses

- Public Transit
- School Bus Grants
- School Bus Idling
- Shuttles

Chip Reflash for Diesel Trucks

Heavy Duty Vehicle Inspections (Periodic Smoke Inspection)

Marine

Commercial Harbor Craft

Recreational Marine Engines

Ship Auxiliary Engines

Shore Power

Changes in Fuels

- In 2006, CARB regulations phased in “low sulfur” fuel (15 ppm S; down from 50 ppm and 500 ppm)
- CARB diesel also had lower aromatic content and CARB set lubricity standards
- CARB diesel decreased emissions of PM (mass), NOx, PAH, nitro-PAH, and many other constituents (total hydrocarbons)

Changing fuels and other controls influences emissions

- Relative amounts of various constituents change with engine, fuel type and mixing ratio, engine load
- Fuels changing beyond "CARB diesel"
  - Biodiesel
  - Blends of petrol-based and biodiesel
  - "Renewable" diesel
- Number of studies evaluating changes in constituents with the changing fuels present a complex picture
- Complicates finding a good biomarker or exposure

Biomarker Candidates Most Explored

- Urinary excretion of parent or metabolites of a number of PAHs and oxy-PAHs
- Carbonyls such as formaldehyde and other aldehydes
- Specificity problem, lots of confounders for most of the candidates including tobacco smoke, cooking foods, other fuel combustion
- Short half lives of urinary metabolites a possible problem for infrequent exposures (less so for occupational exposure)
- Inter-individual variability in metabolite production complicates use of urinary metabolites as a biomarker for general population exposure

Biomarkers explored

- Nitro-PAHs may be another route to a biomarker, e.g. urinary metabolites of 1-nitropyrene, found especially in diesel exhaust, less so in other sources
- Dr. Chris Simpson will discuss his methods and results using a number of hydroxylated metabolites of 1-nitropyrene as potential biomarkers for diesel exhaust exposure

Potential Biomarkers

- Other possibilities include hemoglobin or other circulating protein adducts with diesel-exhaust specific compounds
- Generally longer half-lives of adducts than urinary metabolites a benefit
- Specificity still an issue with a number of potential adduct biomarkers
- If need a blood draw, more invasive and more expensive than collecting urine

No "Grand Slams" yet