



|| SCHIRRMESTER || DIAZ-ARRASTIA || BREM LLP ||

Direct Examination of Dr. Shanna Collie

Andrew Schirrmester

Andrew Schirrmester
acs @ sdablaw.com
Schirrmester Diaz-Arrastia Brem, L.L.P.
Pennzoil Place – North Tower
700 Milam – 10th Floor
Houston, Texas 77002
713.221.2500
www.sdablaw.com

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ABC's Best Solvent

❖ Does ABC Solvent Contain Benzene?

NO

❖ What are the ingredients?

- Toluene 35%
- Xylene 40%
- N-Hexane 20%
- Naphtha 5%

❖ Do these ingredients cause cancer?

NO



ABC's Best Solvent

- ❖ Does Toluene Cause Cancer? **NO**
- ❖ Does Xylene Cause Cancer? **NO**
- ❖ Does N-Hexane Cause Cancer? **NO**
- ❖ Does Naphtha Cause Cancer? **NO**
- ❖ Who says these do not cause cancer?
 - International Agency for Research on Cancer
 - National Toxicology Program
 - U.S. Environmental Protection Agency
- ❖ Does ABC Solvent Cause Cancer? **NO**



Benzene is Everywhere: The Dose Makes the Poison



Dose Makes the Poison

- ❖ Paracelsus (1567) stated “*All substances are poisons*”
- ❖ Examples
 - One aspirin prevents heart attacks; two aspirins cure a headache; 100 aspirins can be lethal
 - Water is necessary to life; 17-20 liters of water consumed in a short timeframe is lethal

What is Benzene?

- ❖ Colorless liquid with sweet odor that evaporates quickly
- ❖ Benzene is formed from both natural processes (e.g. volcanoes, forest fires) and human activities
- ❖ Ranks in top 20 chemicals for production volume
 - More than 3 billions gallons produced in U. S. each year
 - More than 2500 facilities in U.S. manufacture or process benzene
 - Used to make gasoline, plastics, resins, nylon, synthetic fibers, rubbers, lubricants, dyes, detergents, drugs, pesticides
- ❖ Is found in air, water, food



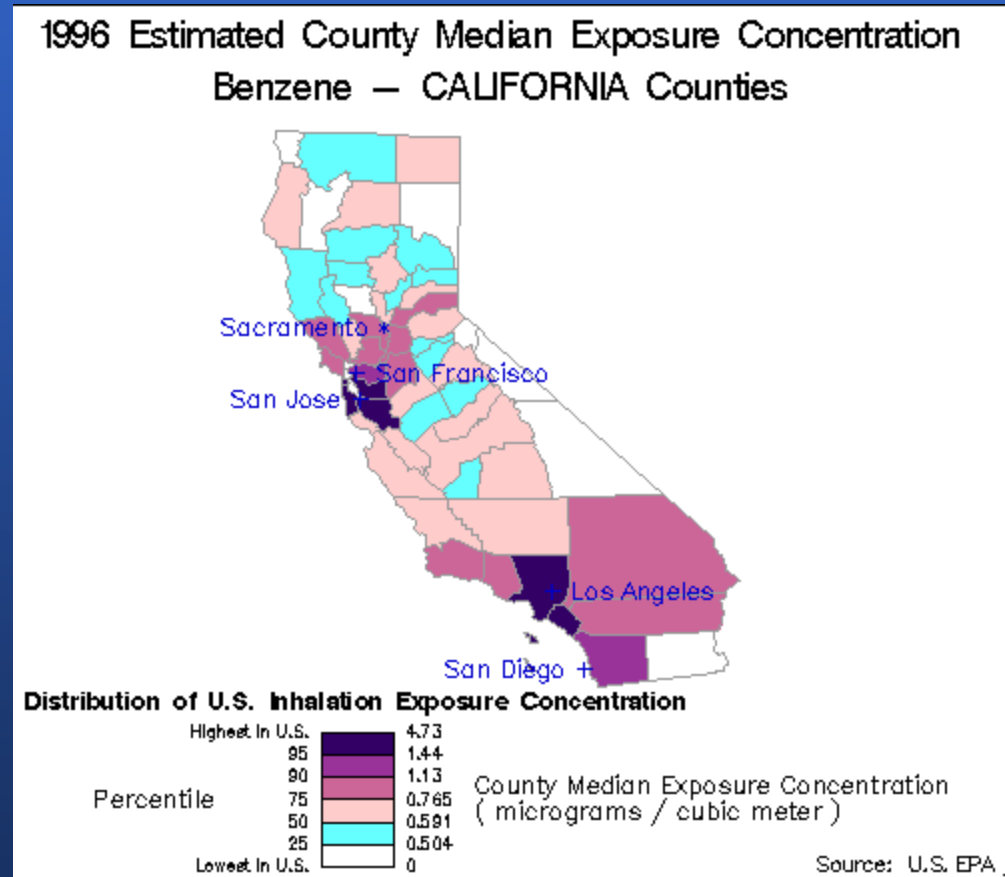
Benzene is Found Everywhere

- ❖ Industrial emissions
- ❖ Automotive exhaust
- ❖ Gasoline
- ❖ Cigarette smoke
- ❖ Household cleaners
- ❖ Drinking water
- ❖ Food
- ❖ Solvents



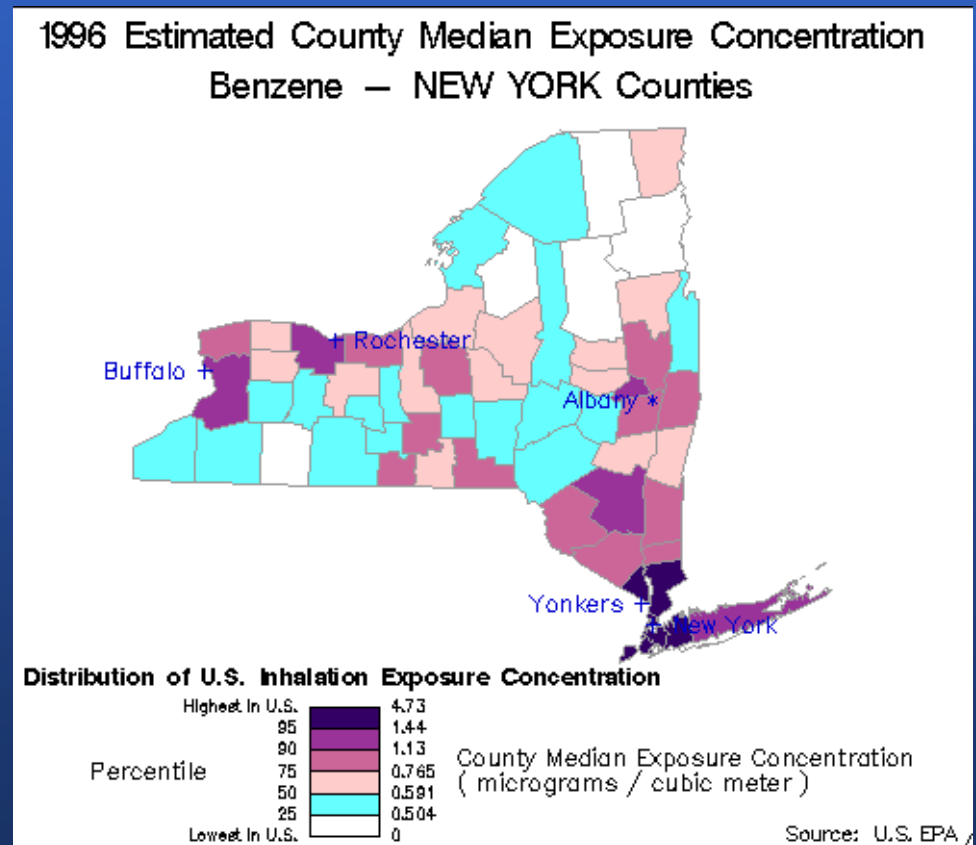
California Benzene Exposure

- ❖ U.S. Environmental Protection Agency (EPA) Region 9
- ❖ Benzene concentrations in Los Angeles were (and are) among the highest in the U.S.
- ❖ Median ~ 4.73 $\mu\text{g}/\text{m}^3$



New York Benzene Exposure

- ❖ U.S. Environmental Protection Agency (EPA) Region 2
- ❖ Benzene concentrations in New York also were (and are) among the highest in the U.S.
- ❖ Median ~ 4.73 $\mu\text{g}/\text{m}^3$





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Leukemia



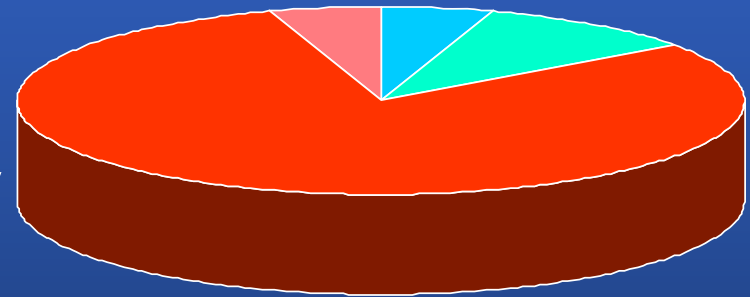
Facts and Figures

- ❖ About 44,000 new cases of leukemia will be diagnosed in the United States during 2007 (American Cancer Society)
- ❖ About 14,000 will be acute myeloid leukemia (AML): most are in adults
- ❖ AML occurs more often in men than women
- ❖ Rate increases with age



Known Causes of Leukemia

- ❖ 80% *de novo* (no known cause)
- ❖ 5% post-chemotherapy
- ❖ 10% smoking
- ❖ <5% potentially related to benzene exposure



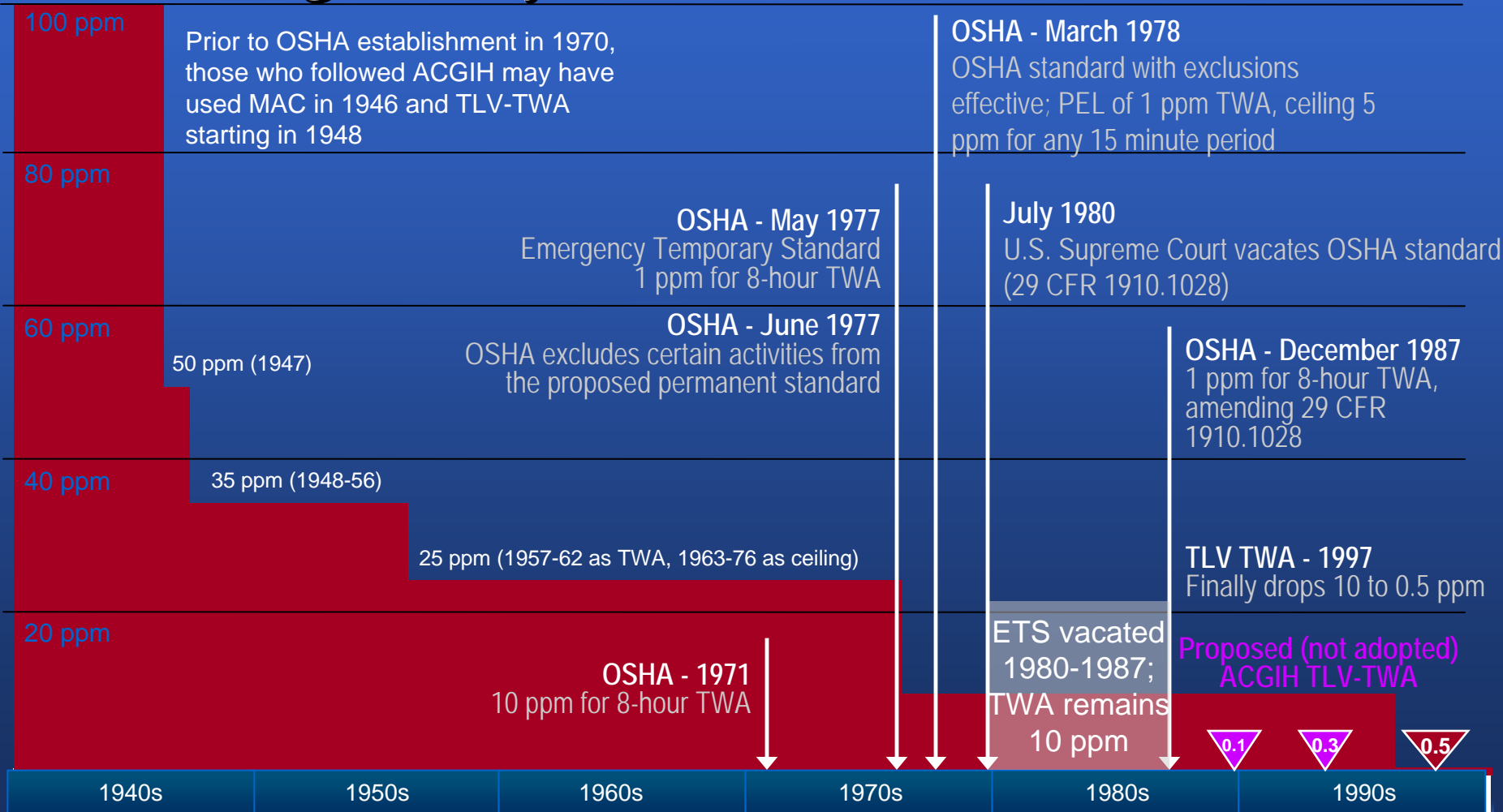


OSHA: Low Levels Are Safe

- ❖ Benzene is a widely used industrial solvent
 - Its use is regulated and monitored
- ❖ U.S. Occupational Safety & Health Administration
 - OSHA (1977) is in charge of ensuring worker safety
- ❖ Benzene Standard, 29 CFR § 1910.1028
 - Comprehensive regulations enacted by OSHA to protect workers from benzene
 - Exempts mixtures containing less than 0.1% benzene



Regulatory and Recommended Limits



Evidence Supports OSHA Exclusion

- ❖ OSHA conducted extensive hearings and examined voluminous evidence in support of its Benzene Standard
- ❖ OSHA published an extensive report of its finding
 - Published in the *Federal Register* – 52 FR 34460
 - “The final standard retains a percentage exclusion [less than 0.1% benzene]... Record evidence indicates that liquid mixtures with less than 0.1 percent benzene are unlikely to cause exposures through dermal absorption and inhalation equivalent to the amount inhaled at the action level [0.5 ppm].”
- ❖ ABC Solvent contains less than 0.1% benzene
- ❖ ABC Solvent does not increase leukemia risk



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Do Pressmen Get Leukemia?

Do Pressmen Get Leukemia? **NO**

- ❖ >95% of studies have no statistically significant increase of leukemia
 - One study with deficit of leukemia mortality
 - Majority with insignificant difference from control populations
- ❖ Of the 25 studies that inform pressmen experience
 - Single study with a statistically significant doubling of risk: Paganini-Hill et al. (1980) for “all leukemia” not just AML
 - Most involved > 20 years experience, all were 1949-1965 union members



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Is There Exposure Evidence? Biomarkers and Human Genes

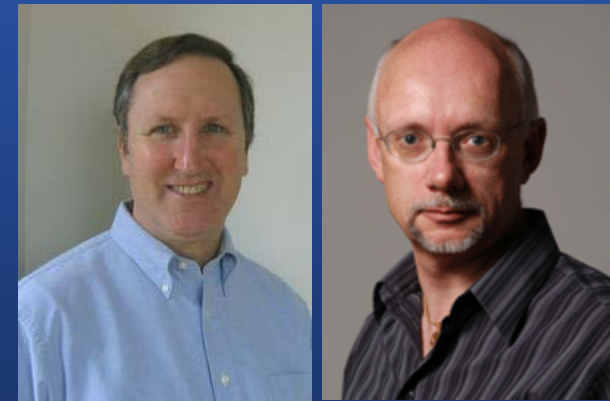


What is *inv*(16)?

- ❖ All the cells in the body carry genetic material that determines how each cell functions. Genes are stored on 23 pairs of chromosomes: each pair is numbered 1 to 22, with the last two chromosomes being the sex chromosomes (X and Y)
- ❖ Inversion 16, also called *inv*(16), is a specific and identifiable genetic defect. A piece of one of the pair of chromosome 16 has been picked out, turned upside down, and returned to the same place.
- ❖ Because of this inversion, the genes don't work properly and this genetic defect can lead to AML.

Chromosomal Aberrations in Humans Exposed to Benzene

- ❖ Comprehensive Study by Scientists at University of California, Berkeley
- ❖ Zhang, Eastmond and Smith MT. 2002. The nature of chromosomal aberrations detected in humans exposed to benzene. *Crit Rev Tox.* 32(1):1-42.
- ❖ Has inv(16) ever been reported in a benzene exposed worker?



NO

Chromosome Changes Due to Benzene

- ❖ 23 cases from 19 reports in Table 1: “extensive but not exhaustive” review: no mention of inv(16)
- ❖ 41 cases with “likely prior benzene exposure” (based on occupation) in Table 2: not a single inv(16) reported
- ❖ Table 3 assesses a large number of patients (n=321): no “preleukemic or benzene-poisoned” patients with any chromosome 16 aberration
- ❖ Not mentioned anywhere on page 12 under review section C, “Structural Chromosome Changes”
- ❖ Neither Table 11 nor Table 12 (entitled, “Prevalence of Specific CA...”) on page 35 list inv(16) as a CA in patients “with likely prior exposure to benzene”

Zhang, Eastmond and Smith MT. 2002. The nature of chromosomal aberrations detected in humans exposed to benzene. *Crit Rev Tox.* 32(1):1-42.



How Much Does it Take? Cumulative Benzene Dose

Cumulative Benzene Exposure

- ❖ There is a threshold of cumulative lifetime exposure to benzene below which there is no risk of leukemia
- ❖ What is the threshold?
- ❖ Studies demonstrate that exposure to benzene at less than 40 ppm-years does not cause AML
 - OSHA
 - Infante/Rinsky ('87) (US Rubber Workers)
 - Gun ('06) (Australian Petroleum Industry)
 - Wong ('87, '95) (US Refinery Workers)
 - Rushton ('97) (UK Petroleum Marketing & Distribution)
 - Swaen ('05) (Dutch Chemical Plant)



Does Smoking Cause AML? **YES**

- ❖ In 2004 the Surgeon General definitively found that smoking causes AML
- ❖ Secondhand smoke has also been designated as a **known human carcinogen**
- ❖ In addition to his own 10 pack years, Jones' father was a heavy smoker

Surgeon General's 2004 Report:

The Health Consequences of Smoking



The Health Consequences of Involuntary Exposure to Tobacco Smoke



Benzene Did Not Cause Mr. Jones' AML

- ❖ ABC Solvent does not contain benzene
- ❖ Ingredients of ABC Solvent (toluene, xylene, n-hexane, naphtha) do not cause cancer
- ❖ Potential benzene contamination levels (less than 0.1%) well below levels found to be safe by OSHA
- ❖ Pressmen Not at Risk for Leukemia
- ❖ Genetic defect inv(16) not related to benzene exposure
- ❖ Cumulative benzene exposure well below any potential AML risk
- ❖ Smoking causes AML