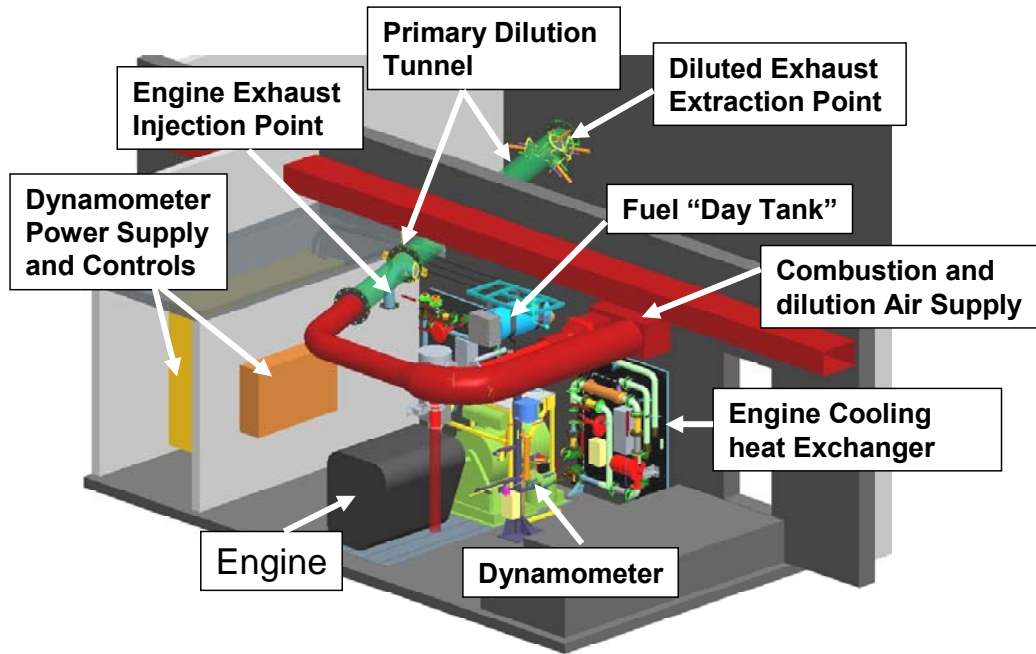


ACES PHASE 3: Chronic Inhalation Bioassay



Joe Mauderly (et many al.)

Lovelace Respiratory Research Institute, Albuquerque, NM

METHODS: RAT STUDY

- **Expose 288 rats/group 16 hr/day, 5 days/wk for 24-30 months**
Harlan HsdRccHan:Wist (Wistar) strain
- **Three dilutions of whole emissions + clean air controls**
Lowest dilution to yield average NO₂ of ~5 ppm
- **184 rats/group committed to carcinogenesis bioassay**
- **80 rats/group allocated for evaluations at 1, 3, 12, & 24 months**

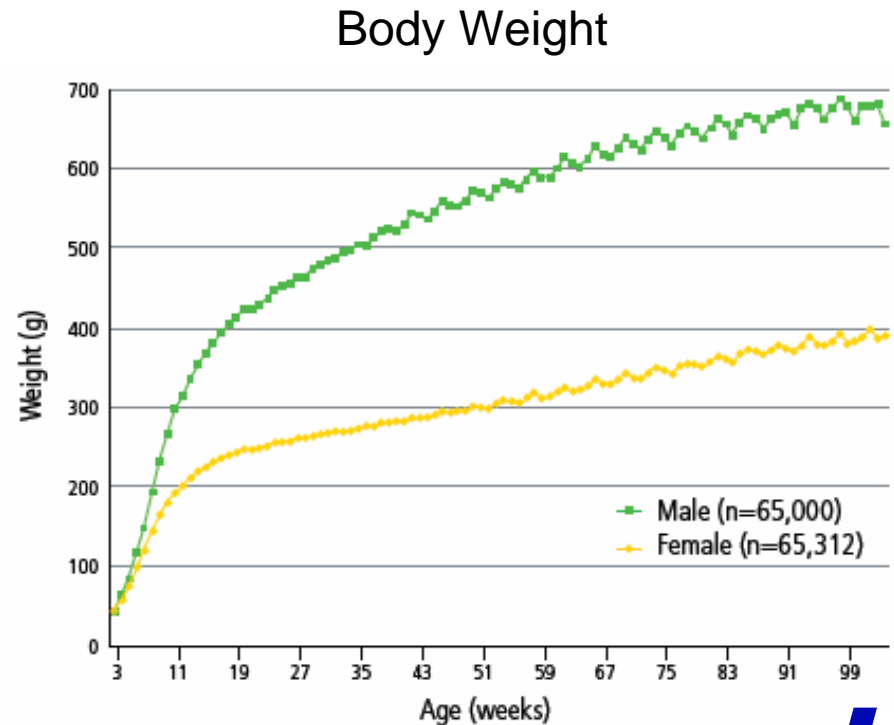
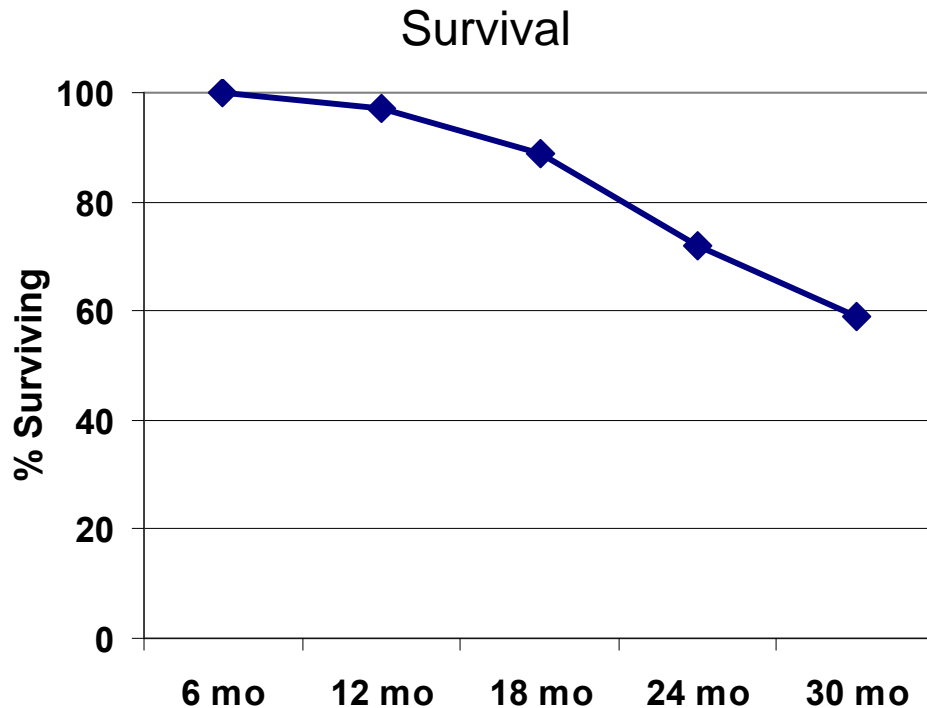
Pulmonary function	Hematology
Bronchoalveolar lavage	Serum chemistry
Cell proliferation	Histopathology

Blood and tissue collected from same rats for ancillary studies
- **24 rats/group to compensate for mortality**

CHARACTERISTICS OF HsdRccHan:Wist RATS

- **Good Survival**
 - **Approximately same in males and females**
- **Low background of lung tumors and other lung lesions**
- **Larger than F344**

Males > 700g
Females > 400g



METHODS: MOUSE STUDY

- **Expose 120 mice/group 16 hr/day, 5 days/wk for 13 weeks**
 - C57BI/6
 - Same control and treatment groups as for rats
- **40 mice/group allocated for evaluations at 1 and 3 months**
 - Bronchoalveolar lavage Serum chemistry
 - Cell proliferation Histopathology
 - Hematology
- **80 mice/group allocated for ancillary studies**
 - Blood and tissue collections

STATUS

Exposure facility is complete

- **Substantial delay caused by problems with dynamometer**
 - Major delay due to problems with dynamometer system
 - Several other operating problems also encountered
- **Now running consecutive 16 hr overnight cycles as possible**
 - Collecting data on chamber atmosphere
 - Gaining confidence in robustness of system

The animal study protocol is under review by HEI

- **Still some details to resolve**
 - Exposure dilutions
 - Lung sectioning strategy

PRELIMINARY RESULTS: Chamber Temperature

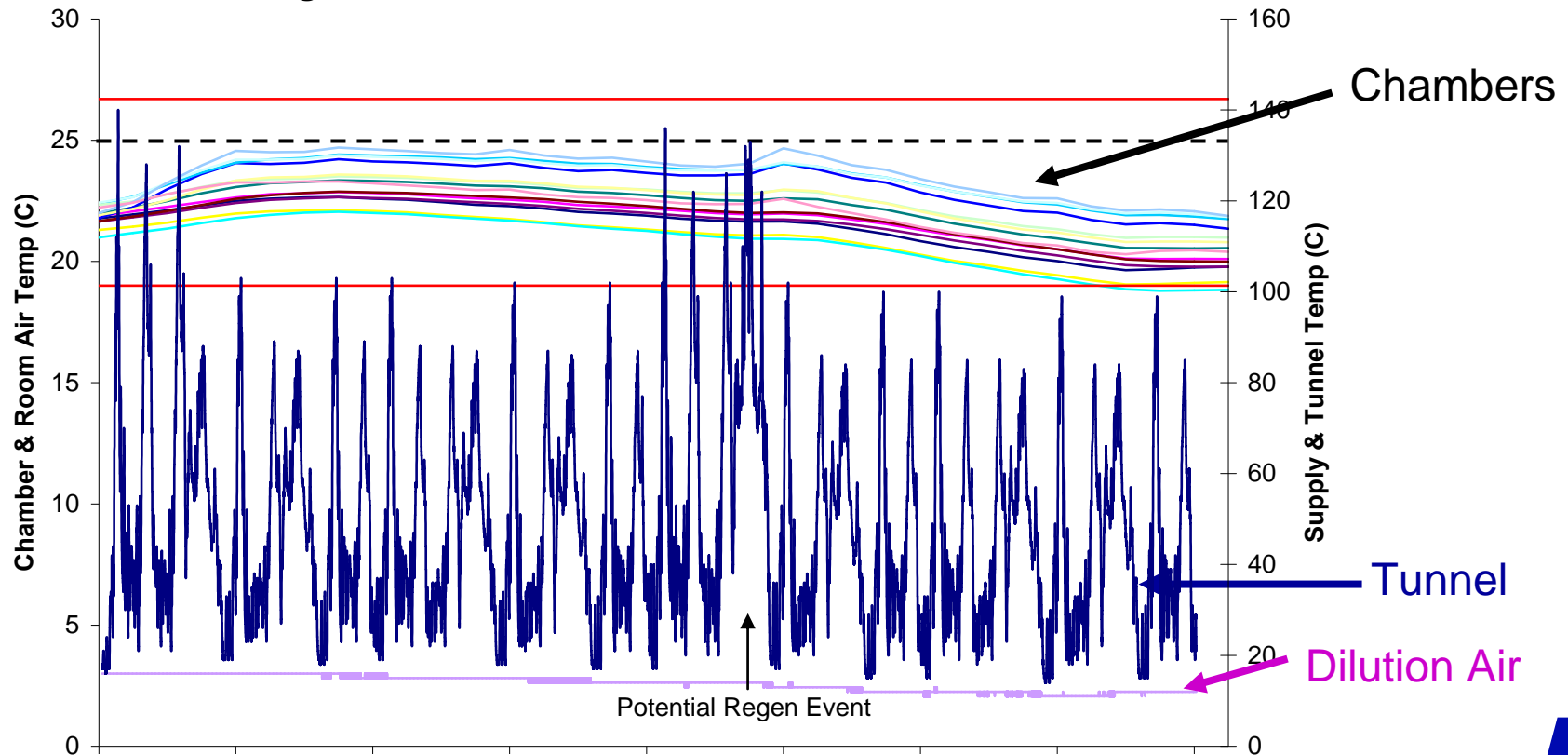
1. Lowest dilution

- Approximately 40:1 dilution required for 5 ppm average NO_2

2. Animal chamber temperature at lowest dilution

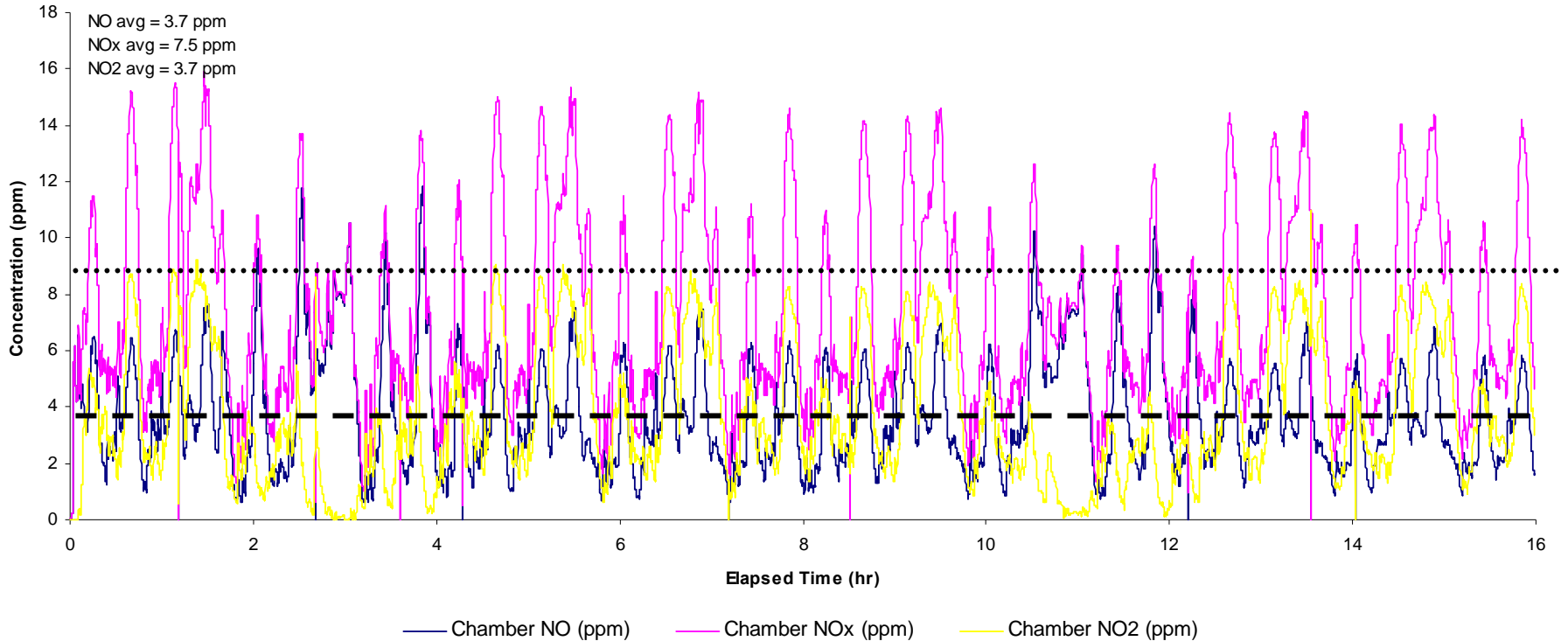
- Chamber temperatures are acceptable at 5 ppm NO_2

Target is maximum of 25°C without animals



PRELIMINARY RESULTS: Gases

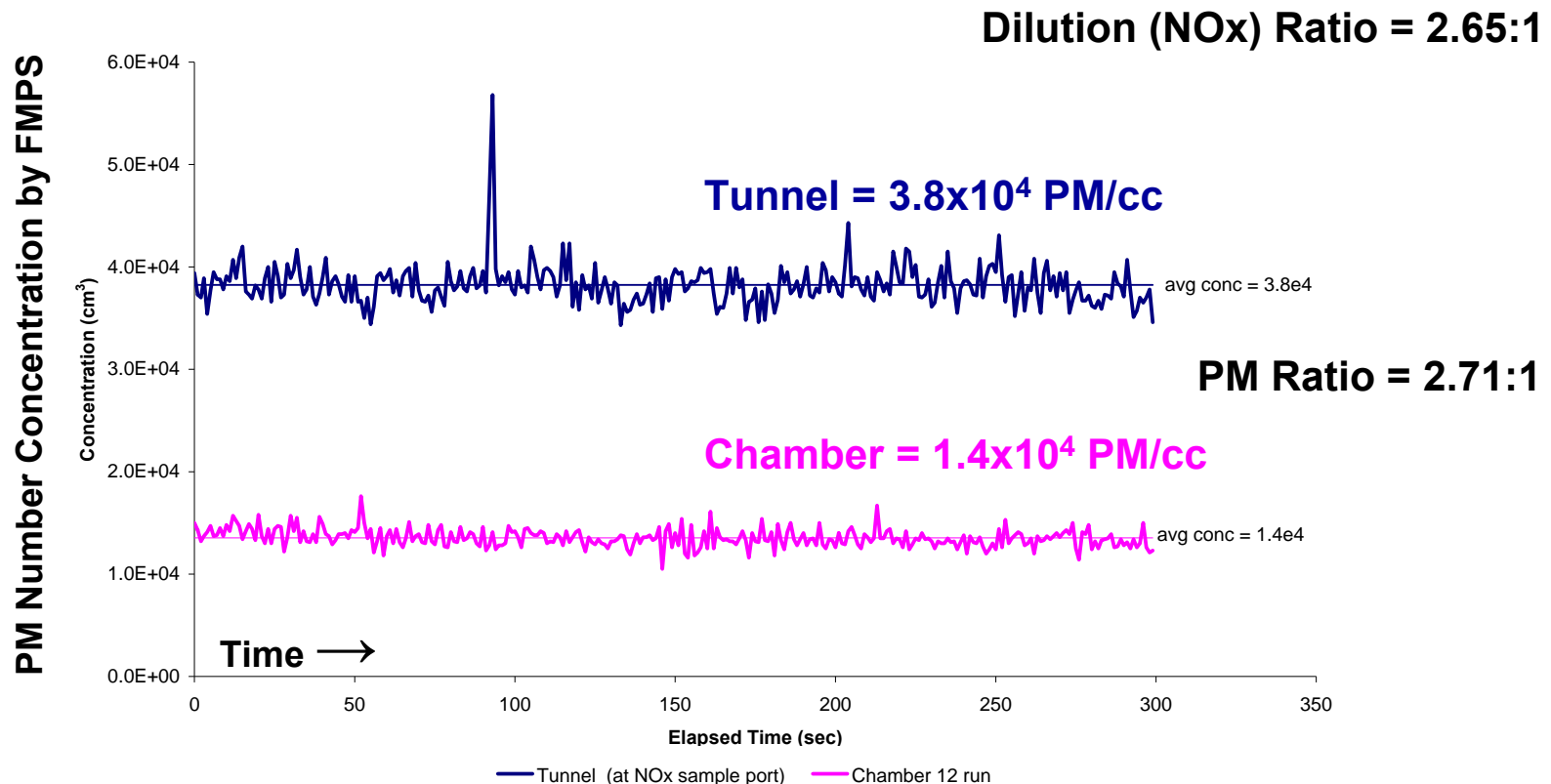
1. At 5 ppm average, NO_2 will peak at ~ 12 ppm during cycle
2. $\text{NO}_2 \approx \text{NO}$



3. $\text{CO} \approx 10$ ppm, $\text{HC} \approx 0.3$ ppm

PRELIMINARY RESULTS: Particles

1. Average PM only $\sim 2 \mu\text{g}/\text{m}^3$ above background
2. Very little PM loss in secondary dilution-distribution system
 - Tunnel:Chamber Ratios at steady-state (1800 rpm, 50% throttle):



SCHEDULE

Assuming that detailed characterization is underway this week, animal exposures can begin by the end of July

To do:

- 1. Approve animal study protocol**

Draft submitted

- 2. Submit PM & gas data at 5 ppm NO₂ for decision on dilutions**

By end of this week (preliminary results presented here)

- 3. Comparisons to SwRI results**

- 4. Detailed characterization at target dilutions**

- 5. Formal report on characterization phase**

- 6. Complete contract for animal study**

Underway