# Dioxins---from the Risk Assessment Perspective

## - - -

Dioxins    family of PCDDs and PCDFs

Dioxins

The following information is essential for policy making

How great is the magnitude of total risks due to dioxins?
(                                    )
Which exposure pathways or sources are dominant?

What risk is action-sensitive ?

# *Target receptor groups*

| Receptor group | Abbreviation | | |
|---|---|---|---|
| General population (*1) | G(1) | | |
| General population (*2) | G(2) | | |
| Local residents | LRs | | |
| Heavy fish eaters | HFEs | | |
| Breast-fed infants | | | |
| Fetuses | (not yet undertaken) | ( | ) |
| Workers | (beyond my scope) | ( | ) |

(*1)  Takayama et al. (1991)
(*2)  Environment Agency (1997)

Estimation of daily dioxin exposure levels in terms of TEQs

(pg/day)

| | | | | |
|---|---|---|---|---|
| 0 | 100 | 200 | 300 | 400 | 500 |

G(1) — 175

G(2) — 75

LR — 238*

HFE — 414

Legend:
- Inhalation:
- Fish:
- Green vegetables:
- Other foods:
- Others:
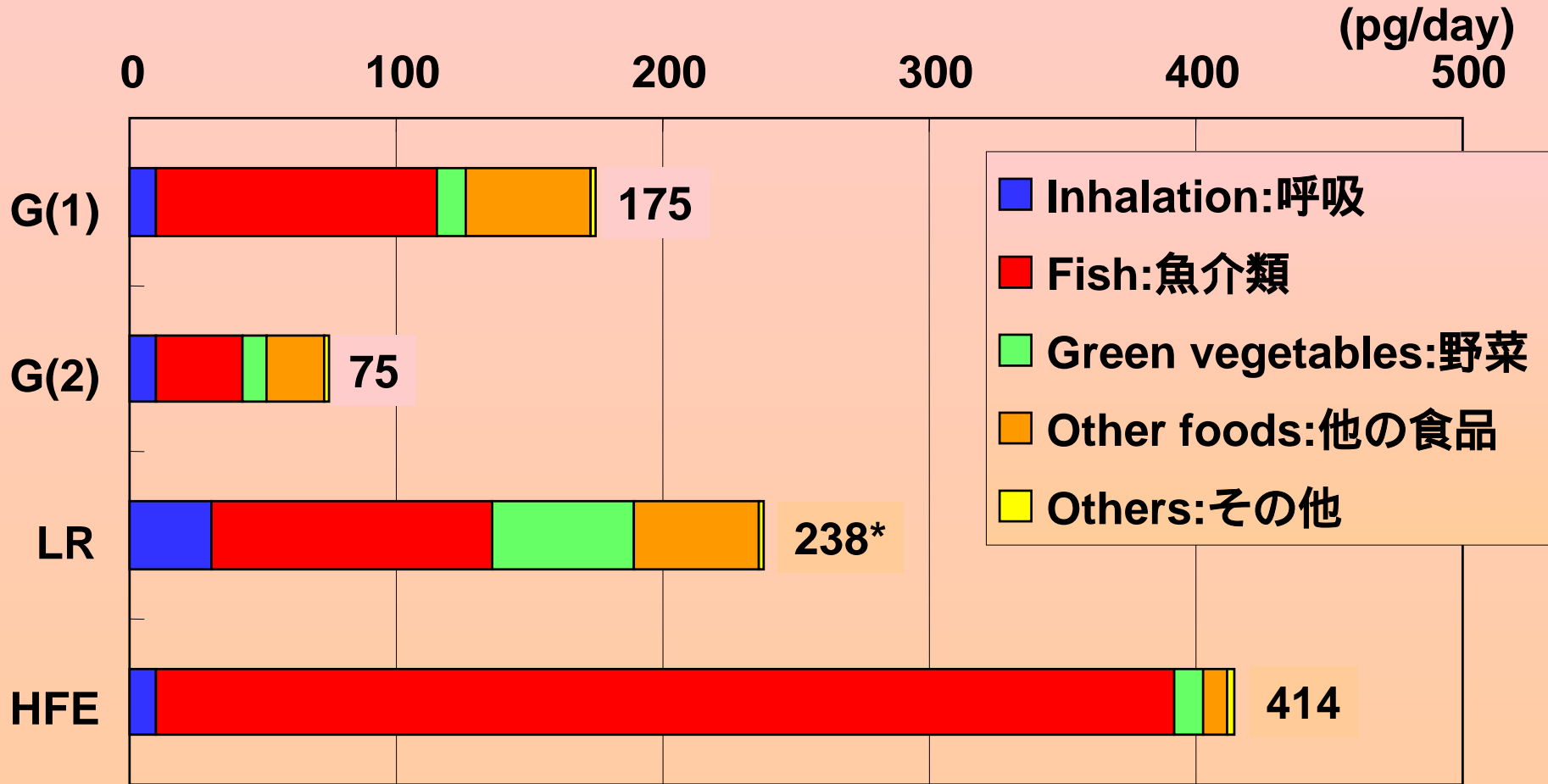
*LADD Lifetime average daily dose
pg=10$^{12}$ gram

# Predicted vs. Observed TEQs tissue levels for general population (Part 1)

**Dioxins in terms of TEQs (pg/g of fat)**

0    10    20    30    40    50

G(2)    G(1)

**Predicted**

**Adipose**

**Blood**

**Maternal milk**

▼ Observed values
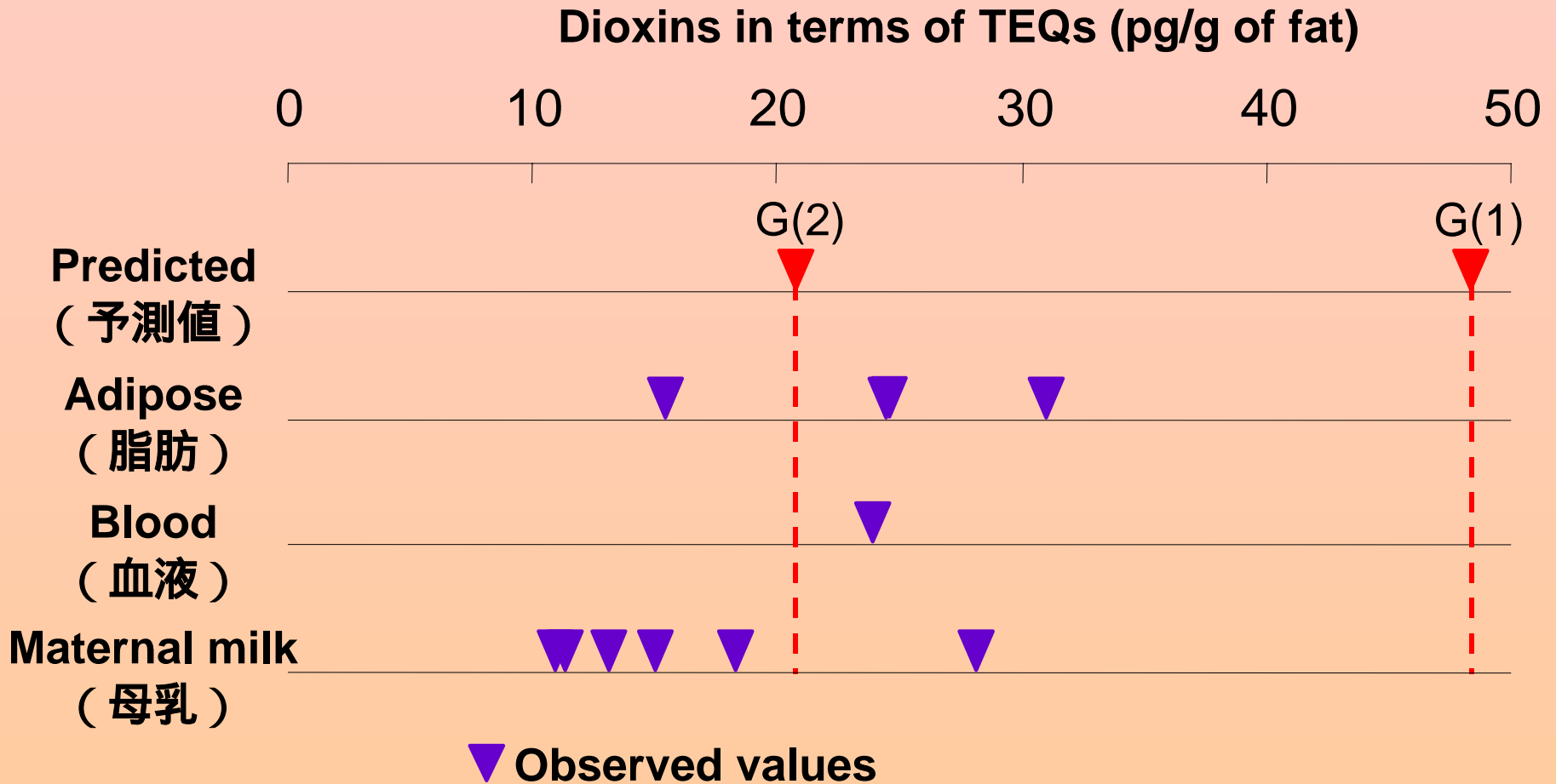
*Predicted vs. Observed TEQs liver levels for general population*

Dioxin in term of TEQs (pg/g of tissue)
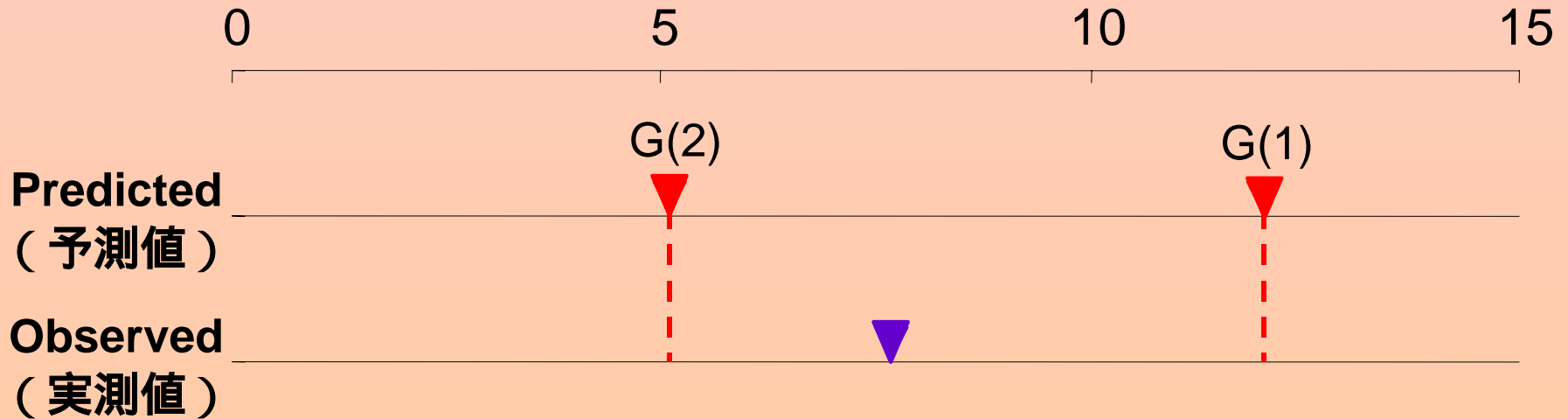
# Exposure estimates for LRs
## (Local residents living near garbage incinerator)
### -- the worst case scenarios and theoretically maximally exposed individual --

1. Dioxin levels

| Media | Dioxin levels |
| --- | --- |
| soil (   ) | 144 pg/g |
| air | 4.9 pg/Nm$^3$* |
| 10 m and larger | (1.5 pg/Nm$^3$) |
| smaller than 10 m | (3.4 pg/Nm$^3$) |
| gas | (0.5 pg/Nm$^3$) |
| intake via green vegetables consumption | 93.4 pg/day |

2. Duration of exposure :  30 years.

*background    large cities    0.6 pg/Nm$^3$

# *Expousure estimation for HFEs ( heavy fish eaters)*

Average daily consumption of fish : 320 g/day

Duration of exposure: 70 years

# *Linearized multistage model*

Cancer risk is estimated using linearized multistage model.
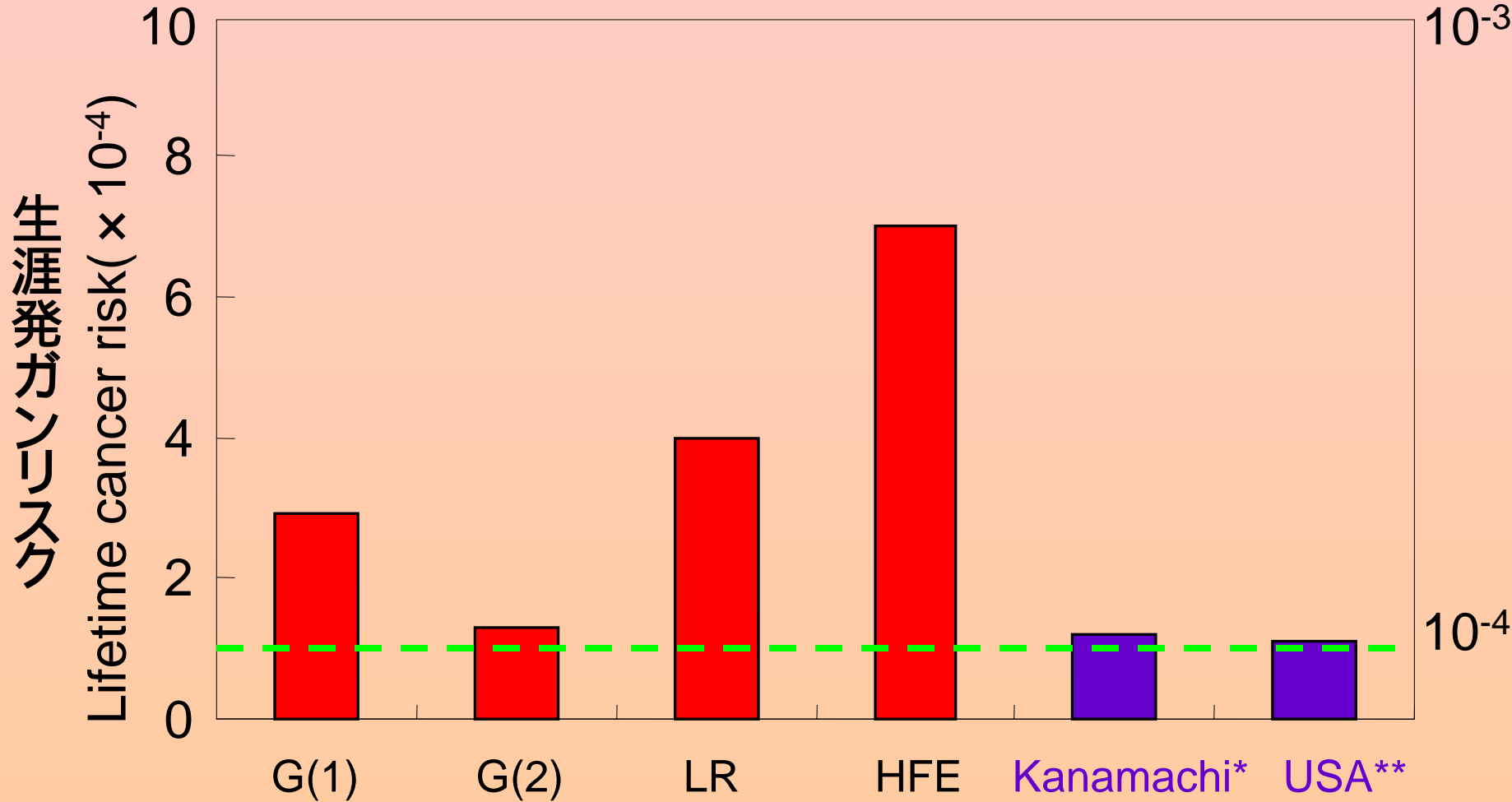(                              )

2378TCDD is thought to be not initiator but promoter. This model is not suitable for promoter such as TCDD. However, it is applied for comparison with other chlorinated compounds, such as chlorination byproducts of water.
(

                                                              )

Oral cancer slope of 10 $^4$(pg/kg/day)$^{-1}$ is used.[*1]

[*1] EPA(1994)

Cancer Risk Estimates (Linearized Multistage Model)
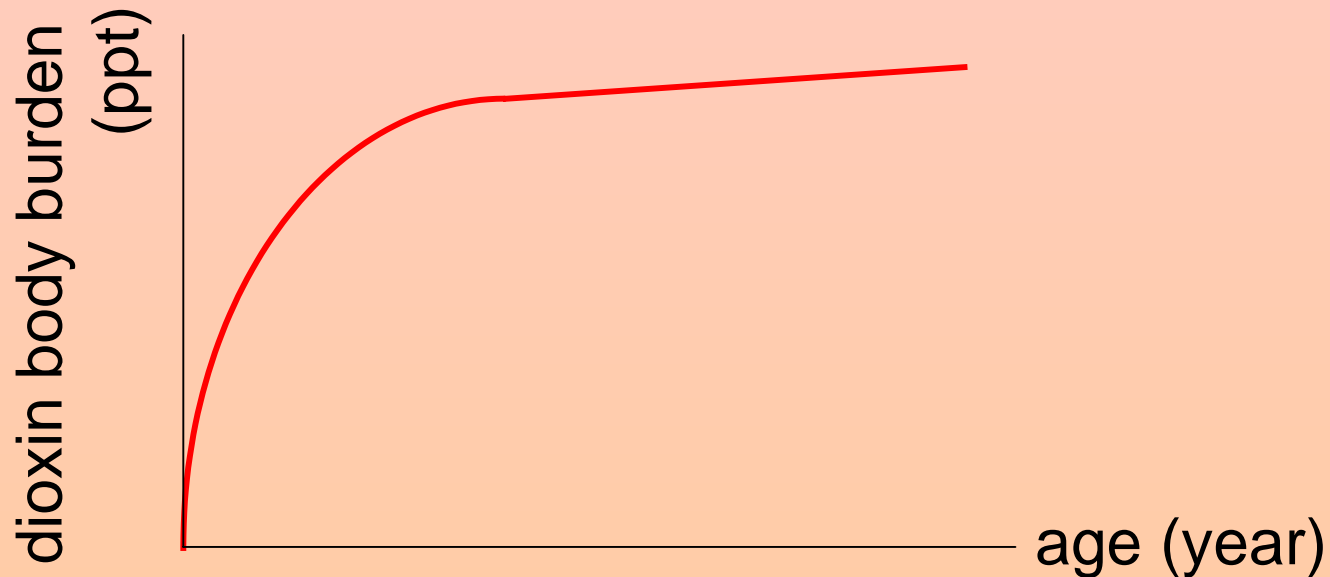
*Since dioxins persist over years in the body, dosimetry of the body's burden retention of dioxins must be used. Here, the area under the curve (AUC) for lifetime is used.*
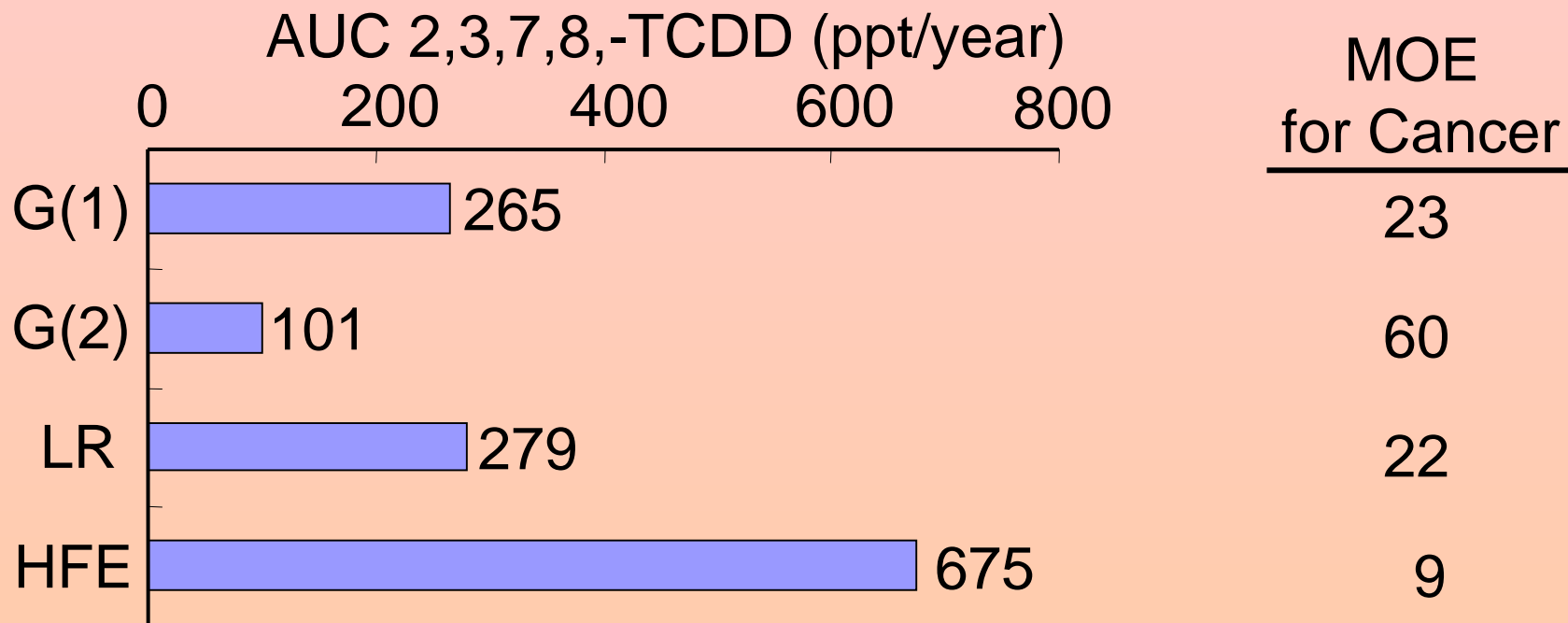
*AUC=                                    ,   POPs=*



dioxin body burden (ppt)

age (year)

$$AUC = \int_0^{t'} C\,dt = \frac{D}{k} \int_0^{t'} \{1 - \exp(-kt)\}\,dt,$$

where k = 0.1066 (1/year) = overall elimination rate constant, t'=70 years, D = yearly dose (1/year)

# AUC 2,3,7,8-TCDD Levels and Corresponding Cancer Risks



| | AUC 2,3,7,8,-TCDD (ppt/year) | MOE for Cancer |
|---|---|---|
| G(1) | 265 | 23 |
| G(2) | 101 | 60 |
| LR | 279 | 22 |
| HFE | 675 | 9 |

NIOSH (National Institute of Safety and Health ) cohort was used as a reference. According to the analysis by Aylward et al., the AUC serum lipid TCDD levels of 6059 ppt  year is an average for an apparent "no-effect level" group in the NIOSH cohort.

$$MOE = \frac{exposure}{\text{no-effect exposure level}} = \text{Margin of exposure}$$

## Table 6. MOE Values for Three Endpoints
### - 1996 Proposed Guidelines -

| Endpoint / Receptor | Cancer | Reproductive Dysfunction | Endometriosis |
|---|---|---|---|
| G(1) | 98 | 98 | 13 |
| G(2) | 228 | 228 | 30 |
| LR | 72 | 72 | *9* |
| HFE | 41 | 41 | *5* |

*MOE*

* Estimated from LOEL value.

# *Exposure estimation*

1) For all the four receptor groups, fish ingestion is the dominant route for dioxin exposure. The ratio of exposure from fish consumption to exposure via all routes is 60 % for G(1) and 91% for HFE.

2) Among the four groups, the most highly exposed group is HFE.

3) For LR , ingestion of green vegetables harvested in the proximity ( within 1000 m ) of the incinerator is the second dominant exposure route.

# *Risk   Analysis. (Part 1)*

1) Assuming the linear dose response relationship at low doses, the excess lifetime cancer risk evaluated on the basis of TEQs is in the range of less than $10^{3}$ and more than $10^{4}$ for all the four receptor groups.

2) The MOE values were calculated on the basis of TEQs according to the 1996 Proposed Guidelines . The MOE values for cancer and reproductive dysfunction are large enough to guarantee safety but those for endometriosis are marginal.
(                              MOE
                                              )

# *Risk   Analysis. (Part 2)*

3)  Considering the persistency of dioxins, risks should be evaluated on the basis of the AUC rather than the LADD. The analysis based on the AUC 2,3,7,8-TCDD shows that the MOE values for G(1), G(2) and LR lie in the range of 22 to 60 and are large enough to guarantee safety, but the MOE for HFE is 9 and is marginal. Although this analysis is promising, there are many problems to be solved.

MOE

ACU = Area under the curve
LADD = Lifetime average daily dose

# *Subjects in the coming year*

1) To evaluate the cancer risks not in terms of MOE but LLE.
   LLE

2) To evaluate the risks of other endpoints than cancer.

3) To evaluate the risks for breast-fed infants and fetuses.