

# **Estimation of Dioxin Risk in Japanese by Mathematical Models**

**数理モデルから見たダイオキシン類  
のリスク**

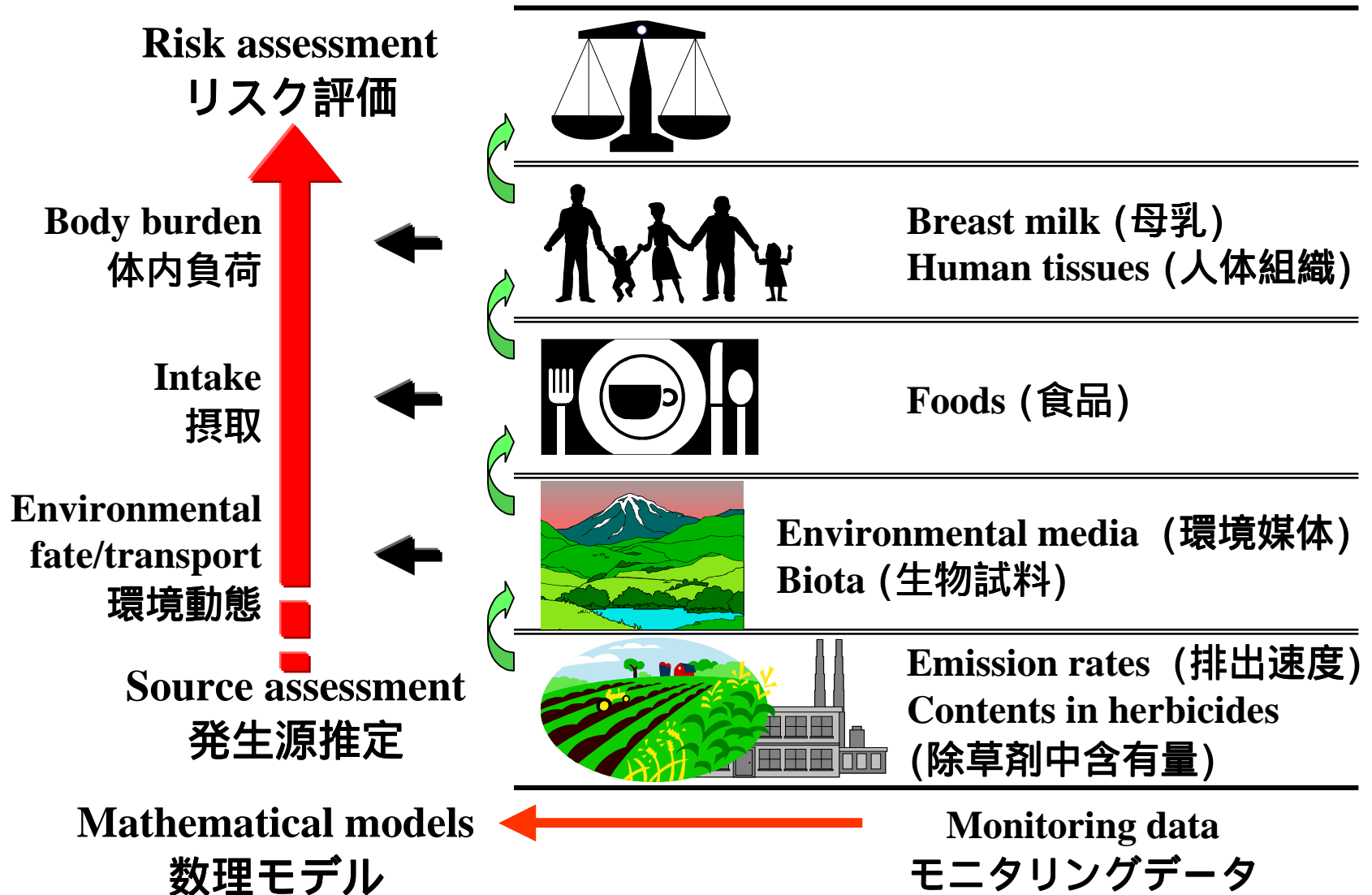
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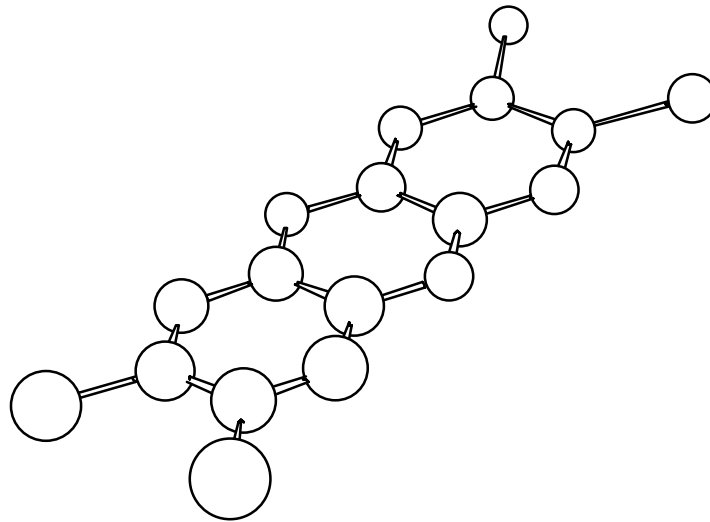
# Mathematical models in assessment of human health risk caused by PCDD/Fs

## ダイオキシンによる健康リスクと数理モデル



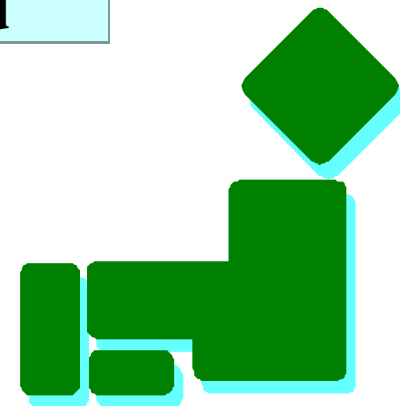
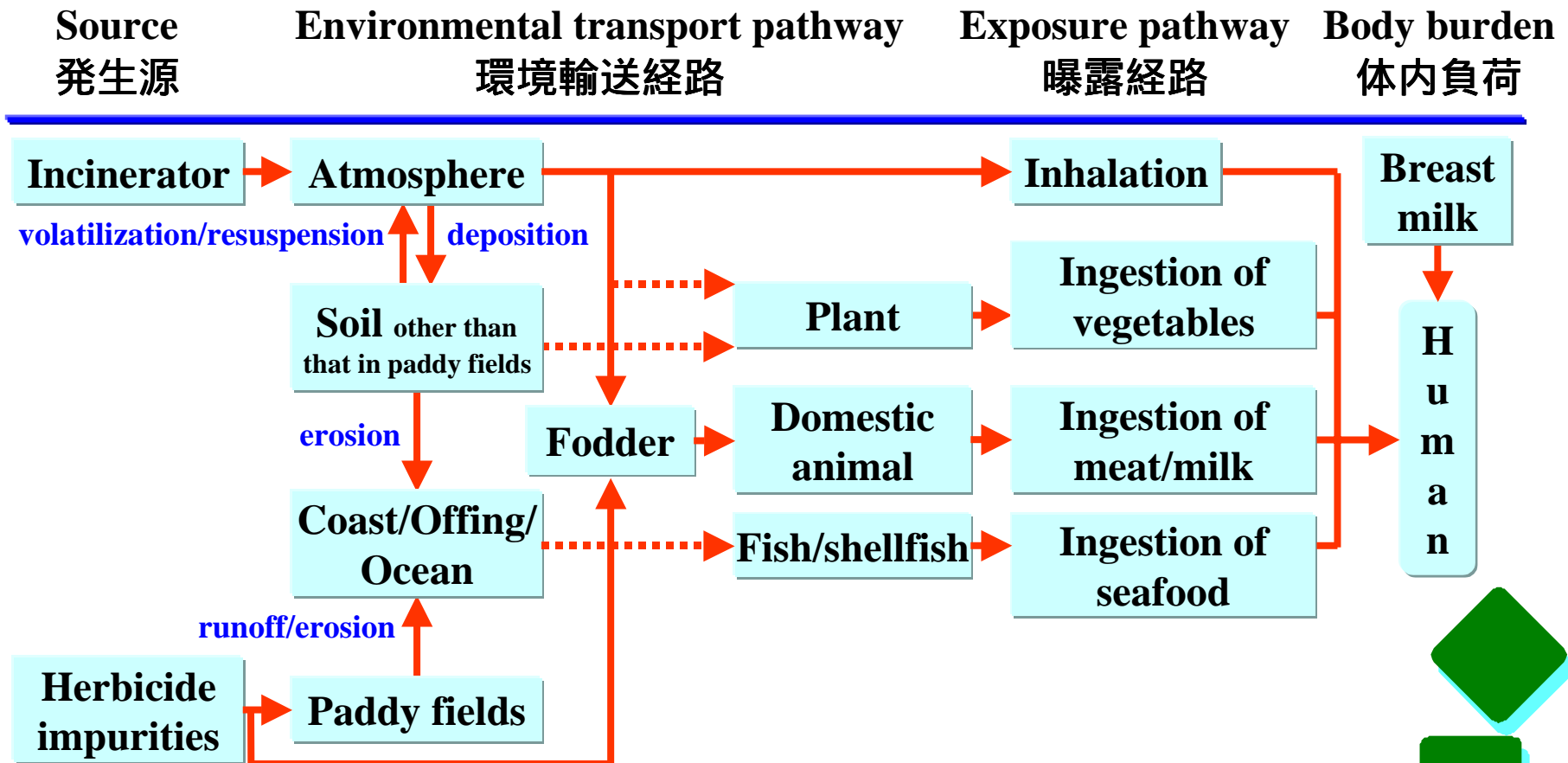
# Description of Modeling and Risk Assessment

## モデル化及びリスク評価法



# Transport pathways of congeners of PCDD/Fs from sources to human body

発生源から人に至る輸送経路

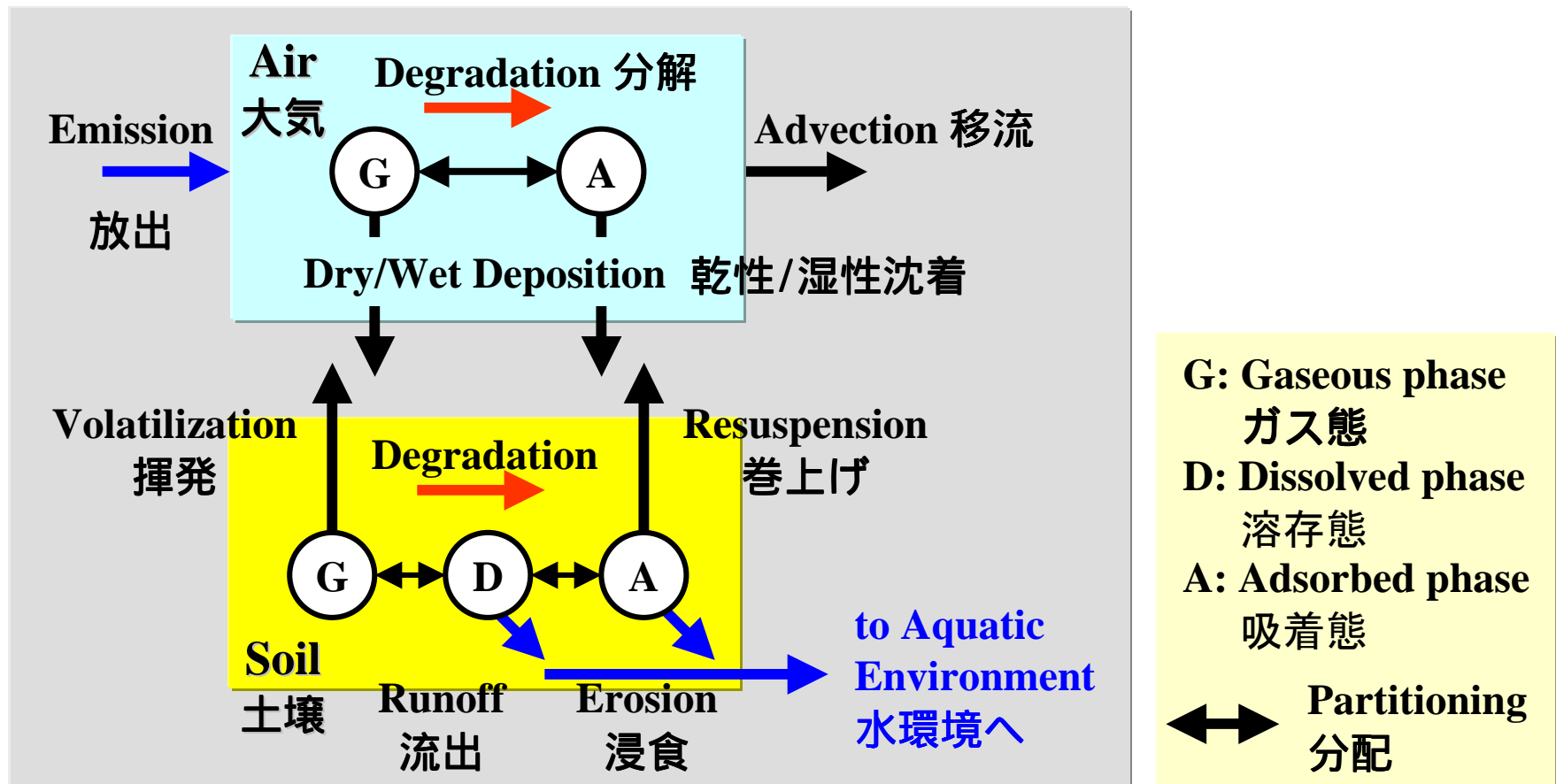


# Estimation of environmental dynamics of PCDD/F congeners emitted from incinerators

大気及び非水田土壌でのPCDD/Fs異性体の動態推定

Processes considered in air/soil two-compartment model

大気/土壌 2 コンパートメントモデルで考慮する過程

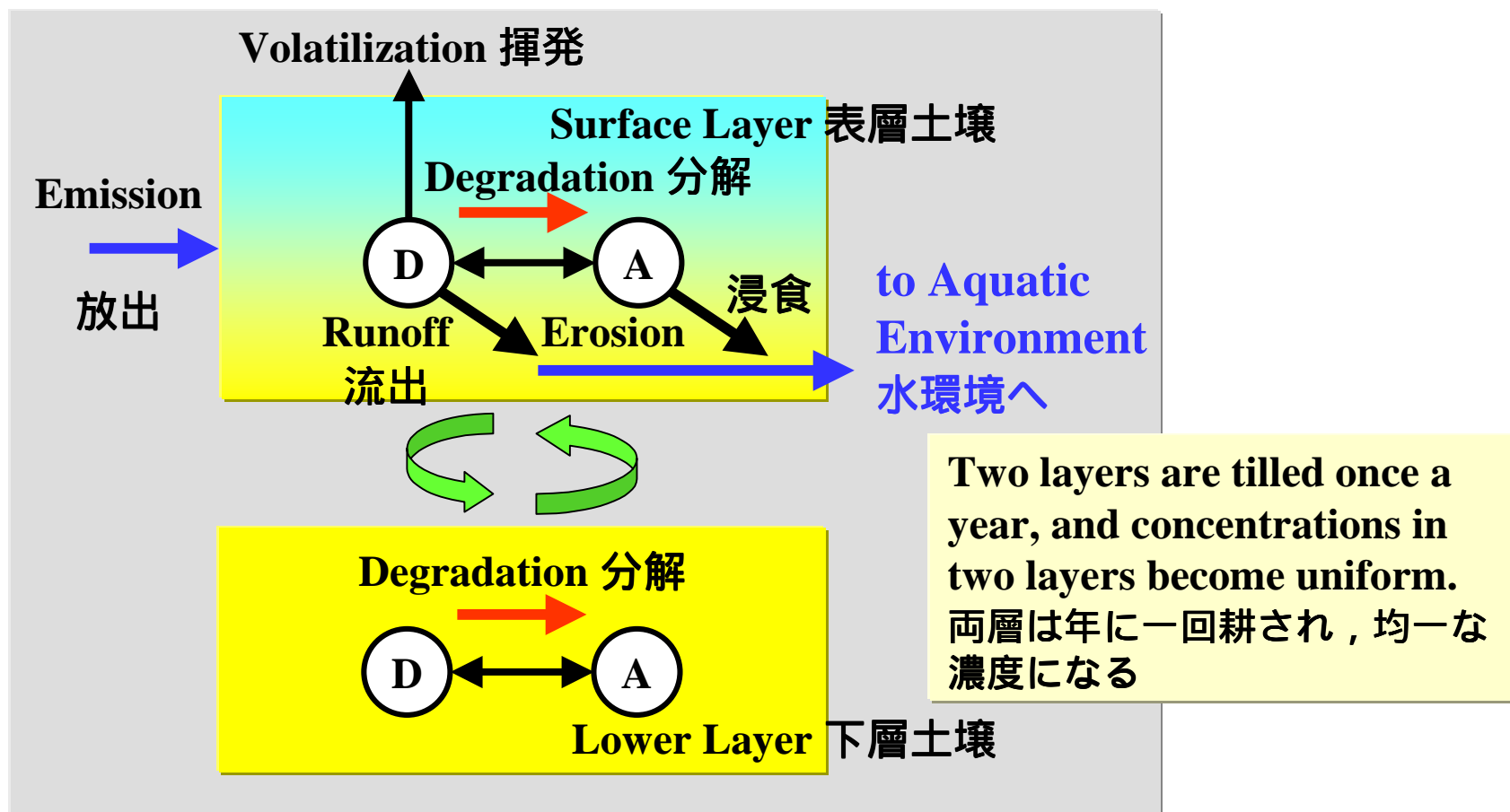


# Estimation of environmental dynamics of PCDD/F congeners in paddy fields

## 水田でのPCDD/Fs異性体の動態推定

Processes considered in soil one-compartment model

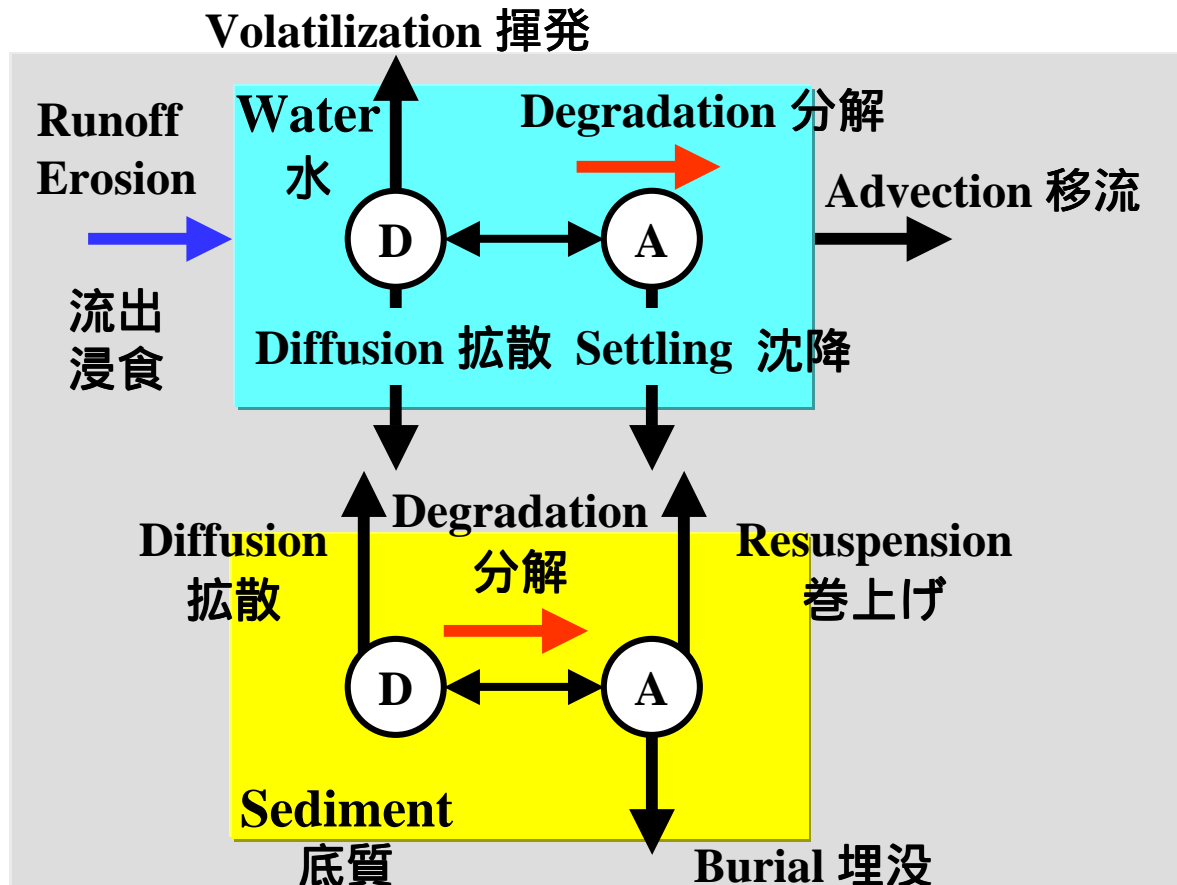
土壌1コンパートメントモデルで考慮する過程



# Estimation of dynamics of PCDD/F congeners in coastal environment

## 沿岸域でのPCDD/Fs異性体の動態推定

Processes considered in water/sediment two-compartment model  
水/底質 2 コンパートメントモデルで考慮する過程



# Estimation of daily intakes of PCDD/F congeners

## PCDD/Fs異性体の一日摂取量の推定

- **Daily intake:** product of concentration in intake medium and ingestion or inhalation rate of intake medium  
一日摂取量：摂取媒体中濃度と媒体摂取速度の積
- **Concentration in coastal fish:** assumed equilibrium between the concentrations in water and fish  
沿岸魚中濃度：魚中濃度と水中濃度間での平衡成立を仮定
- **Concentrations in crops/meat/dairy products:** methods described by the U.S. EPA (1994)  
作物/肉/乳製品中濃度：米国EPAの方法で推定
- **Epidermis of rice plants:** contaminated by PCDD/Fs  
稲の表皮：PCDD/Fsで汚染されると仮定  
**Residual culms and blades after threshing rice:** fed to domestic animals as fodder  
脱穀後の稲の茎葉：家畜に飼料として与えられる



# Estimation of congener-specific body burden and concentration in breast milk

## PCDD/Fs異性体の体内負荷量と母乳中濃度の推定

### ■ Body burden, $C_{\text{human}}(t)$ 体内負荷量

$$C_{\text{human}}(t) = \frac{\text{ABS} \times \text{IT}(t)}{k_e \times \text{BW}(t)} \{1 - \exp(-k_e \times t)\}$$

**ABS** : gastrointestinal absorption (消化管吸収率)

**IT(t)** : daily intake at age t (一日摂取量)

**$k_e$**  : 1st-order rate constant for elimination  
(排泄1次速度定数)

**BW(t)** : Body weight at age t (体重)

### ■ Concentration in breast milk, $C_{\text{milk}}(t)$ 母乳中濃度

$$C_{\text{milk}}(t) = \frac{C_{\text{human}}(t)}{\text{Fat}(t)}$$

**Fat(t)** : fat content at age t (体内脂肪含有率)

# Derivation of correction factors for calculating 2,3,7,8-TCDD toxic equivalent body burden

毒性等価体内負荷量を算出するための補正係数の導出

- **Toxic equivalent factors (TEFs): based on administered doses**

毒性等価係数(TEFs) : 投与された用量ベースで設定

- **Relative toxic equivalent body burden (relative TEB)**

毒性等価体内負荷量相対値 (relative TEB)

$$\text{relative TEB}_i = \frac{\text{TEF}_{\text{TCDD}}}{\text{TEF}_i} \times \frac{\text{ABS}_i \times \text{DT}_{50,i}}{\text{ABS}_{\text{TCDD}} \times \text{DT}_{50,\text{TCDD}}} \quad (i = 17 \text{ congeners})$$

TEF : WHO-TEF

DT<sub>50</sub> : Half-life 体内半減期

- **Correction factor (CF) 補正係数**

$$\text{CF}_i = \frac{1}{\text{relative TEB}_i}$$

applied rounding-off procedure (nearest 1 or 5)

有効数字1桁目を丸める (1あるいは5に)

# Correction factors for calculating 2,3,7,8-TCDD toxic equivalent body burden

毒性等価体内負荷量を算出するための補正係数

Congener	<i>WHO-TEF</i>	<i>ABS*</i>	<i>DT50*</i> (year)	<i>Relative TEB</i>	<i>CF</i>
2,3,7,8-TCDD	1	0.97	6.2	1.00	1
1,2,3,7,8-PeCDD	1	0.99	8.6	1.42	0.5
1,2,3,4,7,8-HxCDD	0.1	0.98	8.4	13.7	0.05
1,2,3,6,7,8-HxCDD	0.1	0.97	13.1**	21.1	0.05
1,2,3,7,8,9-HxCDD	0.1	0.96	8.5	13.6	0.05
1,2,3,4,6,7,8-HpCDD	0.01	0.86	6.6	94.4	0.01
OCDD	0.0001	0.76	5.6	7080	0.0001
2,3,7,8-TCDF	0.1	0.97	0.4	0.65	1
1,2,3,7,8-PeCDF	0.05	0.99	0.9	2.96	0.5
2,3,4,7,8-PeCDF	0.5	0.98	9.9	3.23	0.5
1,2,3,4,7,8-HxCDF	0.1	0.97	5.7	9.19	0.1
1,2,3,6,7,8-HxCDF	0.1	0.97	6.2	10.0	0.1
1,2,3,7,8,9-HxCDF	0.1	0.95	1.1***	1.74	0.5
2,3,4,6,7,8-HxCDF	0.1	0.96	2.4	3.83	0.5
1,2,3,4,6,7,8-HpCDF	0.01	0.87	0.2***	2.89	0.5
1,2,3,4,7,8,9-HpCDF	0.01	1.00	3.2	53.2	0.01
OCDF	0.0001	0.95	0.2	316	0.005

\*: Liem and Theelen (1997), \*\*: Flesch-Jabys, et al. (1996), \*\*\*: Yoshida (2000)

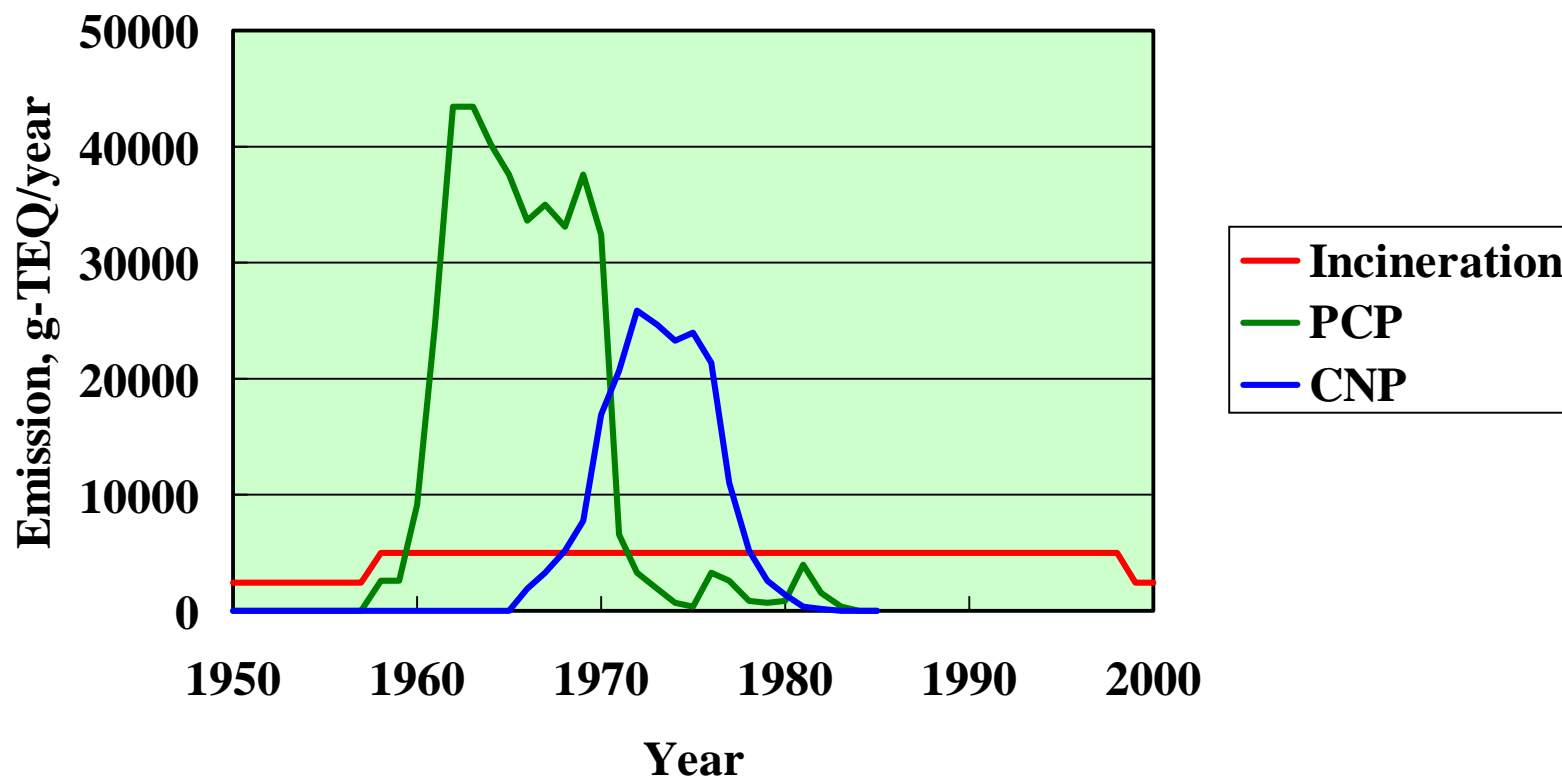
# Endpoint and margin of exposure

## エンドポイントと曝露マージン

- **Endpoint:** morphological reproductive alterations in female offspring exposed prenatally (Gray et al., 1997)  
エンドポイント：胎内曝露女児への形態変化を伴う生殖毒性
- **Body burden for NOAEL:** 28.6 ng/kg (Hurst et al., 2000)  
average body burden of 2,3,7,8-TCDD between gestation day 16 and 21 of rats administered at a dosage level of 50 ng/kg  
最大無毒性量に相当する体内負荷量：28.6 ng/kg  
50 ng/kg 単回投与された雌ラットでの妊娠16日目と21日目の2,3,7,8-TCDDの平均体内負荷量
- **Margin of exposure (MOE):** calculated by dividing the body burden for NOAEL by the estimated maternal body burden  
曝露マージン(MOE)：NOAELに相当する体内負荷量を母親の体内負荷量で割った値

# Emission rates of PCDD/Fs into the Japanese environment

## わが国におけるPCDD/Fsの環境放出量



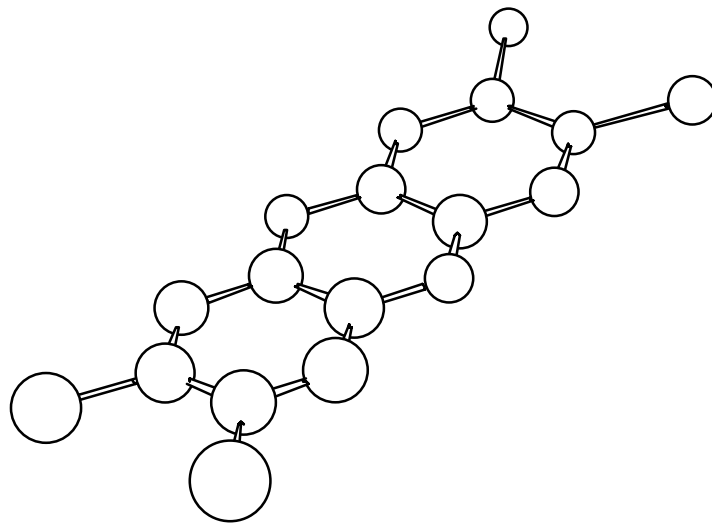
### Congener patterns of PCDD/Fs 異性体パターン

Exhaust gas from incinerators (燃焼排ガス) : Environment Agency, 1999

Herbicide PCP and CNP (除草剤) : Masunaga & Nakanishi, 1999

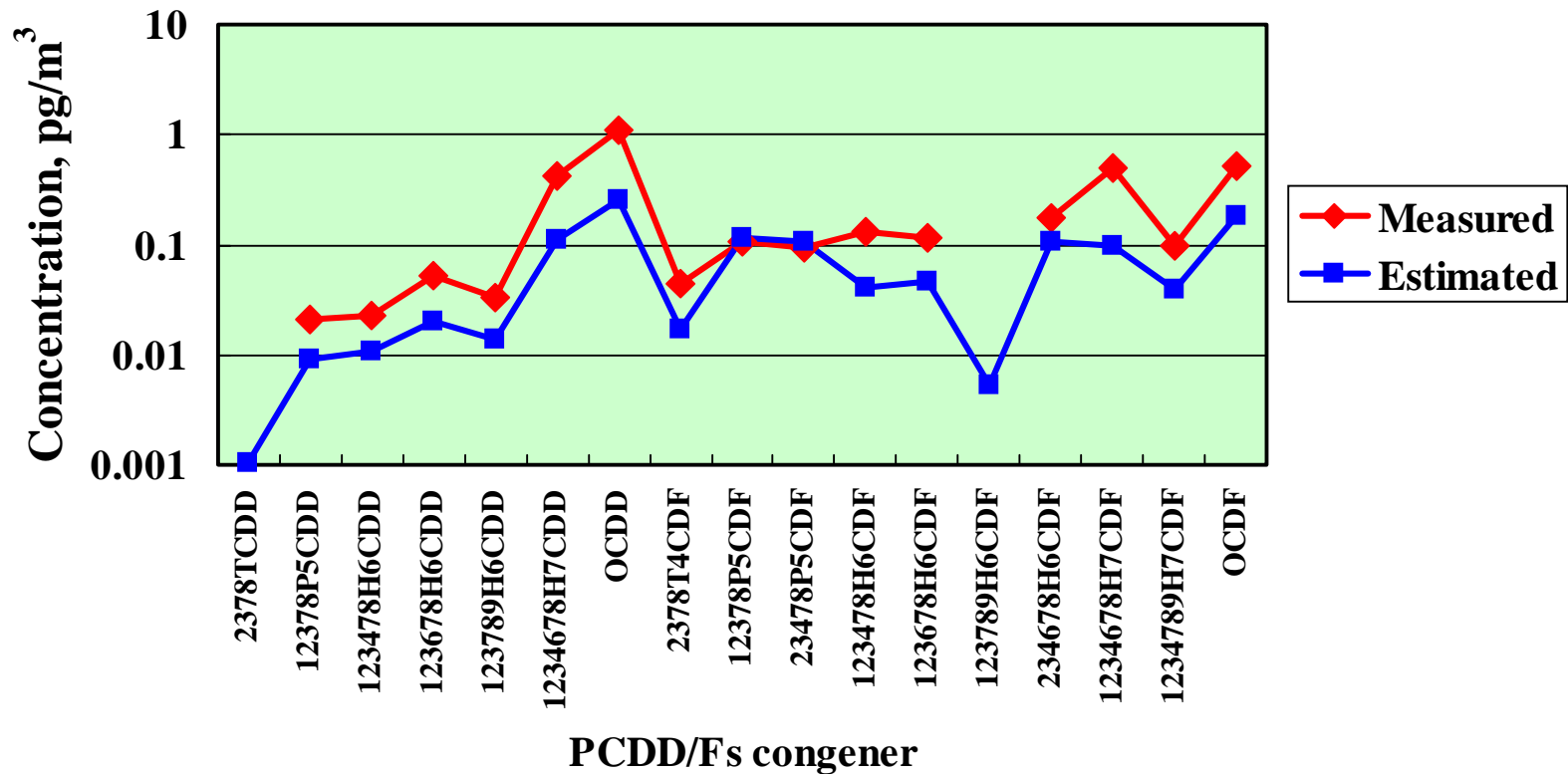
# Results

# 結果



# Comparison of measured and estimated congener-specific concentrations in the air

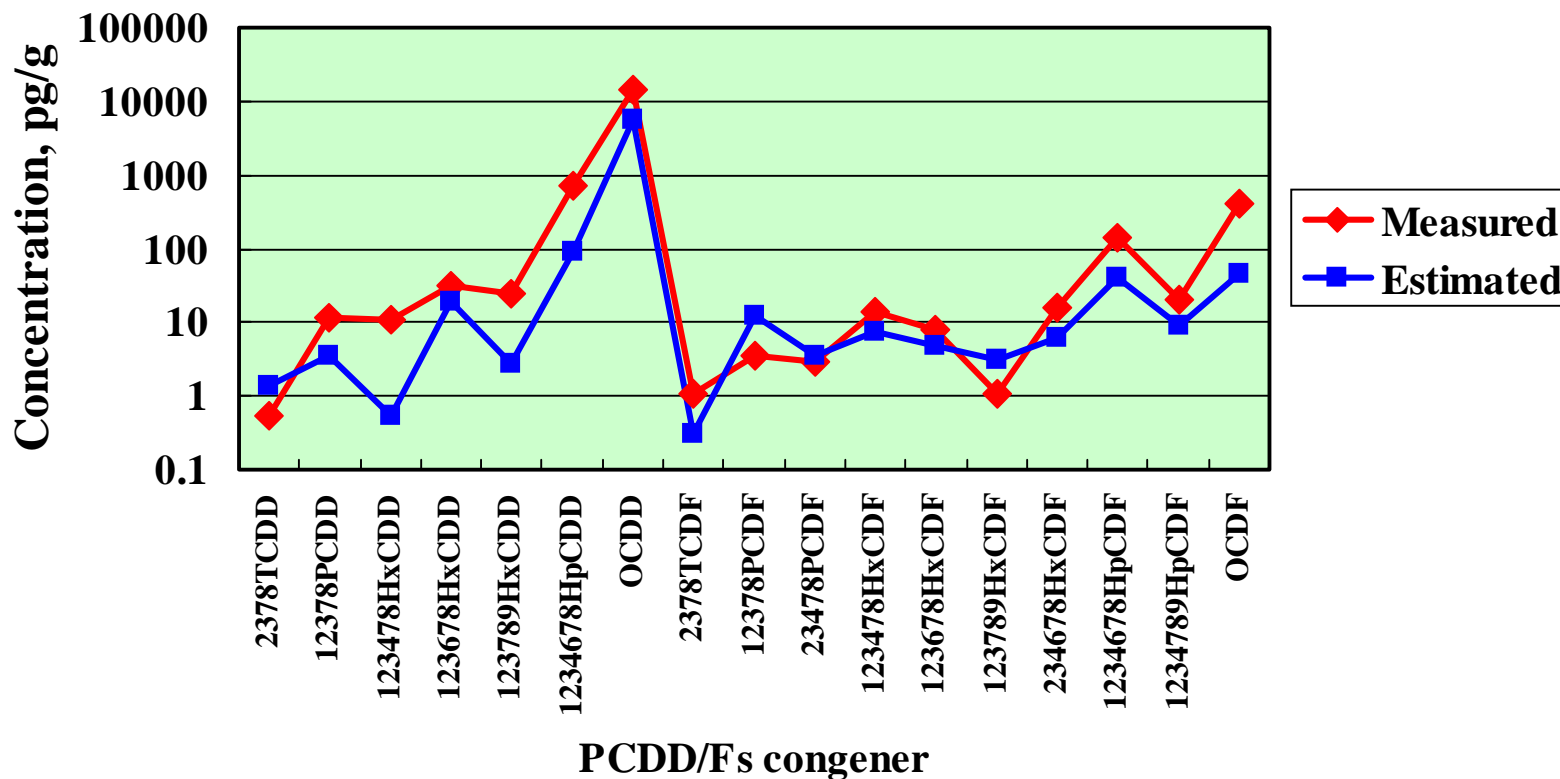
推定された異性体別大気中濃度と測定値の比較



Data: Environment Agency (1999): Results of urgent nationwide survey of dioxins.

# Comparison of measured and estimated congener-specific concentrations in soil of paddy fields

推定された異性体別水田土壌中濃度と測定値の比較

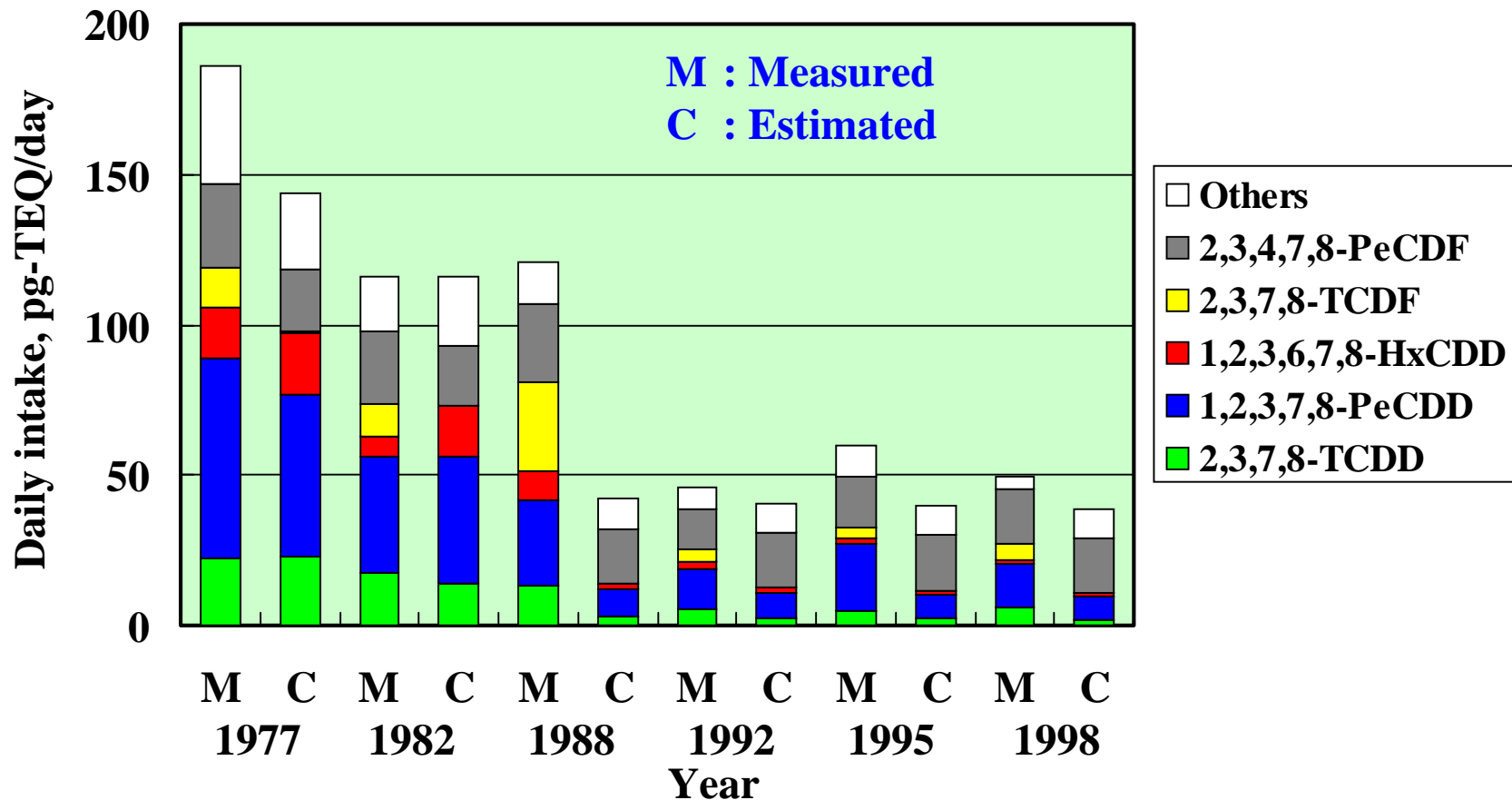


Data: Environment Agency (2000): Results of Survey of Dioxins in Agricultural Land Soil and Products.



# Comparison between measured and estimated congener-specific daily intakes

推定された異性体別一日摂取量と測定値の比較



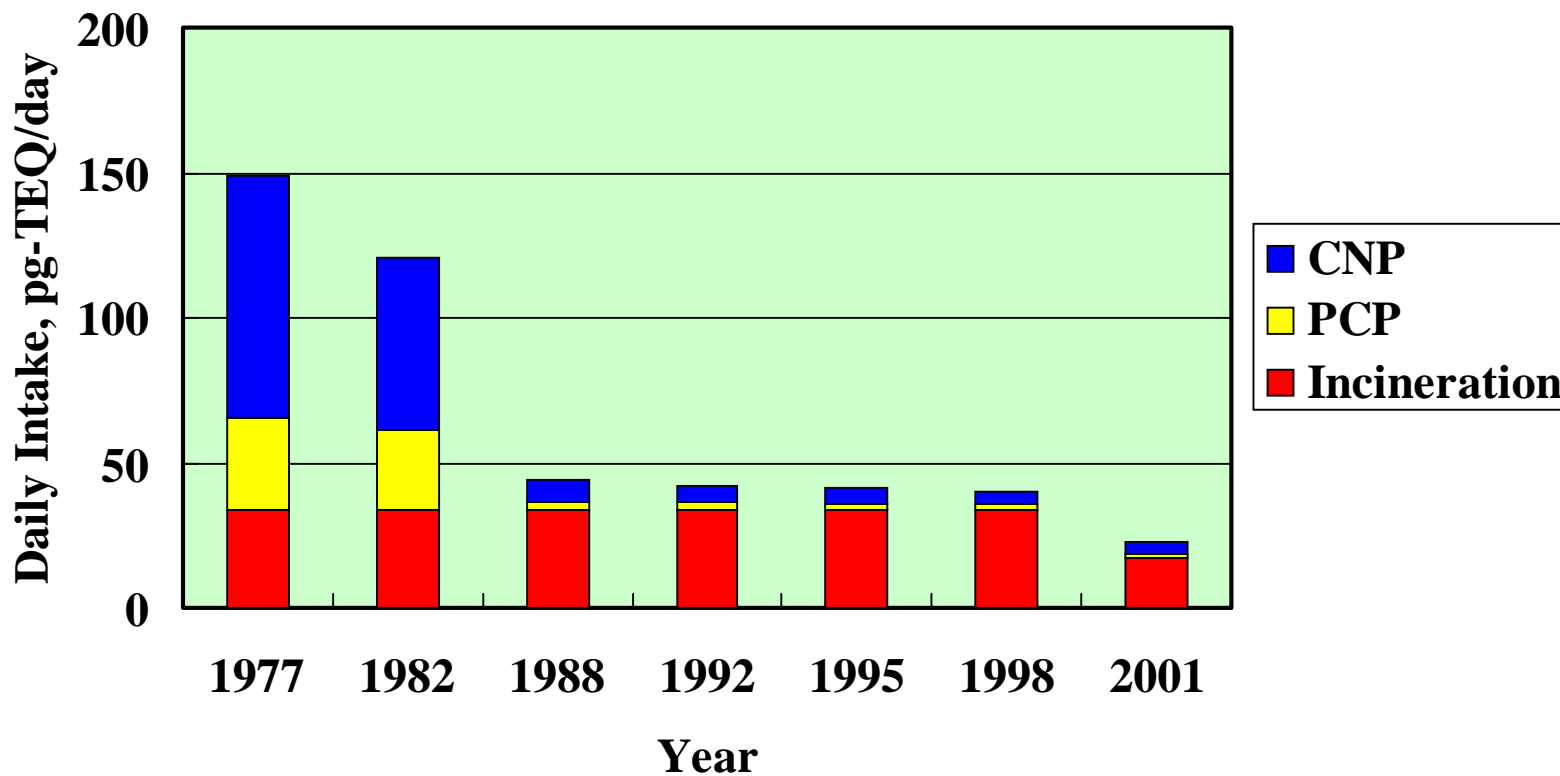
Data: MHW (1999): Results of Survey of Contamination by Dioxins and Related compounds in Foods in 1998.

# Contribution of different sources to daily intake

## 一日摂取量への発生源別の寄与

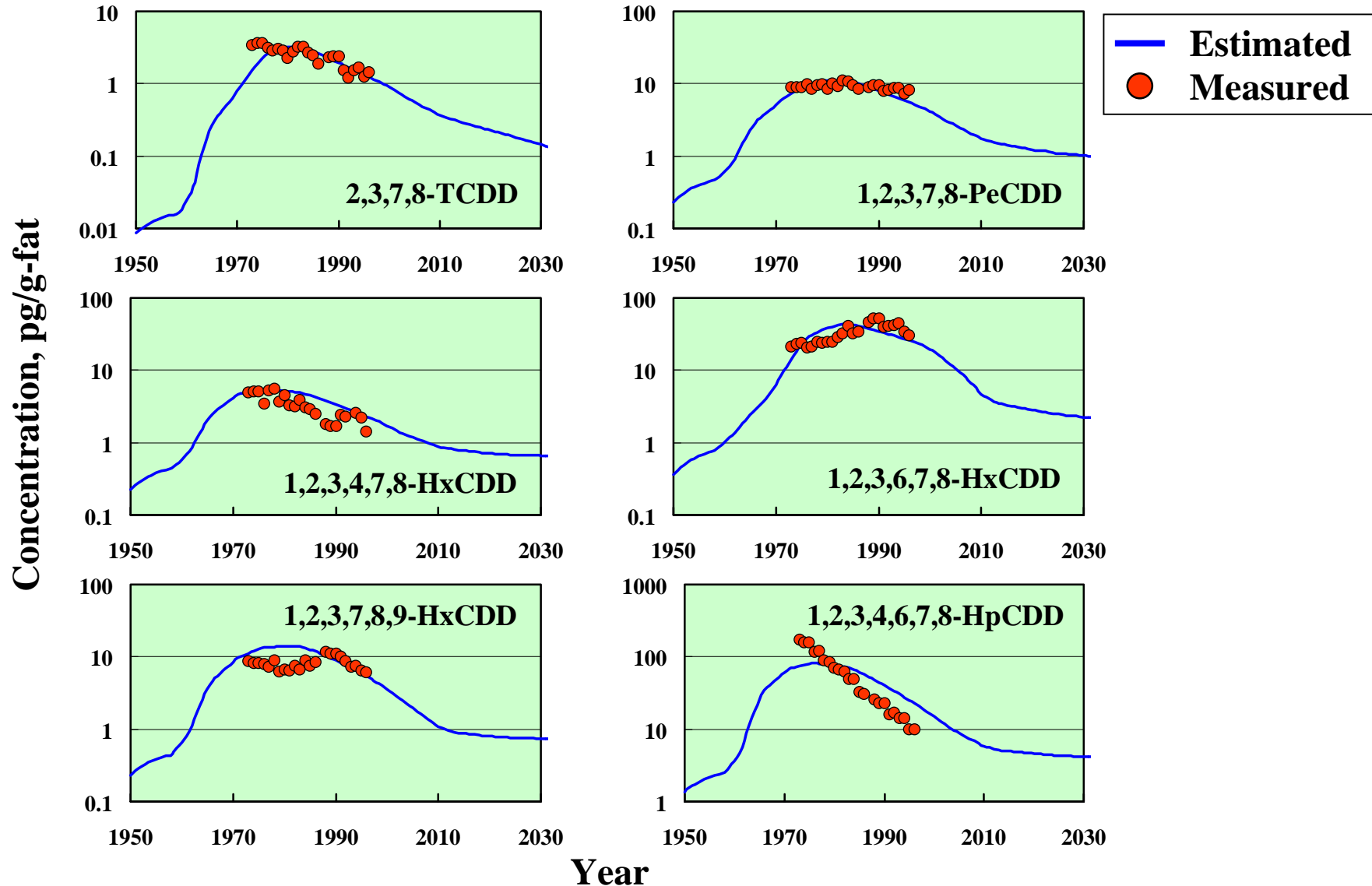
After 1992, daily intake of PCDD/Fs results from incineration processes.

1992年以降のPCDD/Fs一日摂取量には焼却施設が寄与する



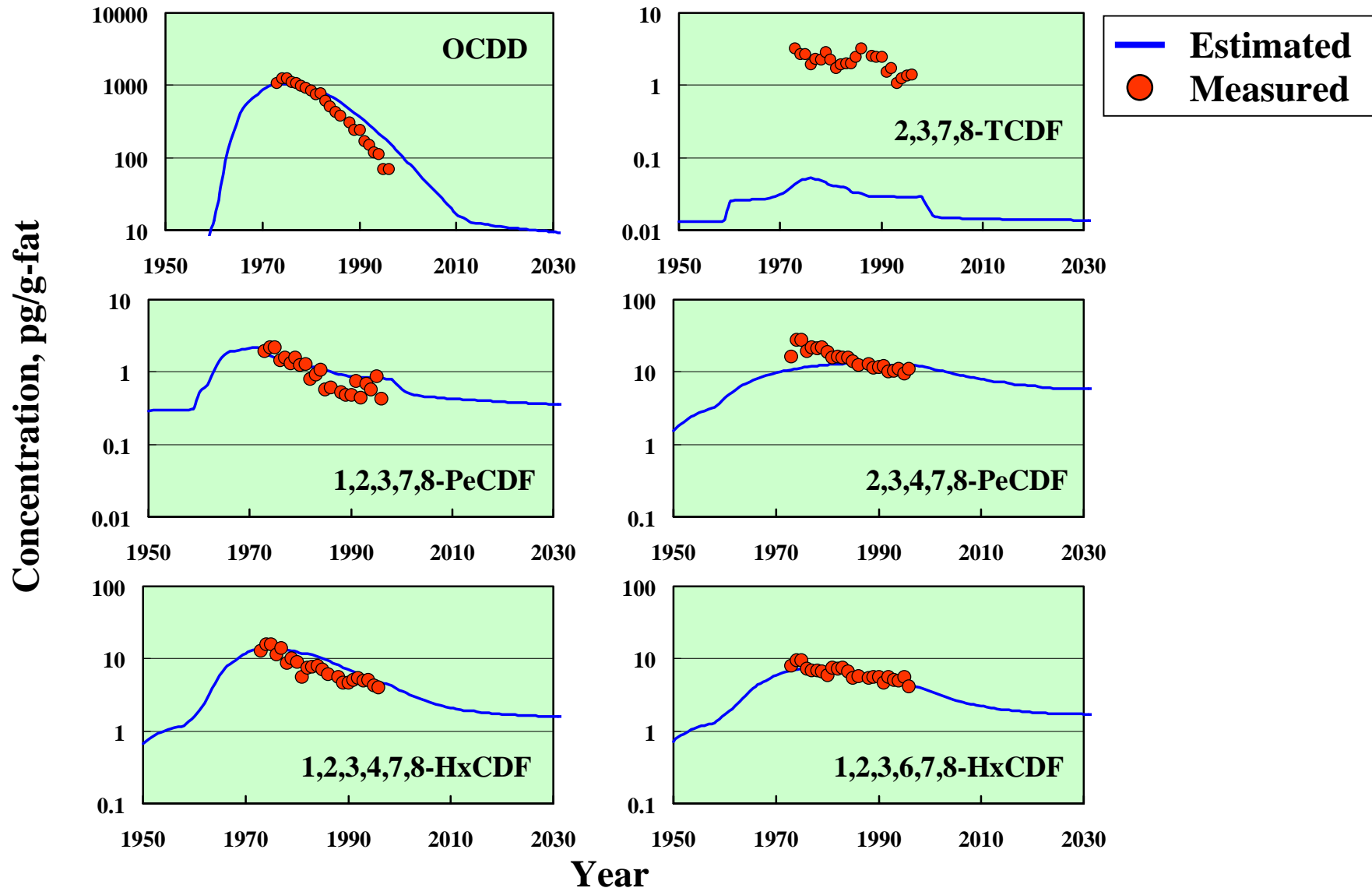
# Congener-specific concentrations in the breast milk of 27-year-old females

27歳女性の脂肪中異性体濃度



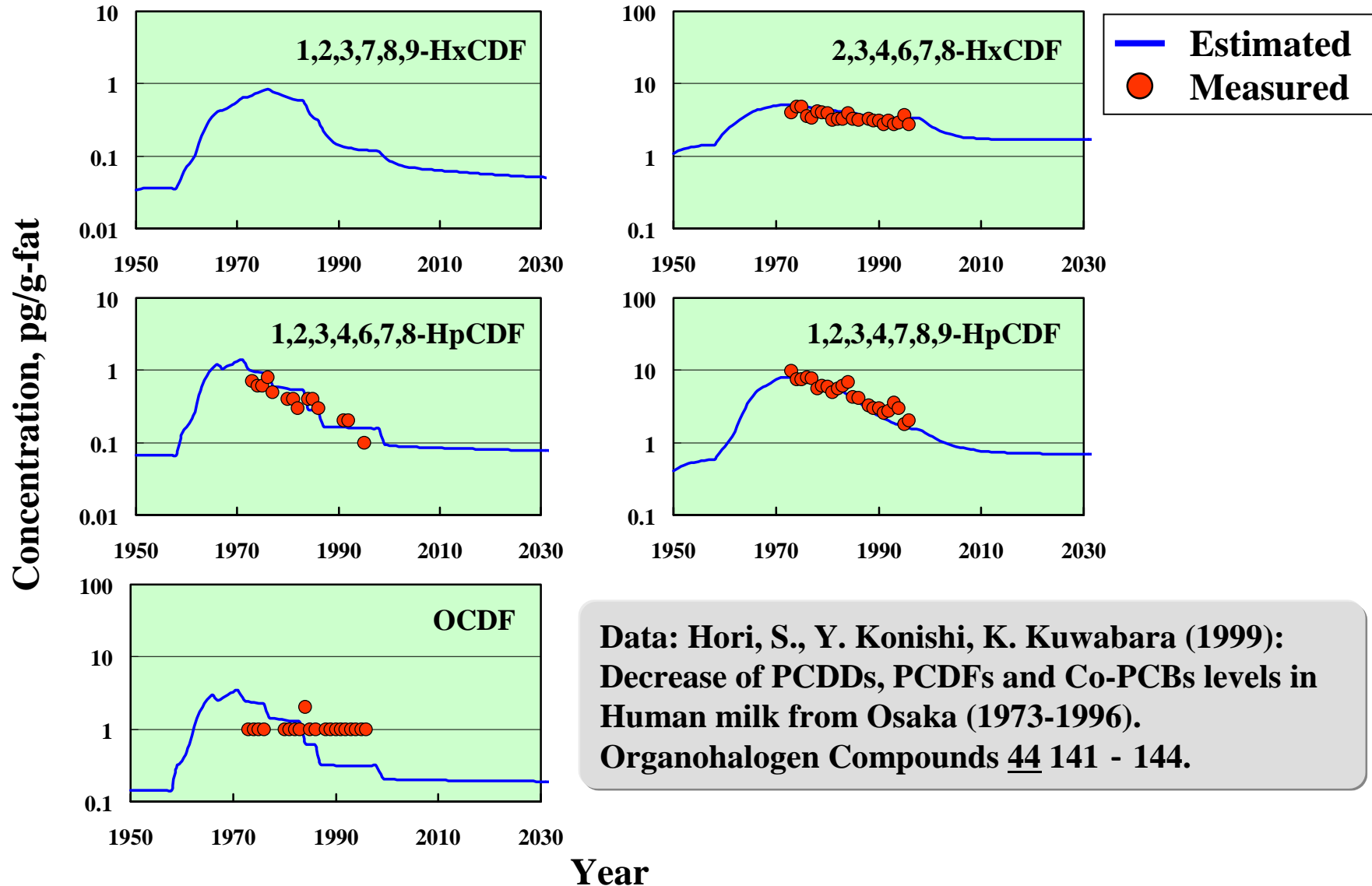
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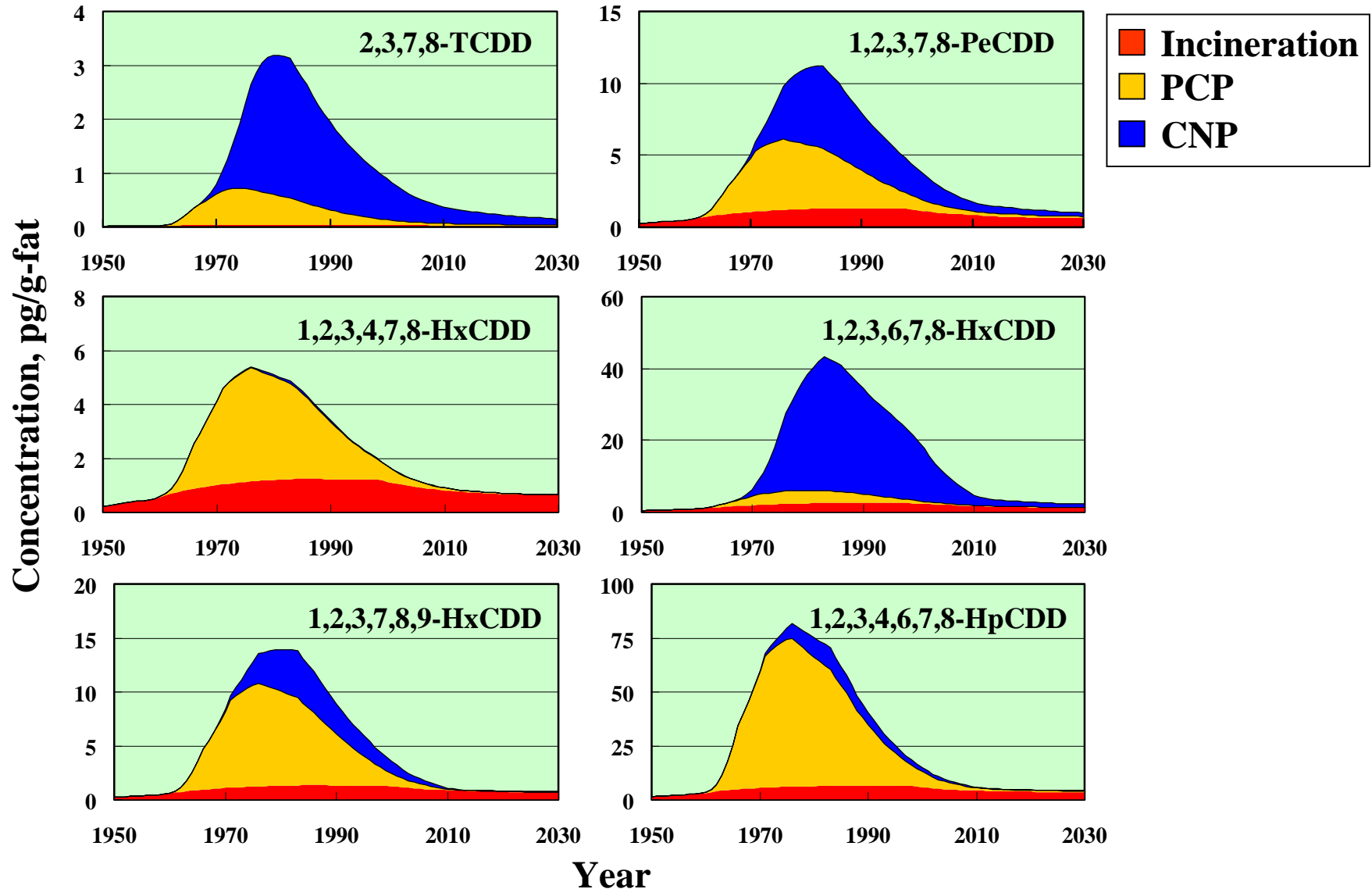


**Data: Hori, S., Y. Konishi, K. Kuwabara (1999):  
Decrease of PCDDs, PCDFs and Co-PCBs levels in  
Human milk from Osaka (1973-1996).**

**Organohalogen Compounds 44 141 - 144.**

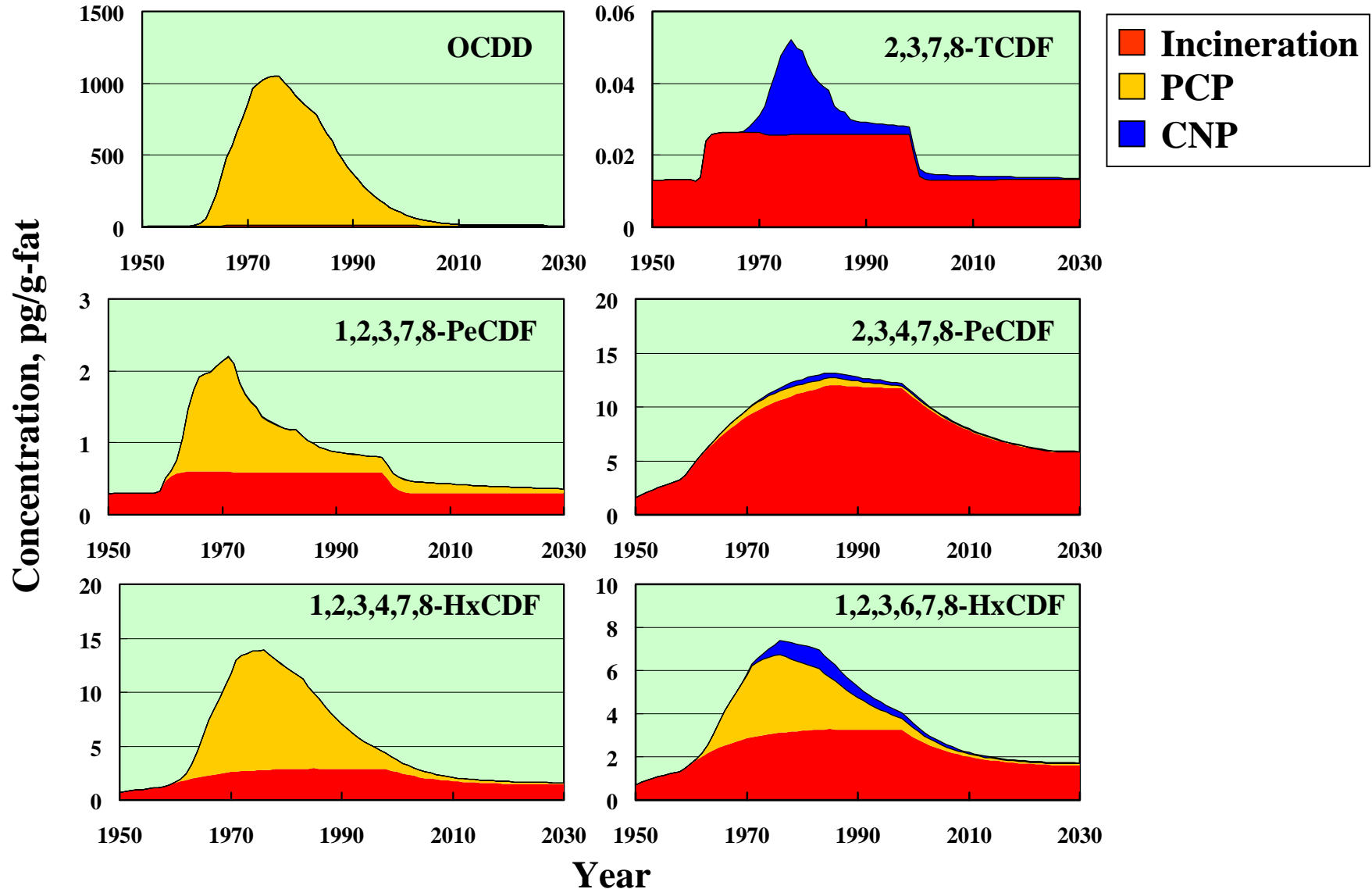
# Contribution of different sources to concentrations of PCDD/F congeners in breast milk

脂肪中濃度への発生源別の寄与



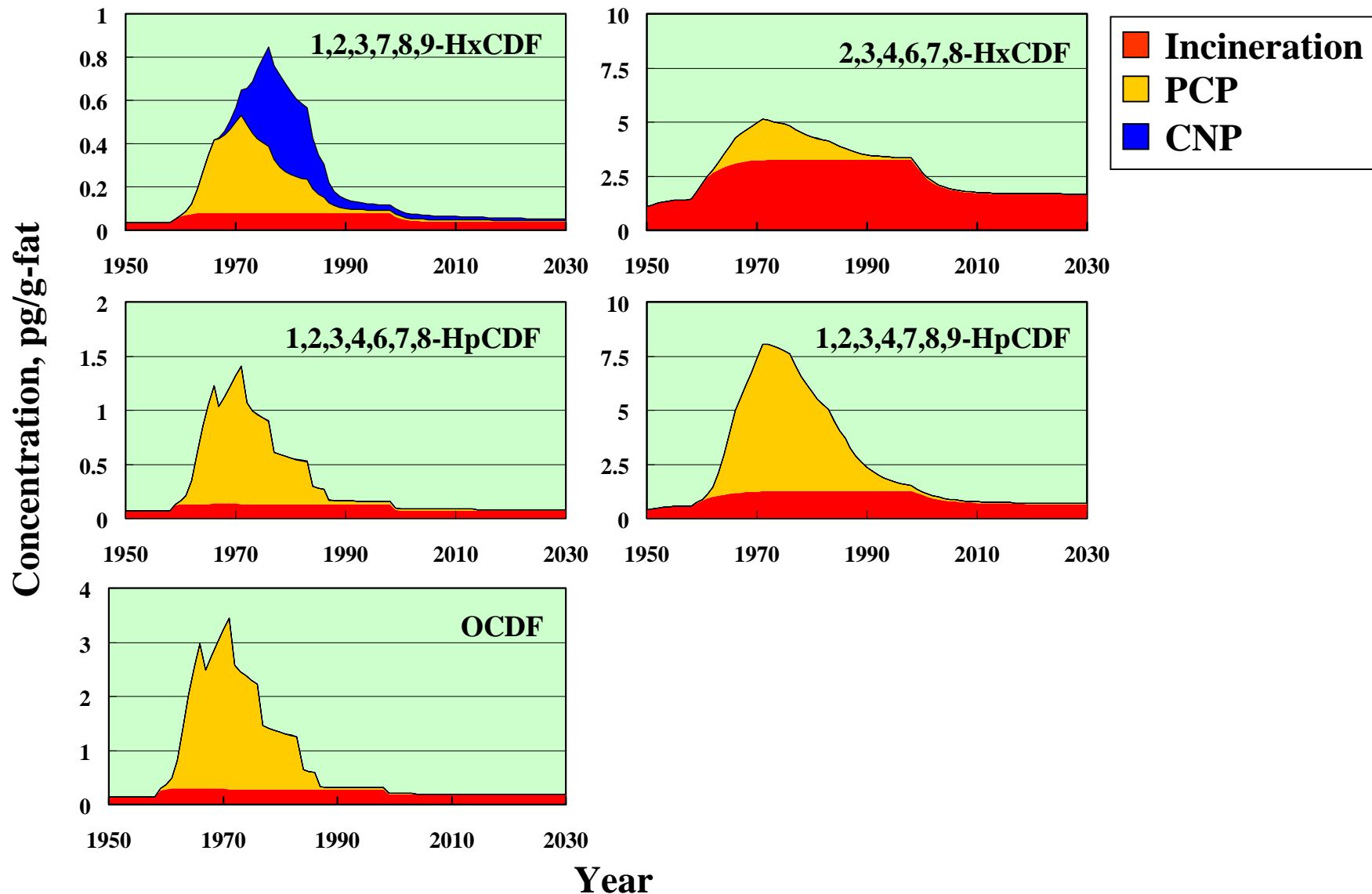
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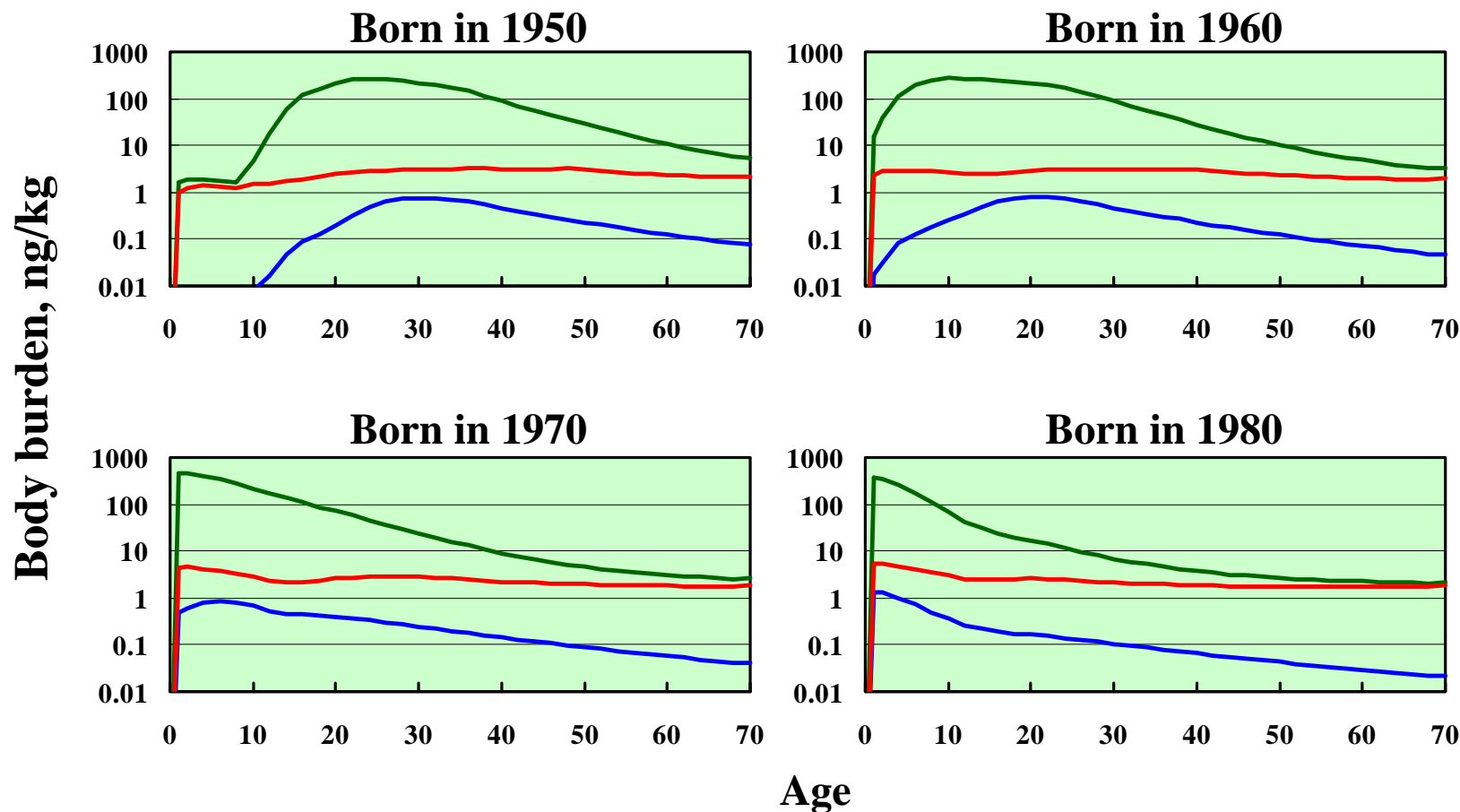
脂肪中濃度への発生源別の寄与





# Estimated time course of body burdens of 3 congeners in females born in 1950, 1960, 1970 and 1980

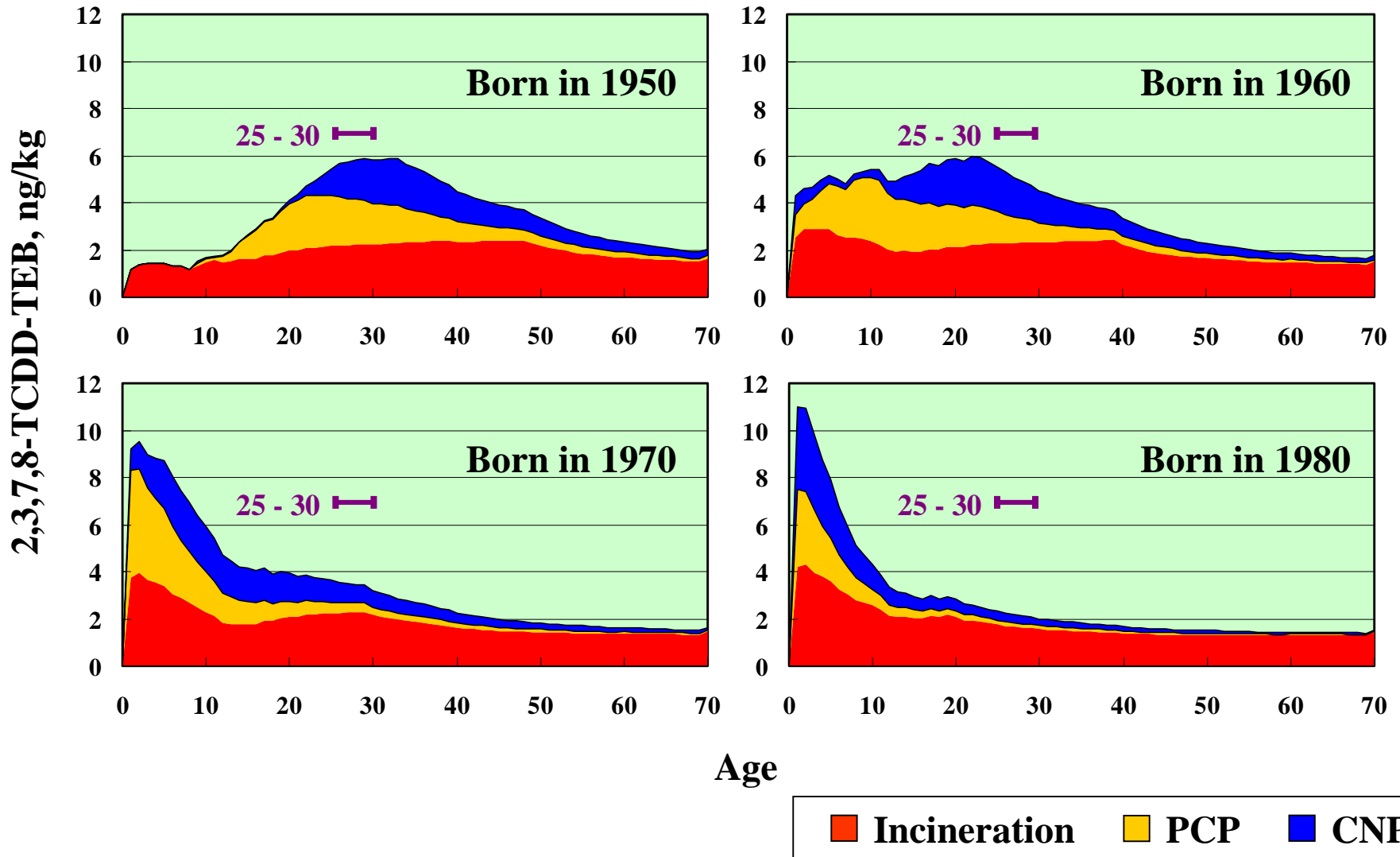
1950, 60, 70及び80年生れの女性における3異性体体内負荷量の経年変化



— 2,3,7,8-TCDD — OCDD — 2,3,4,7,8-PeCDF

# Contribution of different sources to body burden of PCDD/Fs in Japanese Females

日本人女性の体内負荷量への発生源別の寄与



# 2,3,7,8-TCDD toxic equivalent body burden and MOE for female offspring

母親の毒性等価体内負荷量と女兒への生殖毒性に対するMOE

Maternal female 母親		Female offspring 女兒
Year of birth 生年	2,3,7,8-TCDD-TEB ng/kg	MOE 曝露マージン
1950	4.9 - 5.5	5
1960	4.1 - 5.2	5 - 6
1970	2.7 - 3.1	8 - 9
1980	1.7 - 2.0	12 - 14

- The MOE values might not be sufficiently large to guarantee safety for female offspring of maternal females born in 1950 and 1960.

1950年と60年生れの女性が出産する女兒のMOEは余裕がない

- safety factor of 3 – 10: extrapolation from the general population to the sensitive subpopulation (個人差)
- body burden of 2,3,7,8-TCDF was underestimated (過小評価)

# Conclusion

## まとめ

- **Improvement of mathematical models in order to achieve reliable prediction of exposure to many kinds of chemical substances in the environment**

環境中に存在する多種多様な化学物質の曝露をより確実に測るための数理モデルの改良

- **Establishment of procedures to monitor chemical concentrations in the long term to validate the predictability of the models and procedures to compensate the lack of data**

モデルの予測能力を検証するための長期間に亘る濃度モニタリング手法及び欠損データの補完方法の確立