# Bijdrage van nieuwe epidemiologische studies aan de onderbouwing van de classificatie van dieselmotoremissies als humaan carcinogeen

**Roel Vermeulen, PhD**
*IRAS, Environmental Epidemiology Division*
*Utrecht University, the Netherlands*

*Julius Center, Health Sciences and Primary Care*
*University Medical Center Utrecht, The Netherlands*

Universiteit Utrecht

# Monograph 105

## Carcinogenicity of diesel-engine and gasoline-engine exhausts and some nitroarenes

In June, 2012, 24 experts from seven countries met at the International Agency for Research on Cancer (IARC; Lyon, France) to assess the carcinogenicity of diesel and gasoline engine exhausts, and some nitroarenes. These assessments will be published as Volume 105 of the IARC Monographs.[1]

The most influential epidemiological studies assessing cancer risks associated with diesel-engine exhausts investigated occupational exposure among non-metal miners, railroad workers, and workers in the trucking industry. The US miners study included a cohort analysis[3] and a nested case–

with 20 years of employment roughly doubling the risk after adjusting for tobacco smoking. When this study was extended with an exposure assessment involving contemporary measurements and exposure re-construction on the basis of elemental carbon, positive trends were observed

Published Online

International Agency for Research on Cancer

World Health Organization

**PRESS RELEASE**
**N° 213**

**12 June 2012**

### IARC: DIESEL ENGINE EXHAUST CARCINOGENIC

**Lyon, France, June 12, 2012** -- After a week-long meeting of international experts, the International Agency for Research on Cancer (IARC), which is part of the World Health Organization (WHO), today classified diesel engine exhaust as **carcinogenic to humans (Group 1)**, based on sufficient evidence that exposure is associated with an increased risk for lung cancer.

# Outline

- IARC evaluation process
- Exposure to diesel engine exhaust (DEE)
- Human cancer evidence of DEE
  - Evidence available at previous evaluation
  - New epidemiological evidence

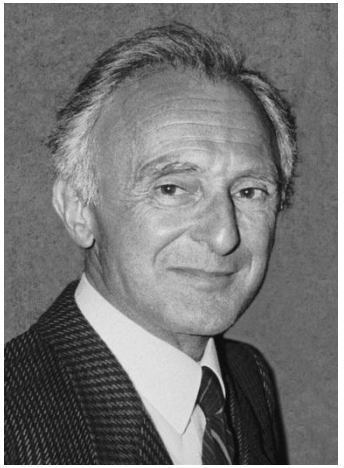
# “The encyclopaedia of carcinogens”

The *IARC Monographs* evaluate

- Chemicals
- Complex mixtures
- Occupational exposures
- Physical and biological agents
- Lifestyle factors

More than 900 agents have been evaluated

- 107 are *carcinogenic to humans* (Group 1)
- 63 are *probably carcinogenic to humans* (Group 2A)
- 271 are *possibly carcinogenic to humans* (Group 2B)

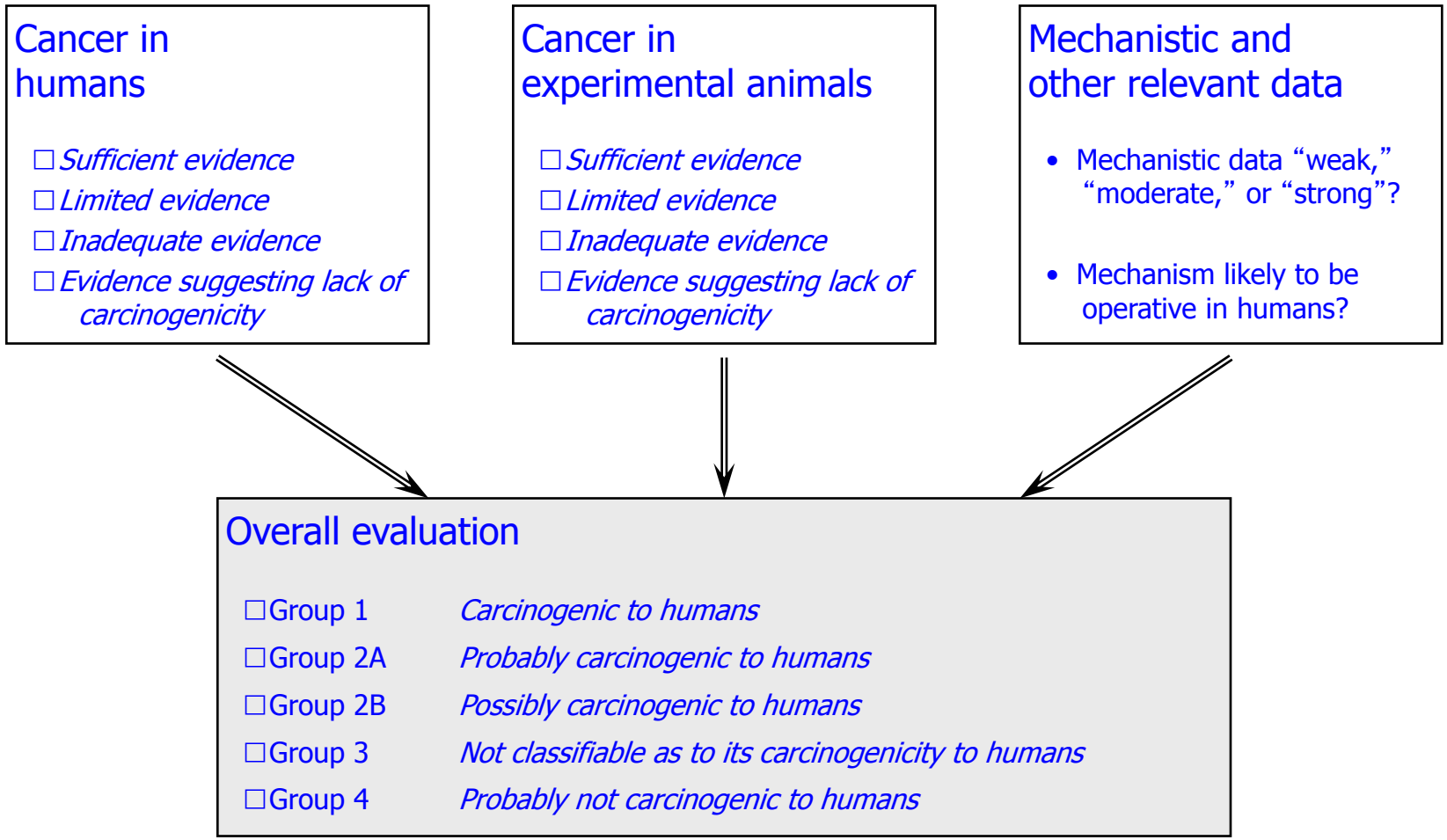


Lorenzo Tomatis
1929-2007

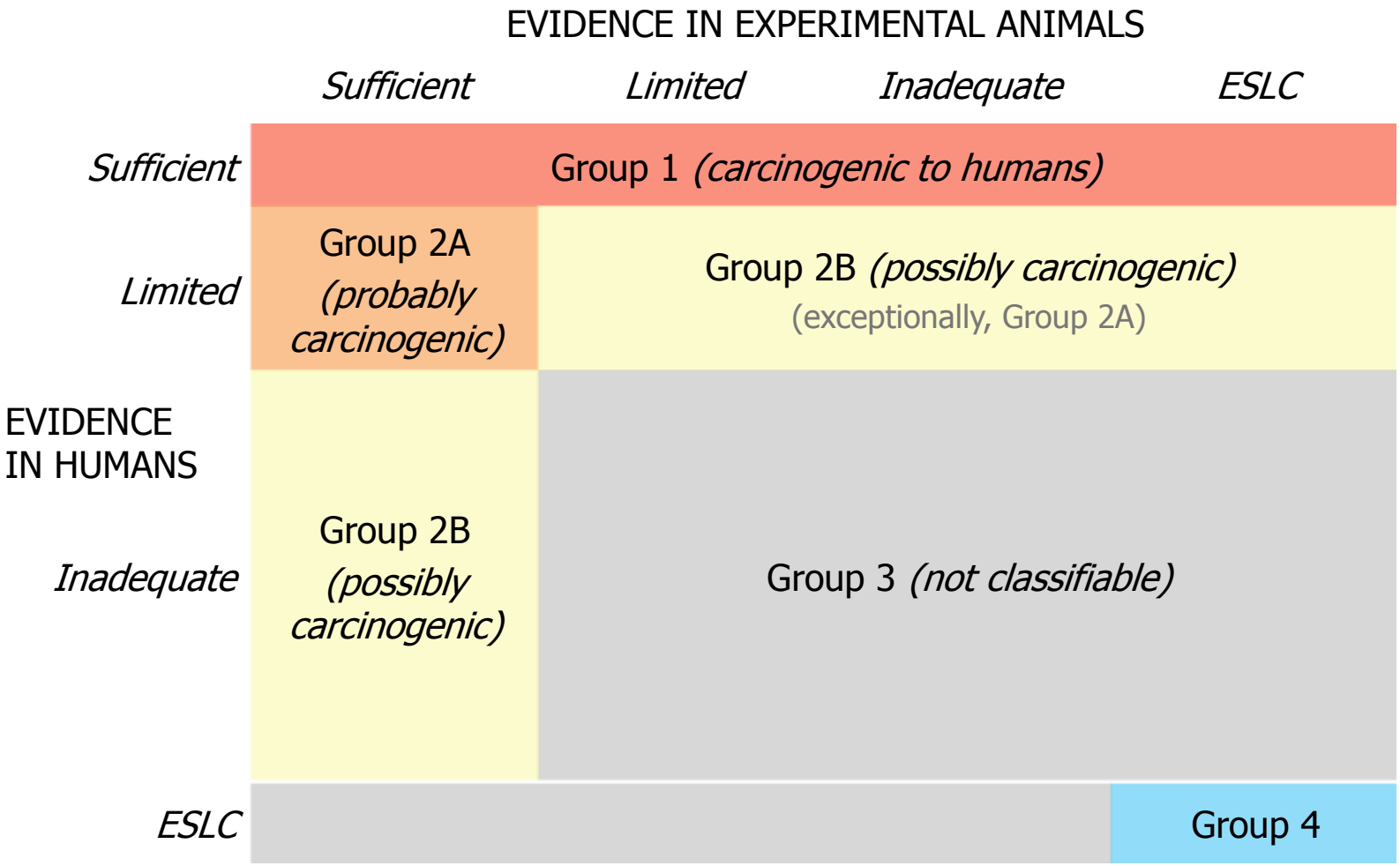
National and international health agencies use the *Monographs*

- As a source of scientific information on known or suspected carcinogens
- As scientific support for their actions to prevent exposure to known or suspected carcinogens

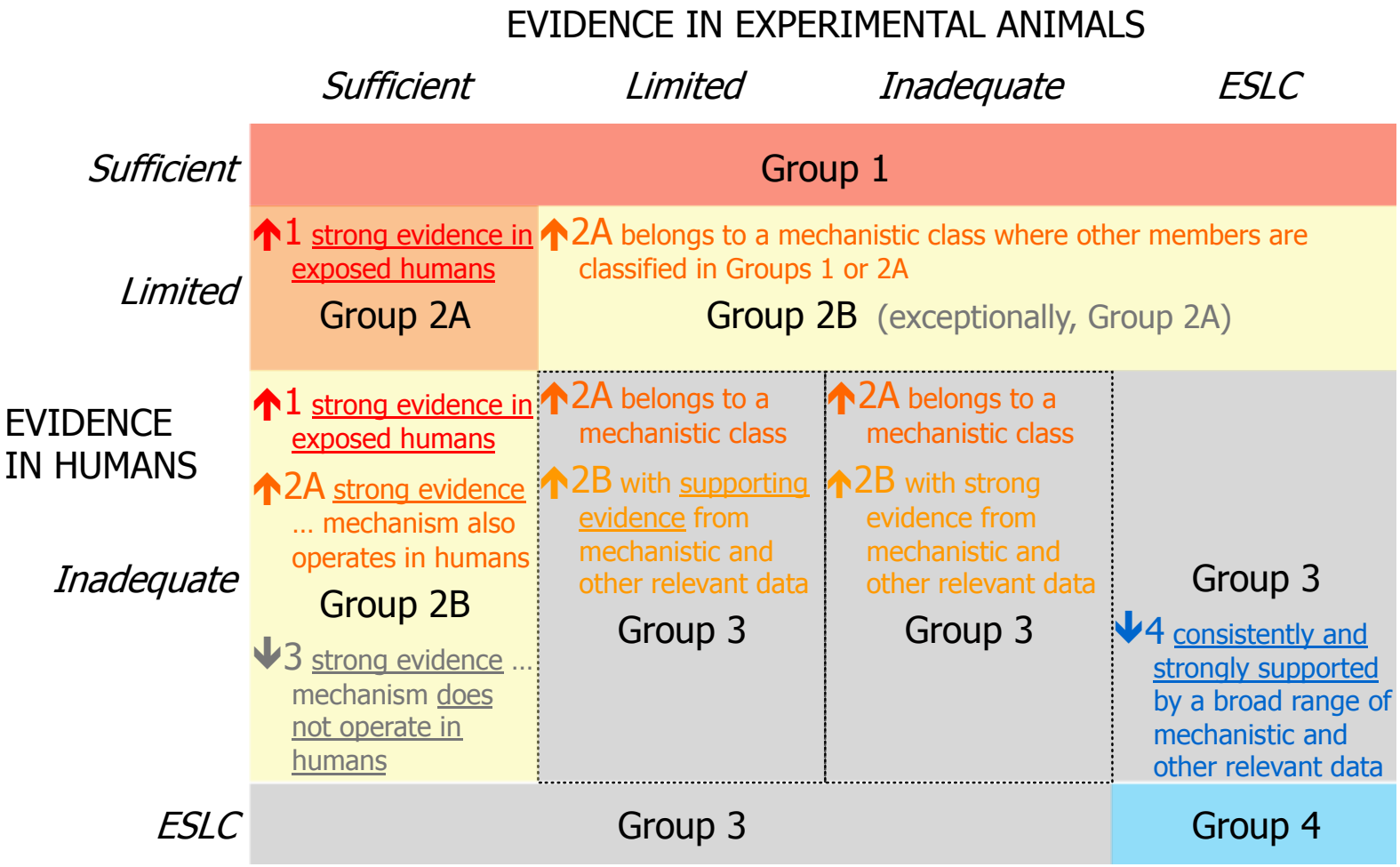
# IARC Evaluations - Subgroup Work



# IARC Evaluations – Dimensions and Classes



# Mechanistic Data can be Pivotal when the Human Data are not Conclusive



# Overall Evaluation – Vol 105, Diesel Engine Exhaust

- There is sufficient evidence for the carcinogenicity in humans of DEE. DEE causes lung cancer. Also, a positive association between DEE and bladder cancer has been observed.

- There is sufficient evidence for the carcinogenicity in experimental animals of whole diesel engine exhaust.

- Overall evaluation
  **DEE is carcinogenic for humans**

# Outline

- IARC evaluation process

- Exposure to diesel engine exhaust

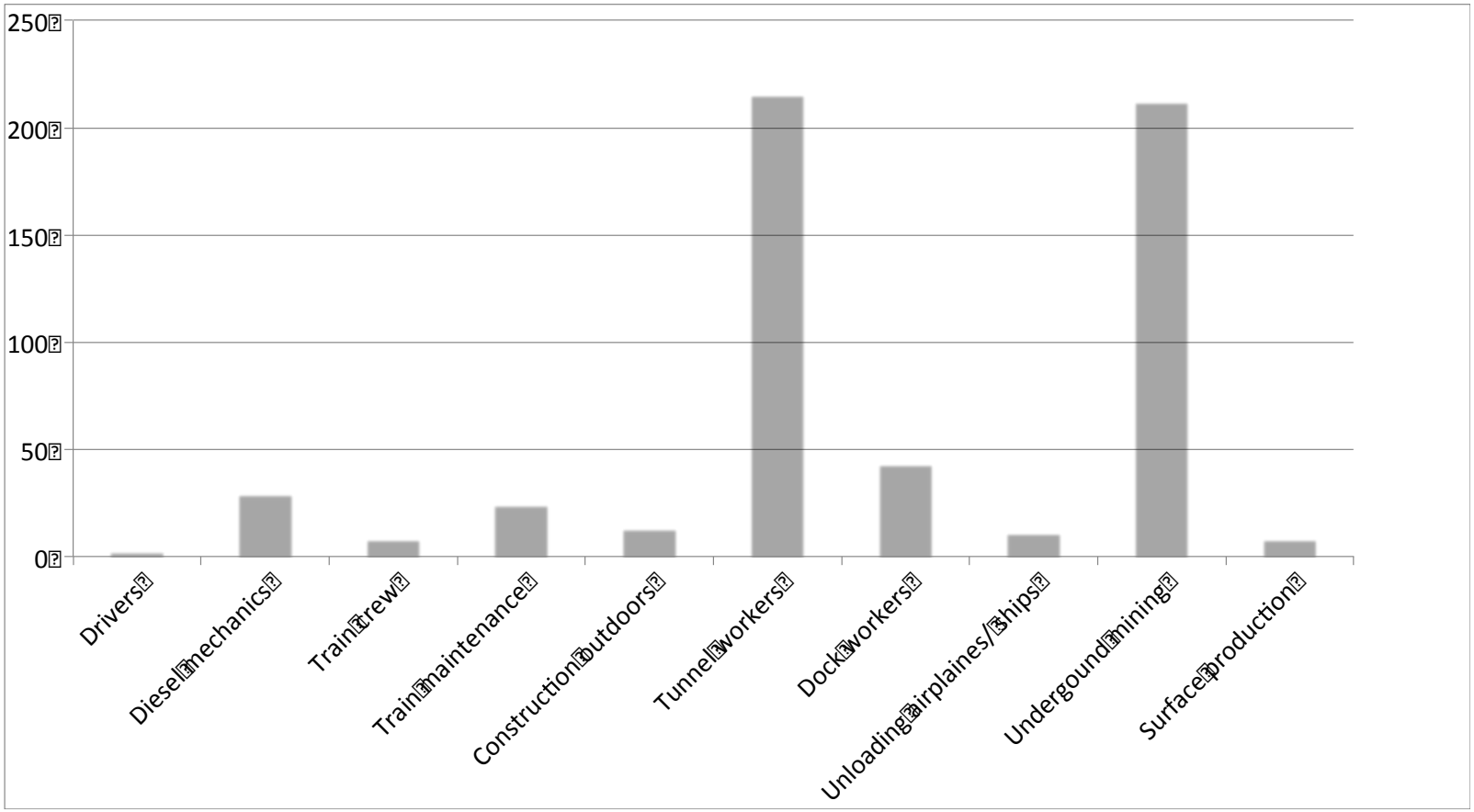
- Human cancer evidence of DEE
  - Evidence available at previous evaluation
  - New epidemiological evidence

# Exposure to DEE

- Diesel engines are predominantly used for heavy duty equipment
  - trains converting to diesel locomotive mainly after World War
  - heavy-duty trucks dieselized primarily during the mid and late 1950s.

- Occupational exposure prevalence (ever)
  - European Union: 12 million workers
  - North America: 12 million workers

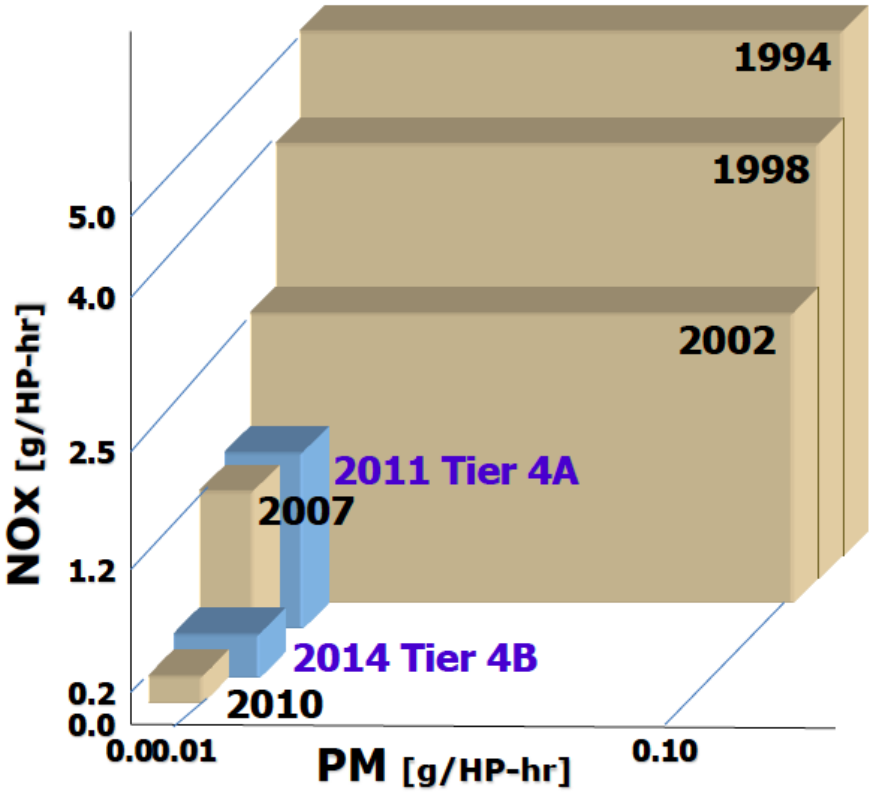
# Average DE Exposure Levels (EC ug/m3) by Occupational Categories

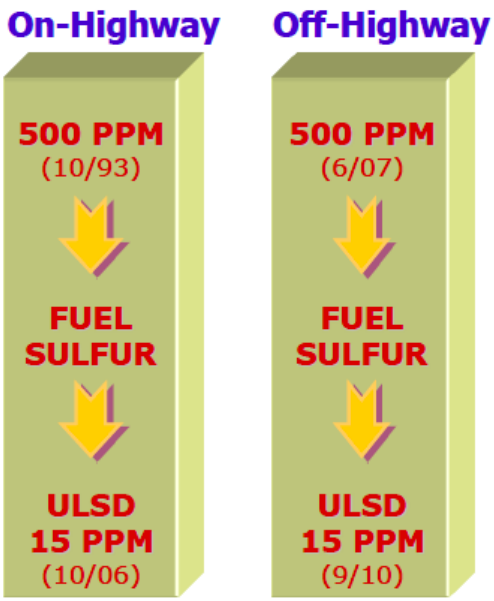



Universiteit Utrecht

# DEE Qualitatively Changes Overtime

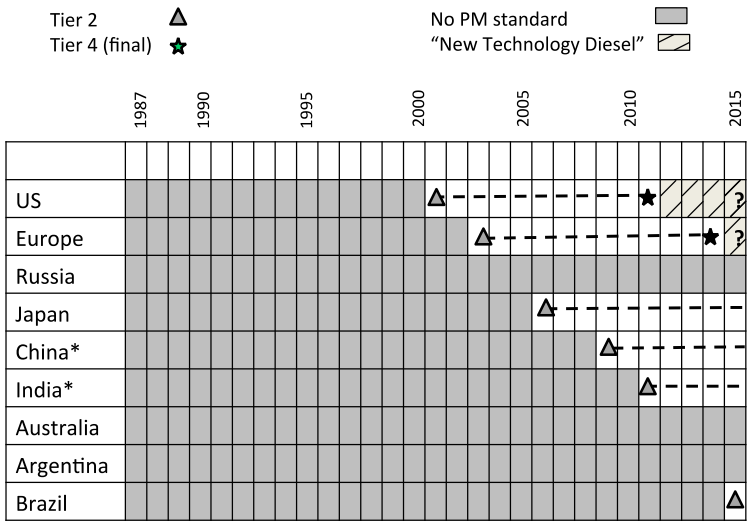
## Evolution of US Heavy Duty Diesel Emission Standards



# DEE Qualitatively Changes Overtime

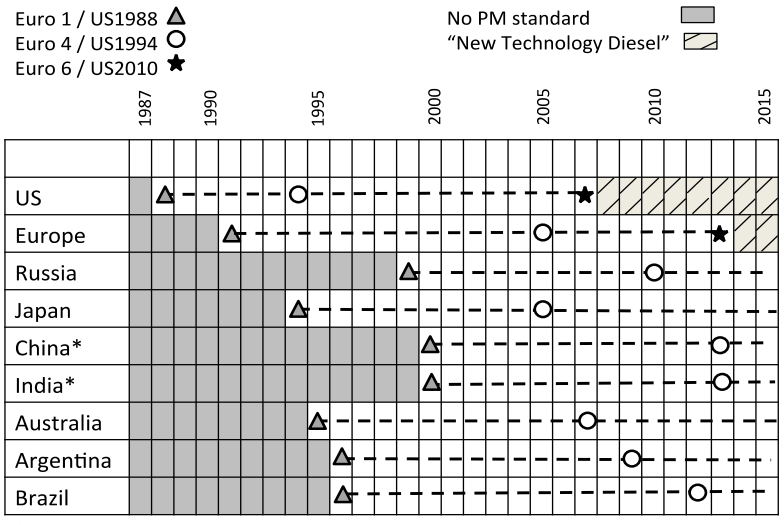
**Implementation Schedule of Global Nonroad Heavy Duty Diesel Emission Standards**




* Nationwide

Data from dieselnet http://www.dieselnet.com/standards/

**Implementation Schedule of Global On-highway Heavy Duty Diesel Emission Standards**




* Nationwide

Data from dieselnet http://www.dieselnet.com/standards/

Universiteit Utrecht

Scheepers and Vermeulen, 2012

# Outline

- IARC evaluation process
- Exposure to diesel engine exhaust
- Human cancer evidence of DEE
  - Evidence available at previous evaluation
  - New epidemiological evidence



Universiteit Utrecht

# Previous Human Evidence

- Moderate increase in risk of lung cancer at levels of exposure experienced by workers
  *(RR 1.33, 95% 1.24 – 1.44, based on 29 risk estimates; Bhatia et al., 1998)*
- Some evidence of a modest increase in risk of bladder cancer among workers exposed to diesel exhaust
  *(RR 1.1 - 1.3; Boffetta and Silverman, 2001)*
- Inconsistent evidence for multiple myeloma, pancreas, prostate, larynx, kidney cancer

# Relative Risks Lung Cancer and Diesel Exposure

TABLE 3. Summary of Pooled Relative Risks

| Group | Number | RR | 95% CI | $\chi^2$ Heterogeneity | Adjusted 95% CI* |
|---|---|---|---|---|---|
| All studies | 29 | 1.33 | 1.27–1.40 | 58.0 | 1.24–1.44 |
| Case-control studies | 14 | 1.33 | 1.21–1.47 | 20.5 | 1.18–1.51 |
| Cohort studies | 15 | 1.33 | 1.26–1.42 | 37.5 | 1.21–1.47 |
| Internal comparison group | 8 | 1.43 | 1.32–1.55 | 11.0 | 1.29–1.58 |
| External comparison group | 7 | 1.22 | 1.12–1.34 | 20.0 | 1.04–1.44 |
| Smoking adjusted | 16 | 1.35 | 1.22–1.49 | 23.4 | 1.20–1.52 |
| Smoking not adjusted | 13 | 1.33 | 1.25–1.41 | 34.5 | 1.20–1.47 |
| Subanalysis by occupation | 24 | 1.37 | 1.30–1.46 | 48.4 | 1.27–1.49 |
| Railroad workers | 6 | 1.44 | 1.30–1.59 | 5.6 | 1.30–1.60 |
| Equipment operators | 3 | 1.11 | 0.95–1.29 | 4.3 | 0.89–1.38 |
| Truck drivers | 10 | 1.49 | 1.36–1.64 | 9.8 | 1.36–1.65 |
| Bus workers | 5 | 1.24 | 1.07–1.43 | 14.8 | 0.93–1.64 |

* Heterogeneity-adjusted confidence intervals using method described by Shore *et al.*[6]



*Bhatia et al., 1998*

# Relative Risks Lung Cancer and Diesel Exposure

TABLE 5. Observed Risks by Employment Duration in Studies Using Internal Comparisons

| Reference | Type | Smoking Adjusted | Occupation | Subgroup (Years) | RR | 95% CI |
|---|---|---|---|---|---|---|
| Boffetta *et al*,[12] 1990 | CC | Yes | Diesel-exposed | 1–15 | 0.52 | 0.15–1.86 |
| | | | | 16–29 | 0.7 | 0.34–1.44 |
| | | | | ≥30 | 1.49 | 0.72–3.11 |
| Damber & Larsson,[14] 1987 | CC | Yes | Driver | 1–19 | 1 | 0.7–1.5 |
| | | | | ≥20 | 1.2 | 0.6–2.2 |
| Garshick *et al*,[41] 1987 | CC | Yes | Railroad worker | 5–19 | 1.02 | 0.72–1.4 |
| | | | | ≥20 | 1.64 | 1.18–2.2 |
| Garshick *et al*,[13] 1988 | RC | No | Railroad worker | 1–4 | 1.2 | 1.01–1.44 |
| | | | | 5–9 | 1.24 | 1.06–1.44 |
| | | | | 10–14 | 1.32 | 1.13–1.56 |
| | | | | ≥15 | 1.72 | 1.27–2.33 |
| Hayes *et al*,[18] 1989 | CC | Yes | Equipment operator | <10 | 1.5 | 0.4–4.3 |
| | | | | ≥10 | 1.3 | 0.6–3.1 |
| | | | Truck driver | <10 | 1 | 0.8–1.3 |
| | | | | ≥10 | 1.5 | 1.1–1.9 |
| | | | Bus driver | <10 | 1.1 | 0.6–2.1 |
| | | | | ≥10 | 1.6 | 0.9–2.8 |
| Steenland *et al*,[39] 1990 | CC | Yes | Diesel truck driver | 1–24 | 1.27 | 0.7–2.27 |
| | | | | 25–34 | 1.26 | 0.74–2.16 |
| | | | | ≥35 | 1.89 | 1.04–3.42 |
| Swanson *et al*,[11] 1993 | CC | Yes | Railroad worker | 1–9 | 1.57 | 0.8–3.11 |
| | | | | ≥10 | 2.46 | 1.24–4.87 |
| | | | Heavy truck driver | 1–9 | 1.56 | 0.95–2.58 |
| | | | | 10–19 | 1.67 | 0.87–3.18 |
| | | | | ≥20 | 2.44 | 1.43–4.16 |

*Bhatia et al., 1998*

# Weaknesses

- Lack of control for confounding
  - Smoking
- Insufficient (quantitative) exposure assessment
- Lack of dose-response within and across occupations

# EPICOH 2013 - Utrecht 18 – 21 June 2013


Universiteit Utrecht