

The 1<sup>st</sup> Online Forum to AVC member countries (ASEAN)

“Moving Forward to the Sustainability  
of PVC Additives System”

*4<sup>st</sup> August 2021, WEB*

**“Trend of Plasticizer towards the  
Sustainability”**

**Phthalates and non-Phthalates**

**~ Safety and in Natural Environment ~**



**可塑剤工業会**

Japan Plasticizer Industry Association

<http://www.kasozai.gr.jp/>

**Dr. Hiromi YANASE**

# Synopsis

JPIA, organized by plasticizer manufactures in JAPAN for the sound development of plasticizer industry **based on science** and promotion of global friendship for more than 60 years.

On the one hand, Phthalates are even now occupies about 65% share of consumption and used as major general plasticizers in global. On the other hand, Phthalates are exposed to scientifically unfair (political) restriction for their use in regulation in EU.

DEHP (DOP) is focused and shown scientifically low toxicity for human beings by species difference between rodents and primates. In the profile of metabolism, DEHP is metabolized in a body and much metabolites are glucuronized to be out of body and mostly not stay in body for primates.

And, JPIA gives a second topic of the fate of Phthalates in natural environment. Degradations of Phthalates in nature occur in different fashions. Such examples are demonstrated for Phthalates to be degradable and not persistent in Nature, indicating data by JPIA Env, Monitoring.

Finally, JPIA answers the question, What is essential for “Sustainability” for plasticizers, for PVC?



可塑剂工业会  
Japan Plasticizer Industry Association

**1957**  
Founded

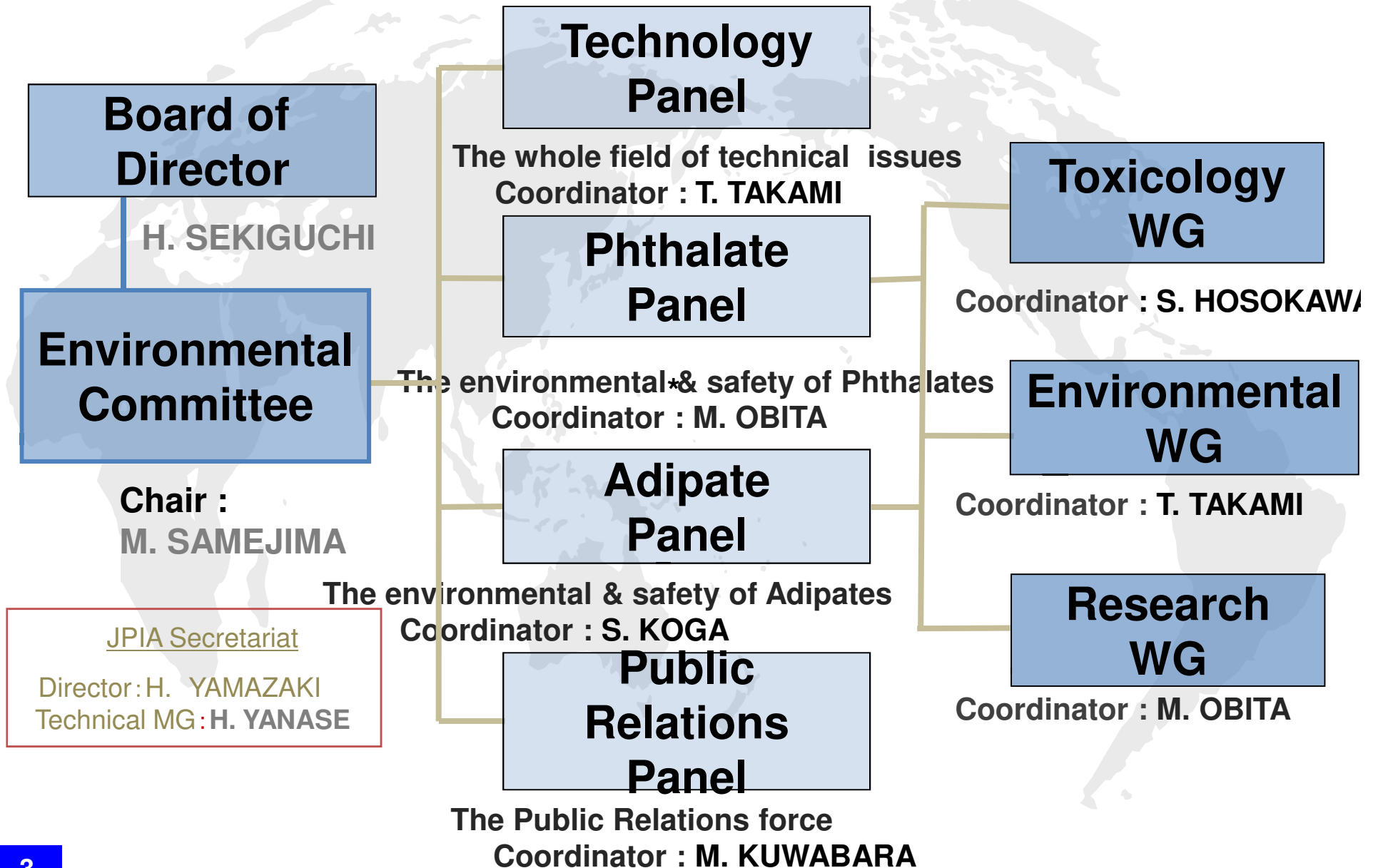
**TOKYO**  
(東京)

**8**  
members

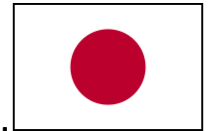
**Plasticizer Industry,**  
**Sound Growth with Science**  
Focused

- CG ESTER Corporation (2000~)
- DIC Corporation
- KUROGANE KASEI CO.,LTD
- SHOWA ETHER CO.,LTD.
- DAIHACHI Chemical Industry CO.,LTD.
- J-PLUS CO.,LTD. (2000~)
- NEW JAPAN CHEMICAL CO.,LTD.
- TAOKA CHEMICAL CO.,LTD.

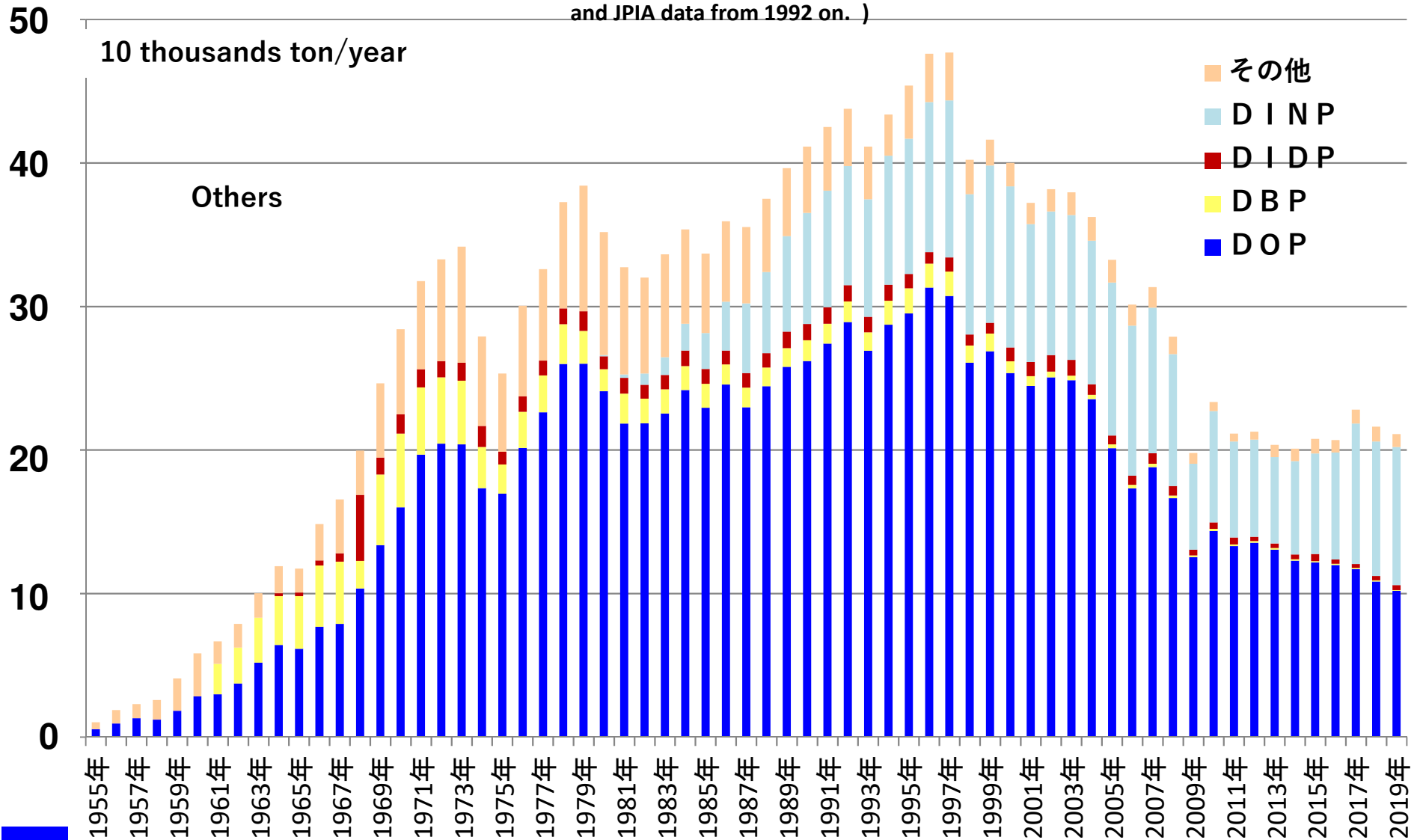
# JPIA Organization 2021



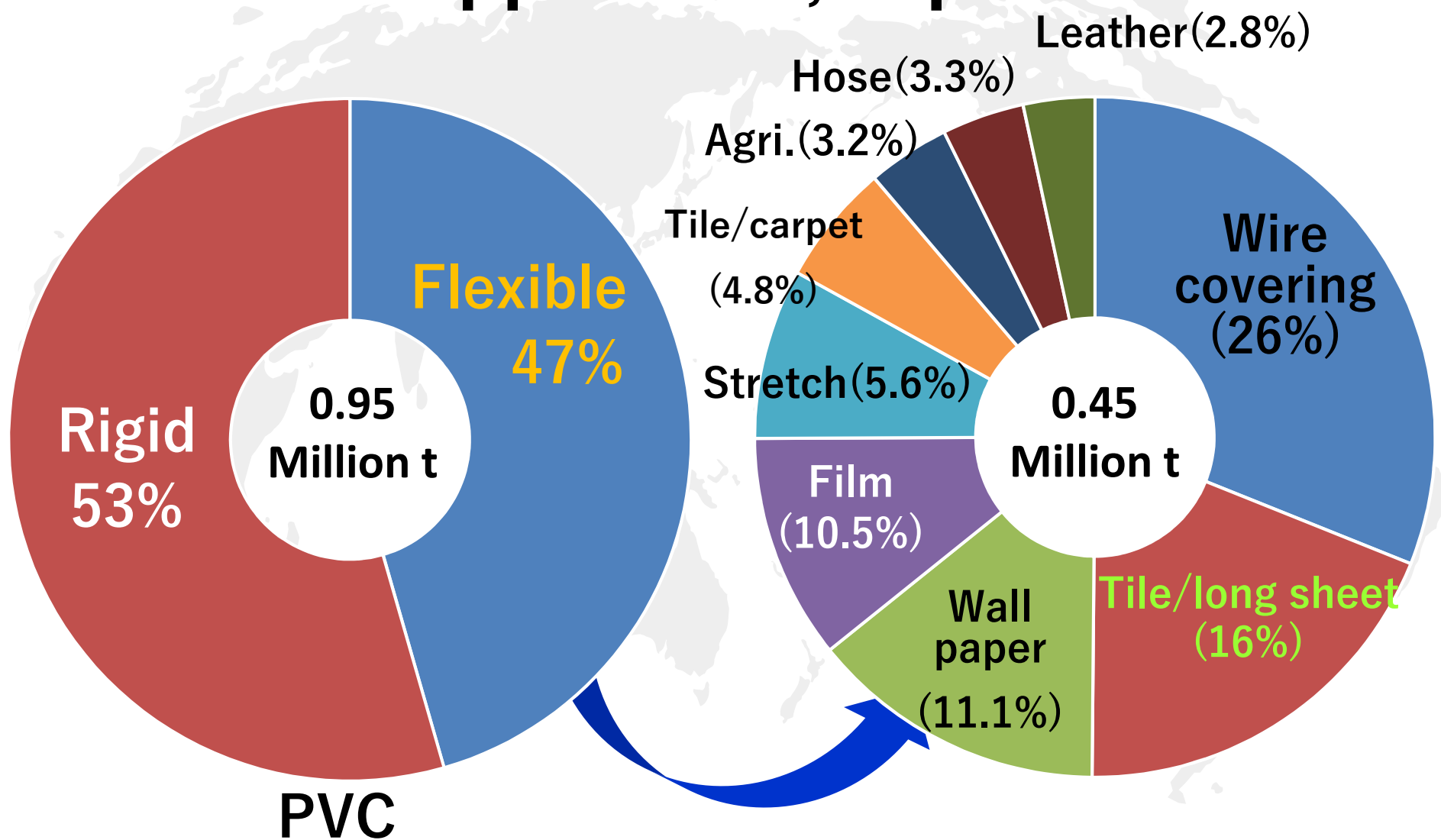
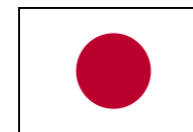
# Progress of Annual Production Amount of Phthalates in Japan



(DEHP and Others from 1955 to 1991 from Annual statistics report of chemical industry (Ministry of Economy, Trade and Industry Japan), and JPIA data from 1992 on. )



# Flexible PVC Market 2020 by Application, Japan

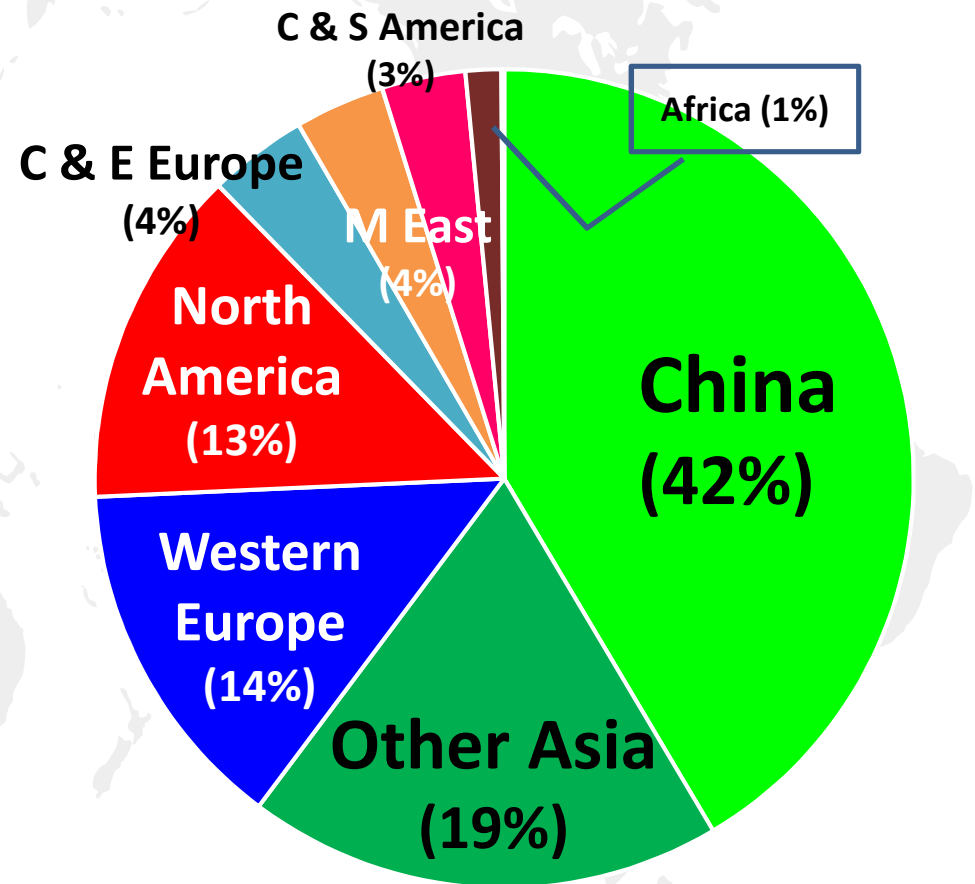
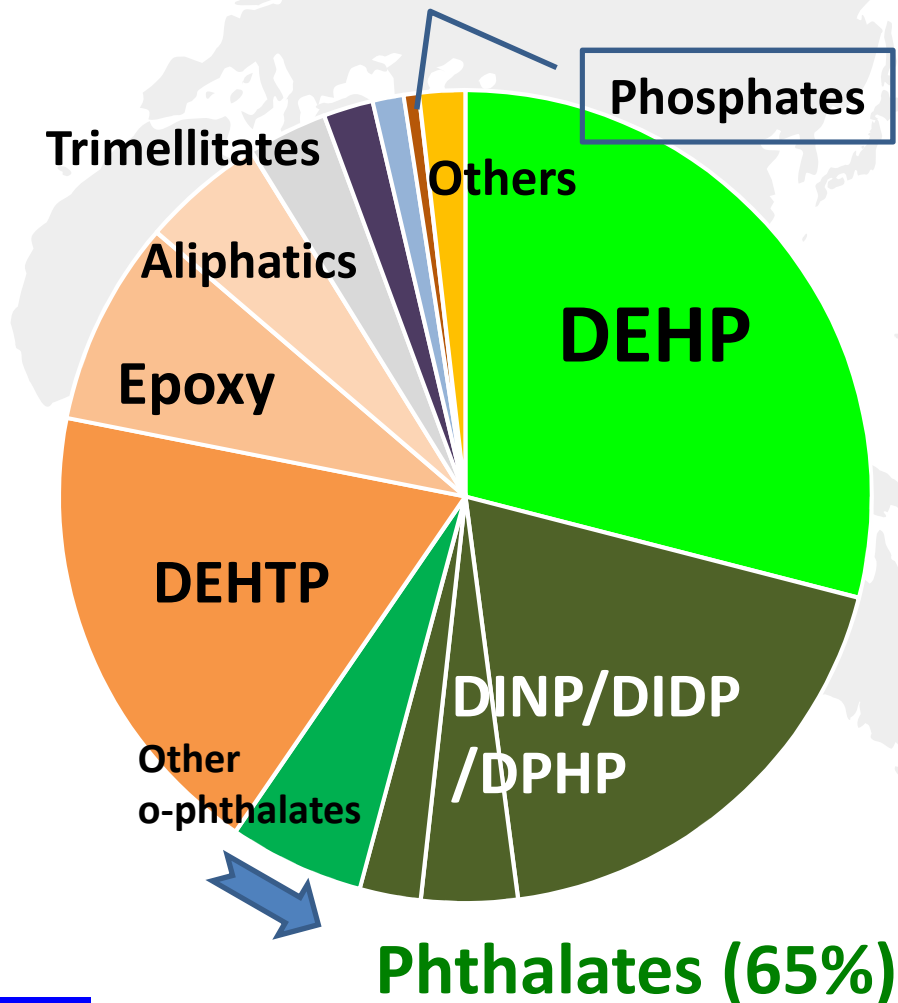


# World consumption of plasticizers 2017




(7.53 mil. t/y)

## by chemical structure

## by region



# Toy Regulation in Japan, EU, and USA 2021

R.		DEHP · DNBP · BBP	DINP · DIDP · DNOP
	Notification 336 of the Ministry of Health, Labor, and Welfare. (2002, 2010)	<ul style="list-style-type: none"> <li>· toys and wrapping, containers contact with oils and fats or foods including oils and fats</li> <li>· toys for below 6 years old</li> <li>· below 0.1% (DBP, BBP from 2010)</li> </ul>	<ul style="list-style-type: none"> <li>· toys essentially for mouthing</li> <li>· for below 6 years old</li> <li>· below 0.1% (DIDP, DNOP from 2010)</li> </ul>
	REACH, Restriction Entry 51(2005, 2018), 52(2005)	<b>DEHP · DNBP · BBP · DIBP</b> <ul style="list-style-type: none"> <li>· toys, child care products and consumer products</li> <li>· below 0.1% (Entry 51 (2020))</li> </ul>	<b>DINP · DIDP · DNOP</b> <ul style="list-style-type: none"> <li>· toys essentially for mouthing</li> <li>· for below 3 years old</li> <li>· below 0.1% (Entry 52 (2005))</li> </ul>
	CPSC Improvement Act (2008, 2017)	<b>DEHP · DNBP · BBP · DIBP · DINP · DPENP · DHEXP · DCHP</b> <b>Children's toys</b> <ul style="list-style-type: none"> <li>· for below 12 years old</li> <li>· below 0.1%</li> </ul>	<b>Child care articles</b> <ul style="list-style-type: none"> <li>· for below 3 years old</li> <li>· below 0.1%</li> </ul>

\*wrapping, containers contact with oils and fats or foods including oils and fats more than 20%, except for dried and solid foods

\*CPSCIA=Consumer Product Safety Commission Improvement Act





# Chemicals Strategy for “Sustainability” (CSS)

REACH shall be amended after more than about 10 years implementation and reflection for sustainability in near future by EU Commission, taking into consideration, Risk evaluation, Regulatory Science, **Science**, . . . .



The "EU chemicals strategy for sustainability" questions regulatory toxicology as we know it: is it all rooted in **sound scientific evidence**? *Archives of Toxicology*, 22 June 2021, 95(7):2589-2601

Says “**facts and evidence**”  
rather than “anxieties or beliefs”.



**JPIA Scientific Approach  
to Toxicology  
and Environment**

**One of **Facts** and **Evidence****

# Scientific Evidences on species difference between rodents and primates



DEHP  
(DOP)

(CAS Number  
117-81-7)

## (1) Marmoset (Primate, Cebidae) studies for reproductive toxicity

- 1) Kurata Y, Kidachi F, Yokoyama M, Toyota N, Tsuchitani M, Kato M., *Toxicological Sciences*, 42, 49-56, 1998. **Adults (成獣)**
- 2) Tomonari Y, Kurata Y, David R M, Gans G, Kawasuso T, Kato M., *Journal of Toxicology and Environmental Health A.*, 69(17), 1651-1672, 2006. **Juvenile (幼若獣)**
- 3) Kurata Y, Makinodan F, Shimamura N, and Kato M., *The Journal of Toxicological Sciences*, 37, 33-49, 2012. **Fetus (胎児)**

## (2) Bio-monitoring study for the profiles of metabolism

- 4) Kurata Y, Kato M. et al., *The Journal of Toxicological Sciences*, 37, 401-414, 2012.

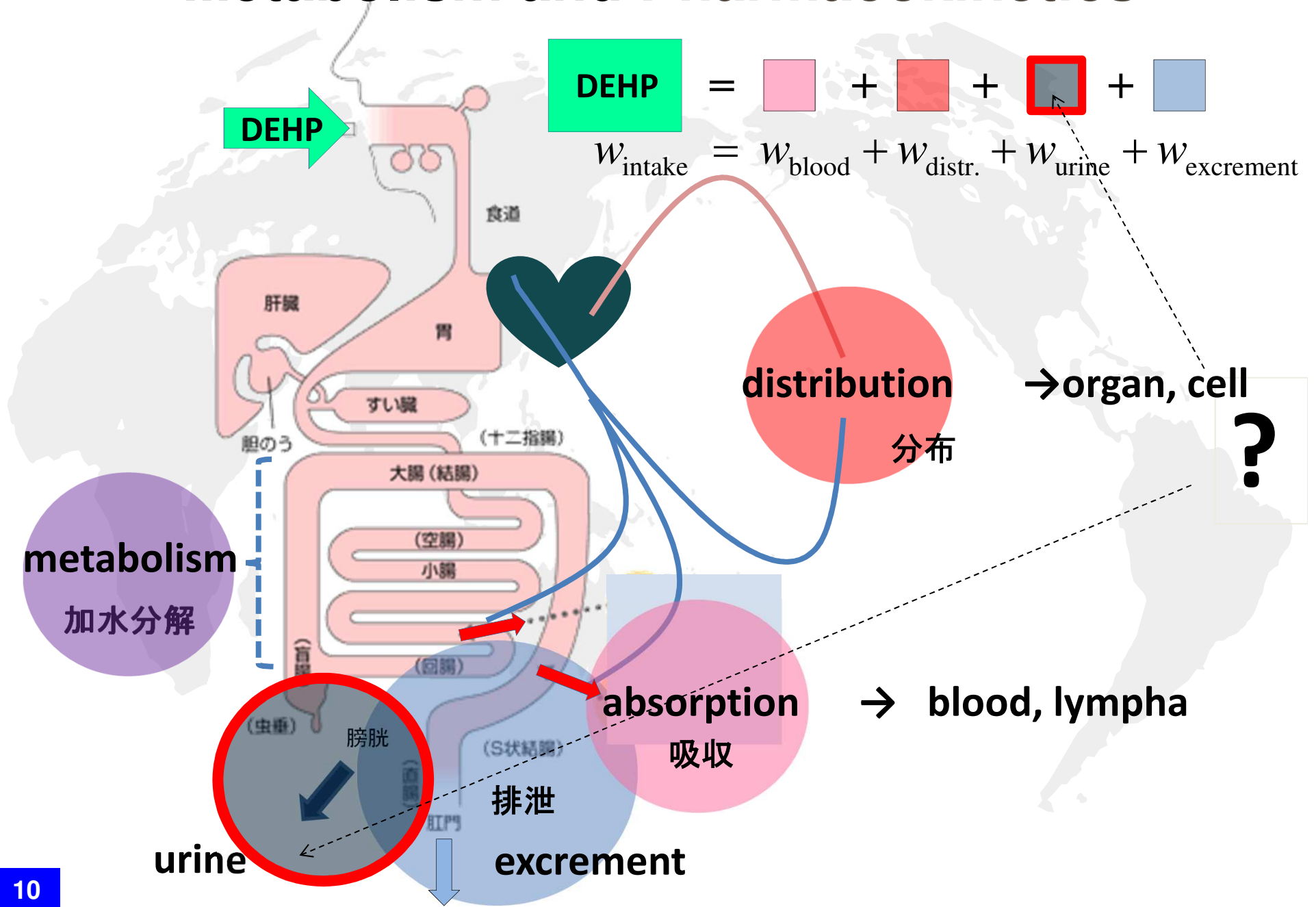


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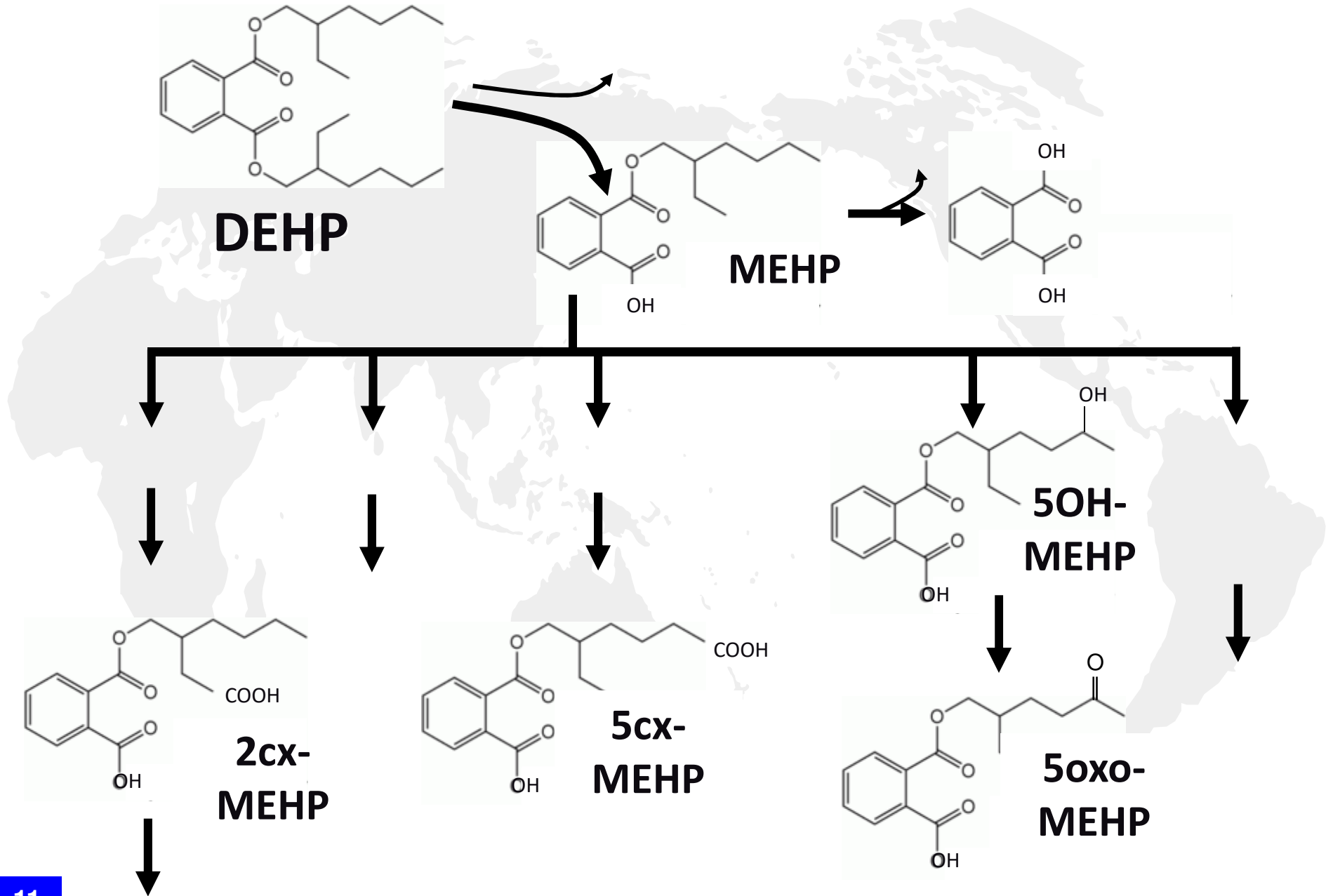


Safer side

# Metabolism and Pharmacokinetics

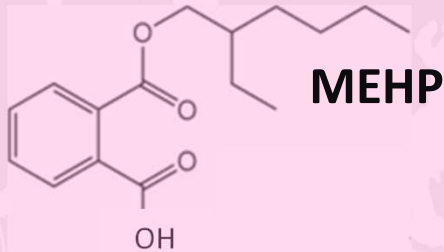


# Outline of DEHP Metabolism



# Two Types of Fast Order Metabolite, MEHP

F-type

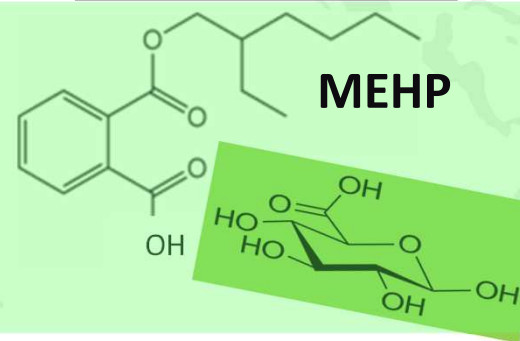


hydrophobic

Apt to stay in  
body

+ glucuronic acid

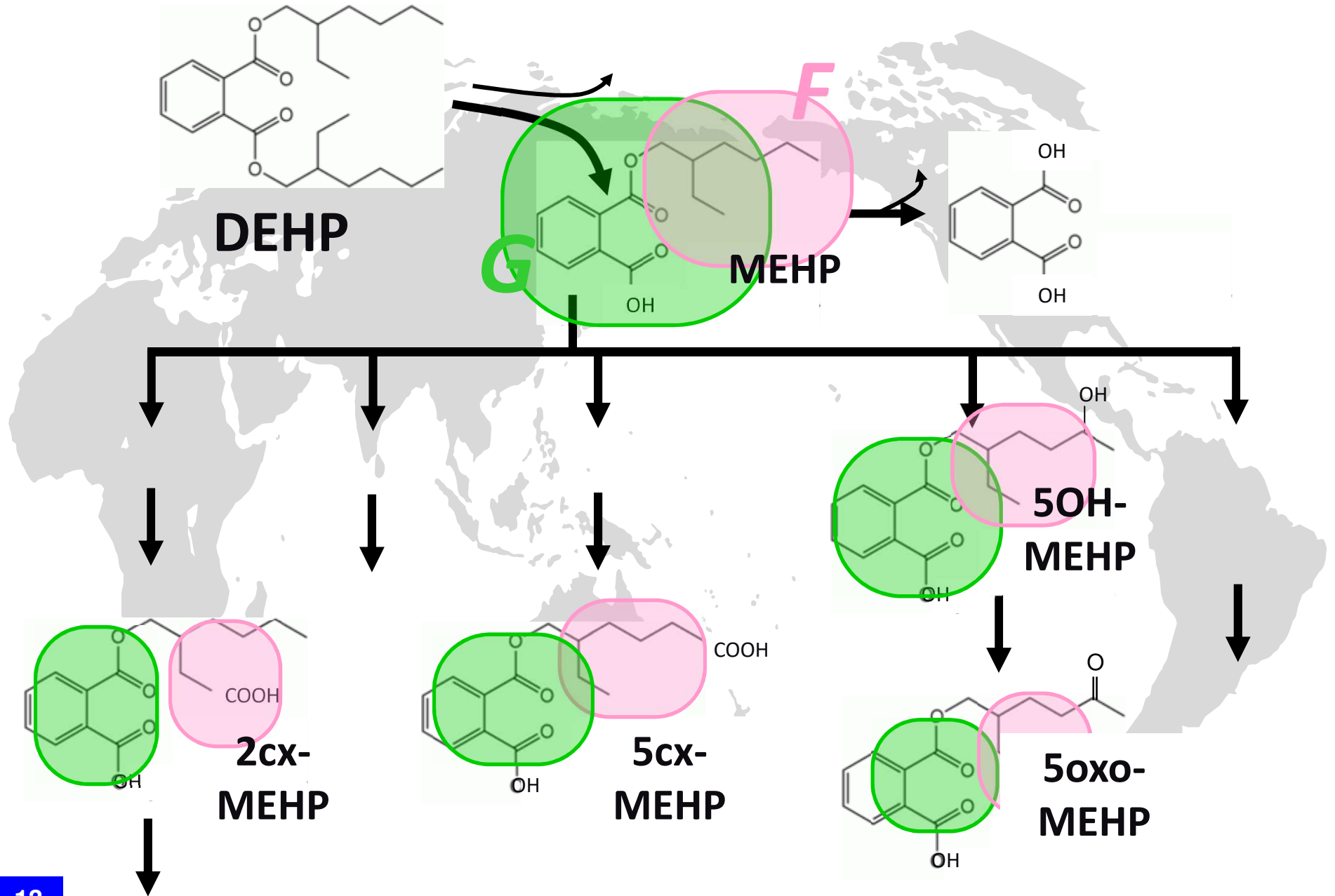
G-Type



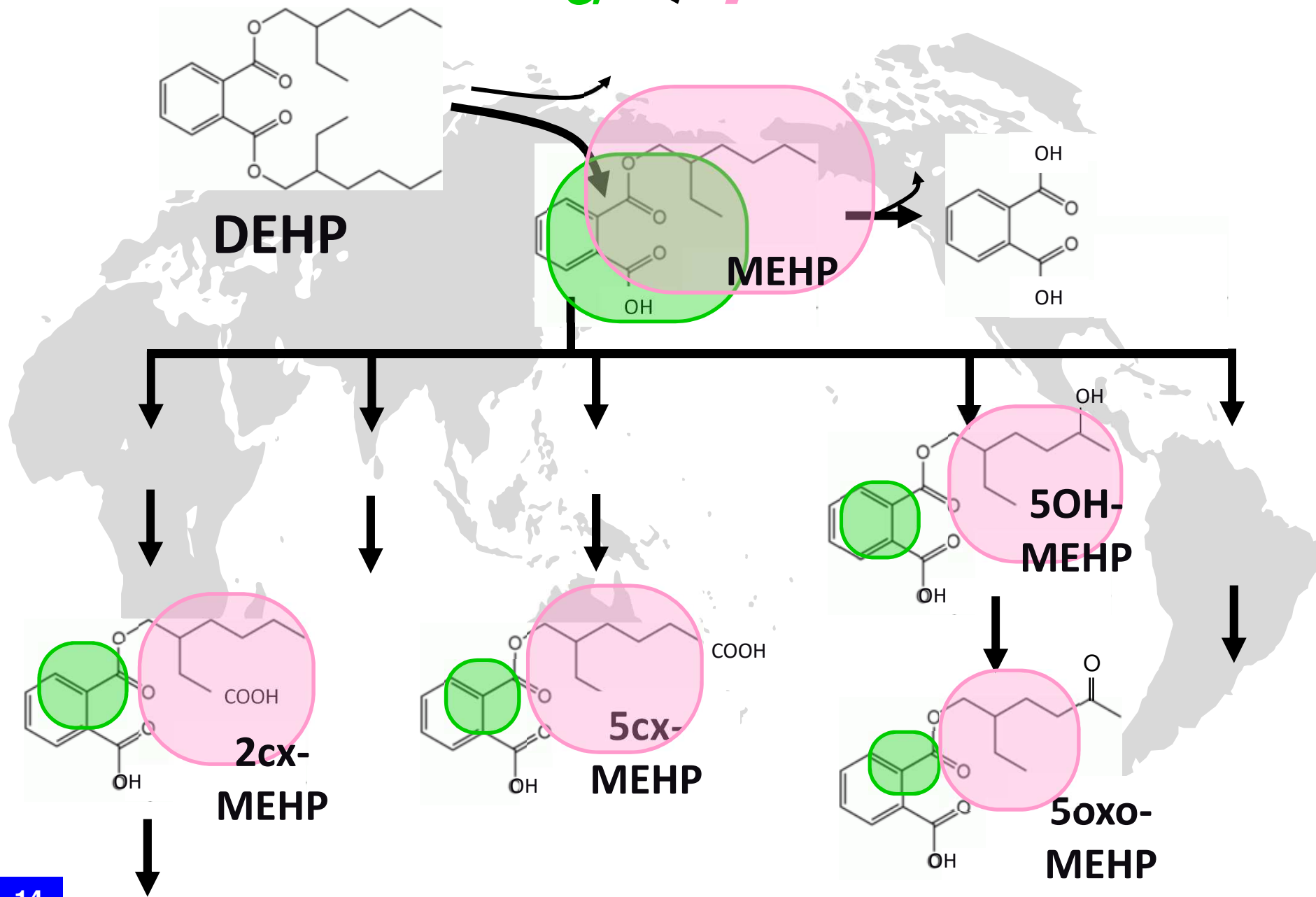
hydrophilic

Easily excreted  
into urine  
(out of body)

# Metabolites *G* & *F* of DEHP

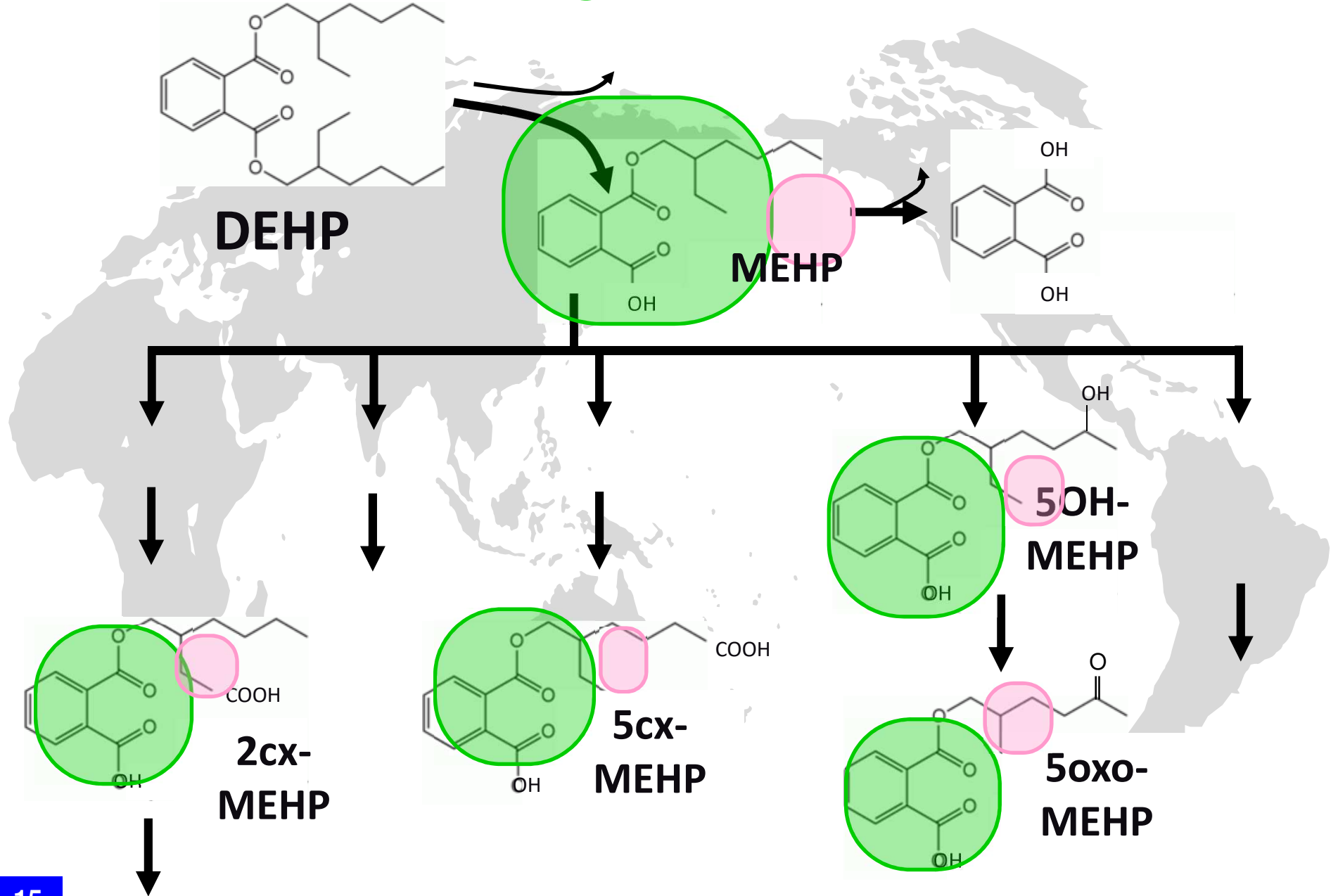


$G < F$



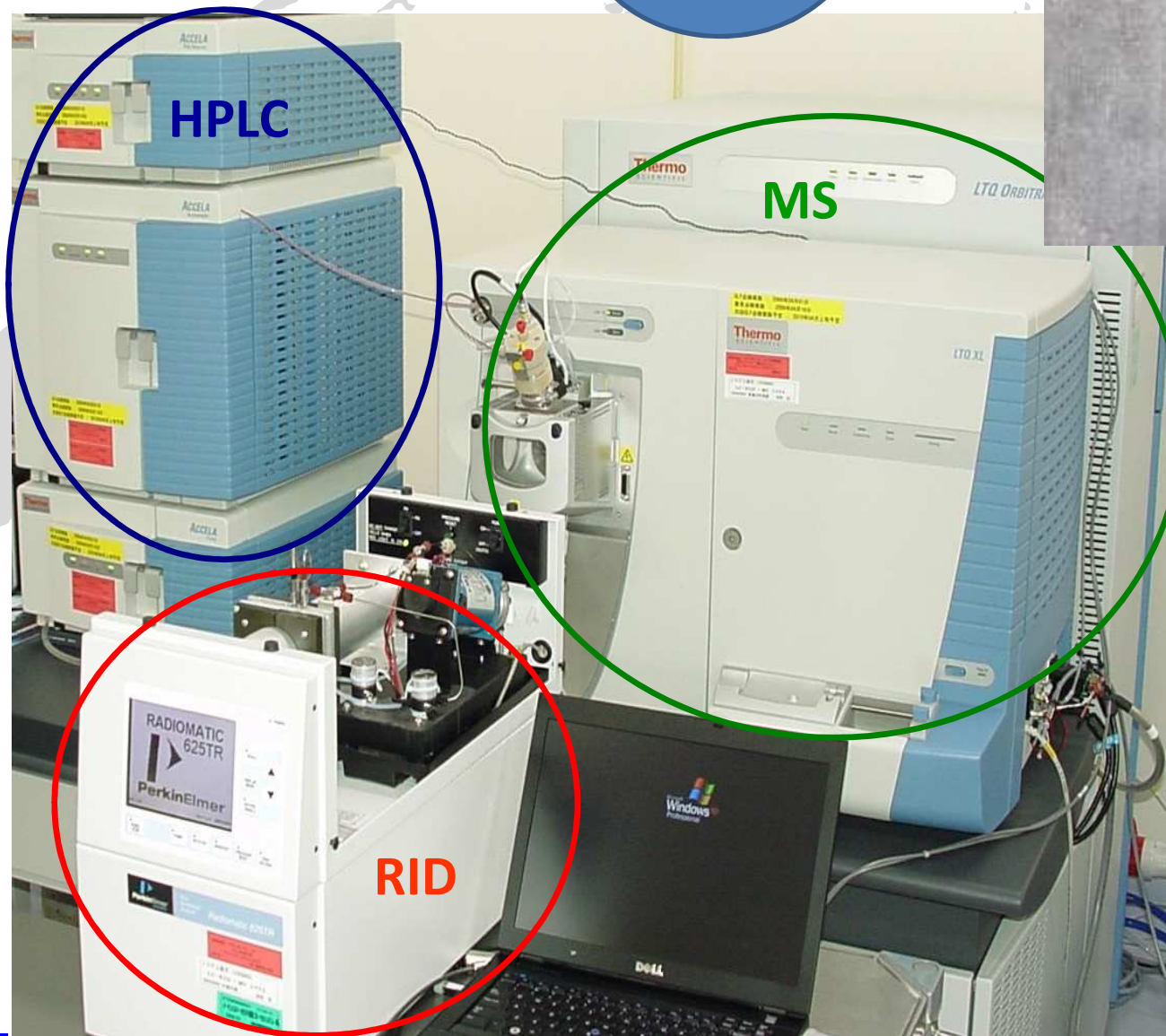


$G > F$



**Oral administration:** d4-DEHP of 3mg/person for each 10 males and females with bread as breakfast.

d4-  
DEHP



**Samples:** urine samples every 4 hours after intake to 36 hours.

**Analytical Method:** *Direct evaluation* of glucuronides and free types of DEHP metabolites by ESI-Negative mass chromatogram

# LC-RID/MS system

Pump

Automatic  
Sample Injector

Column

UV detector

HPLC

MS

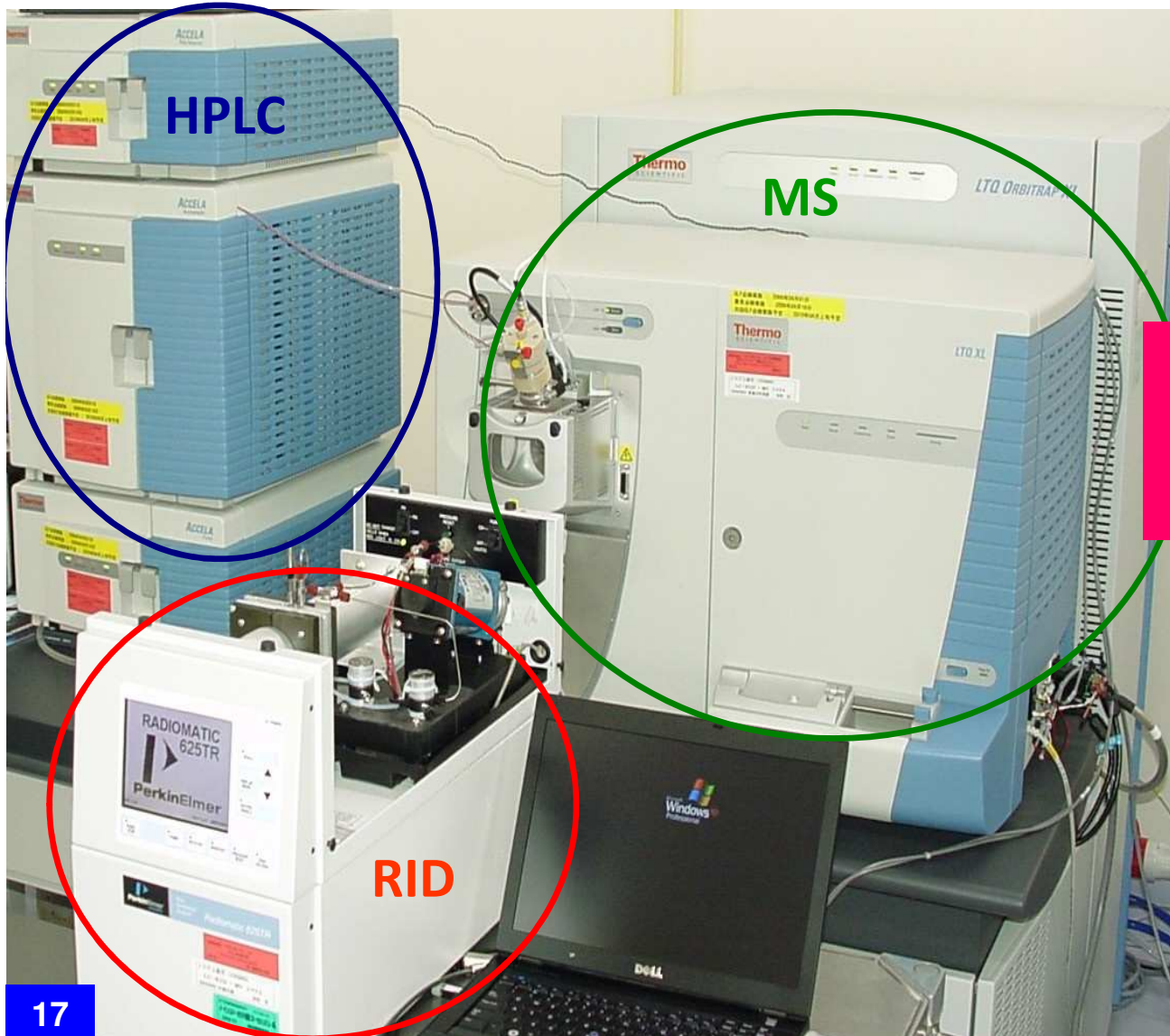
splitter

Radio  
detector

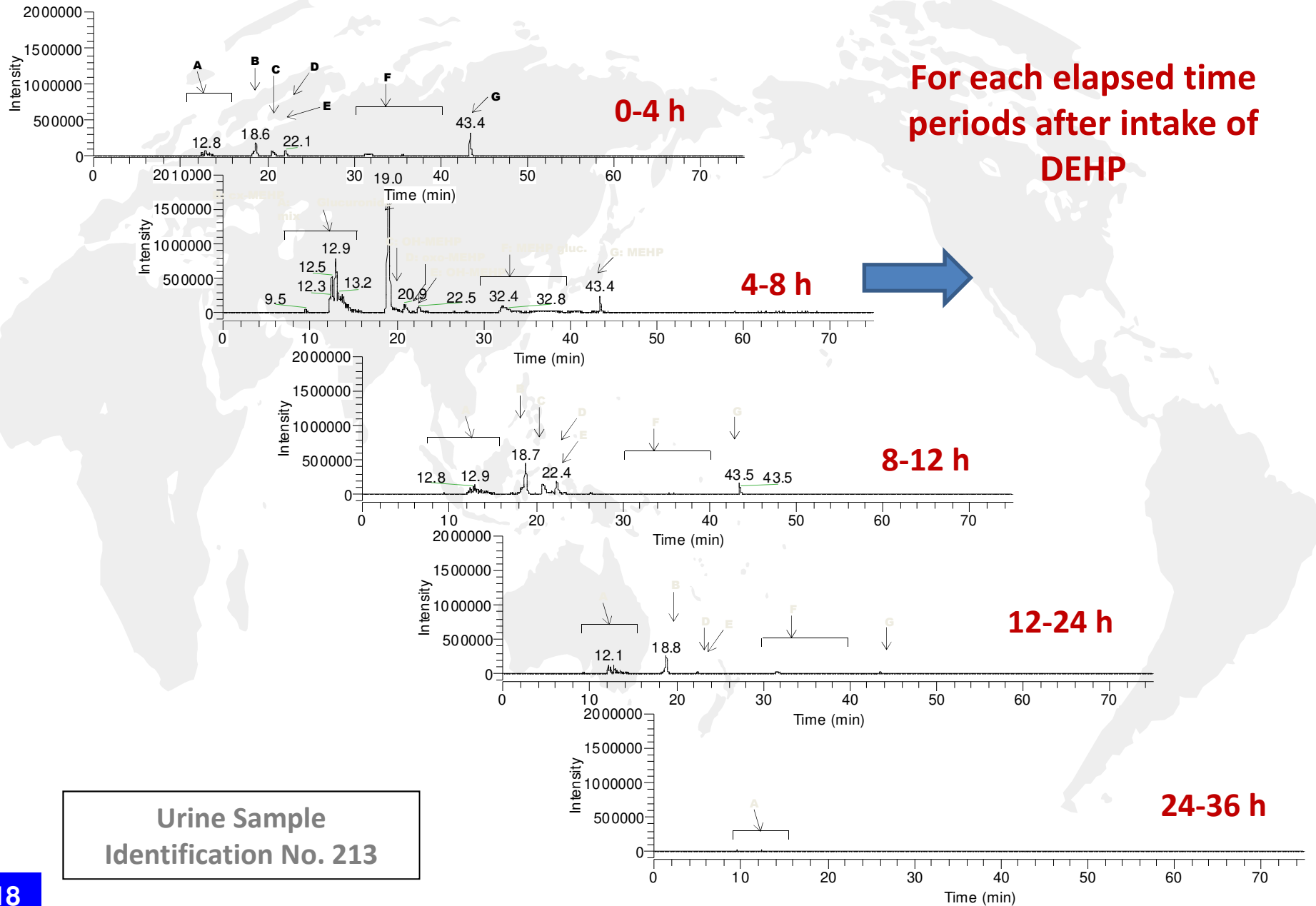
MS/MS<sup>2</sup>  
Spectro  
meter

RID

**Qualitative and  
quantitative data  
can be acquired  
in one injection .**

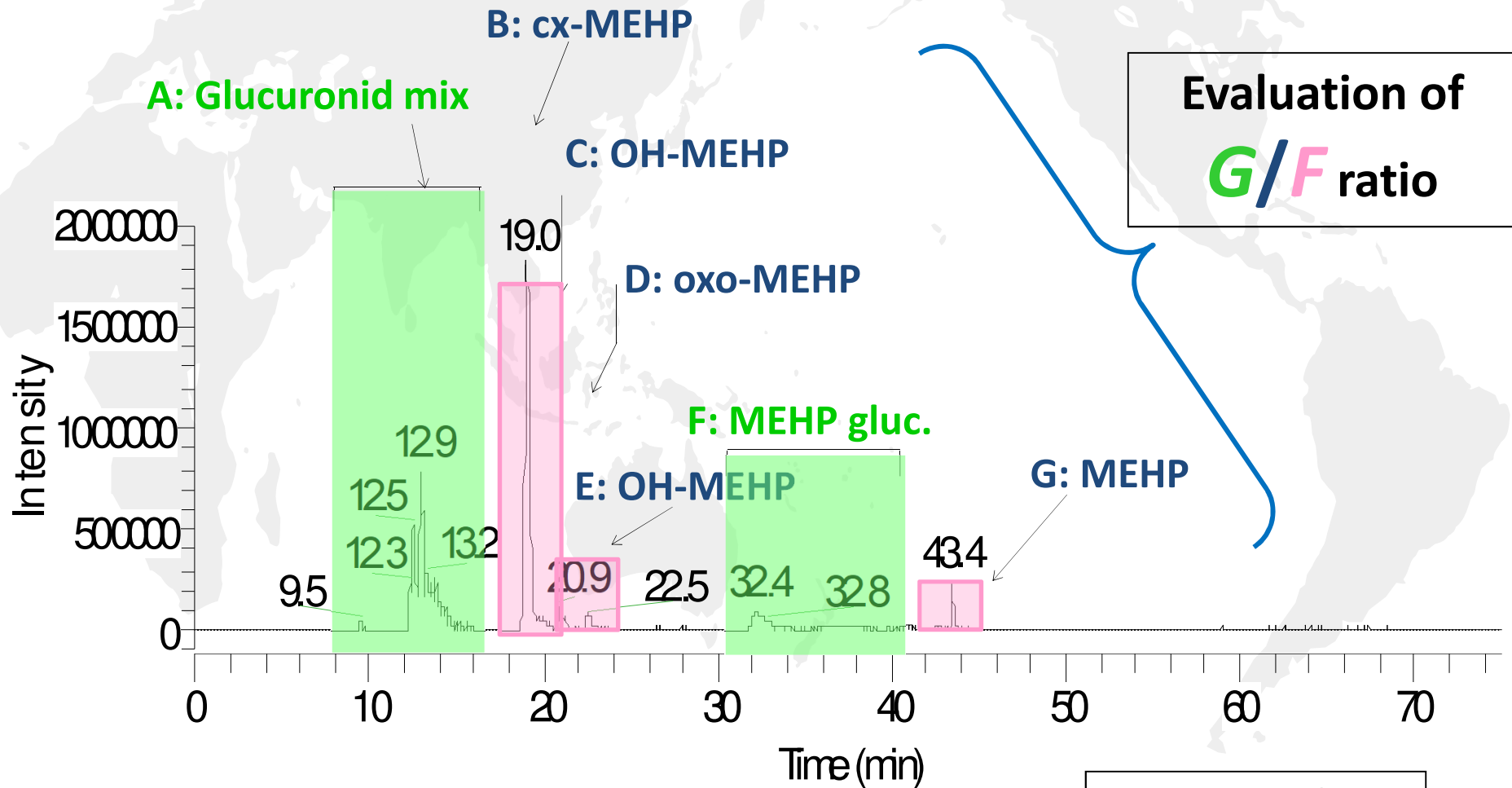


# Profiles of ESI-Negative mass chromatogram



# One Example of ESI-Negative mass chromatogram

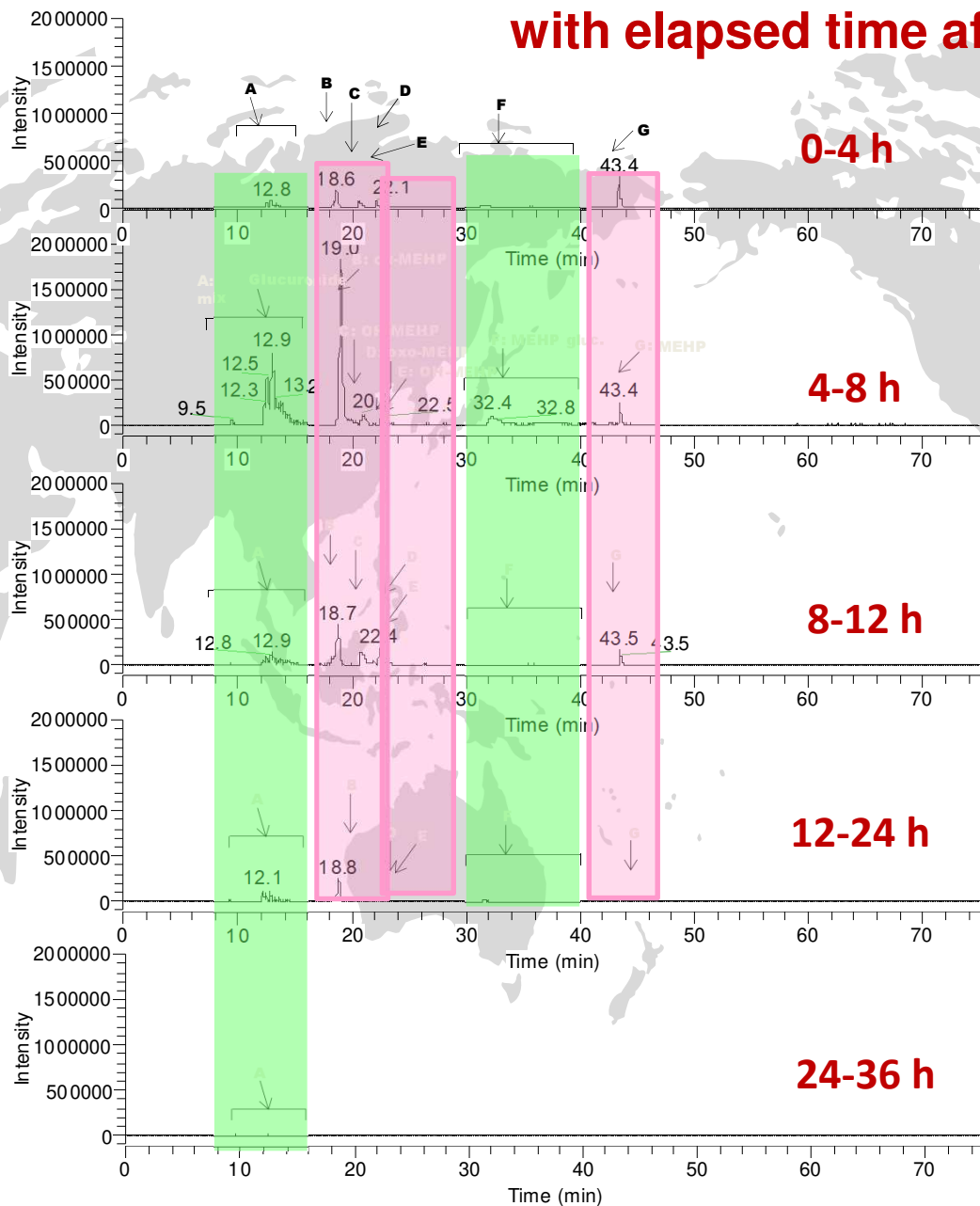
during 4-8h after intake of DEHP



Urine Sample  
Identification No. 213

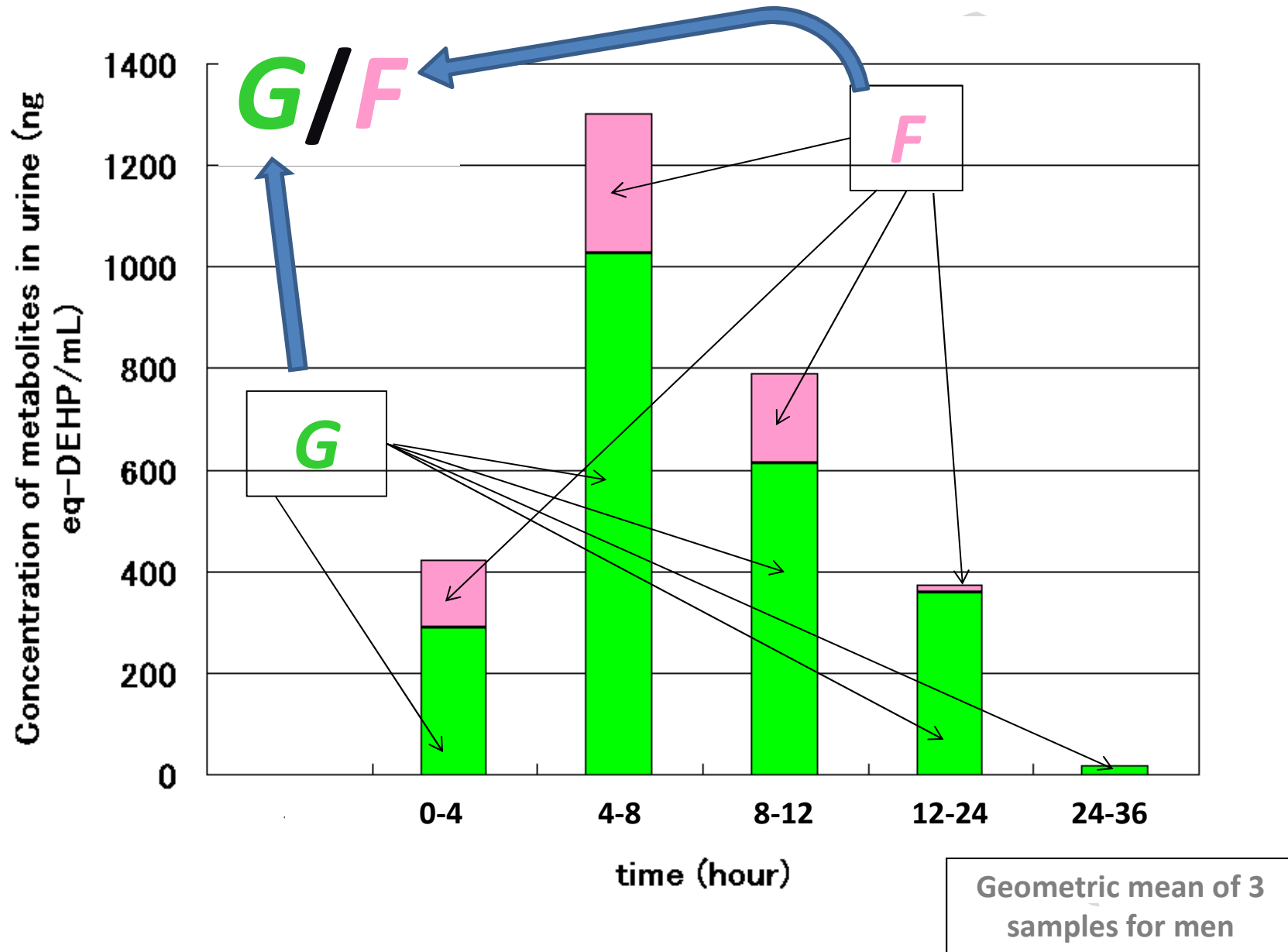
# Identification for **G** & **F**

with elapsed time after intake of DEHP



Urine Sample  
Identification No.  
213

# The time dependence of *G* and *F* metabolites concentration



# Species Difference in Profiles in Metabolism

Species	G / F	To rat
Rat	<b>0.13</b> (Apt to stay in blood)	<b>1</b>
Marmoset	<b>7.12</b>	<b>54.9</b>
Human (male)	<b>3.47</b>	<b>26.7</b>
Human (female)	<b>5.33</b>	<b>41.0</b>

(Easy excretion into urine)



## Experimental Animals



## Human Beings



≠



# Degradation of Phthalates in Environment

Photolysis, Hydrolysis

<

<

**Biodegradation**

# Biodegradation Rates of Phthalates

## Half-life periods

(Under Aerobic circumstance)

2~3 days for DBP, BBP

A few weeks~months for DEHP, DINP

Table 3 Biodegradation half-life of the PAEs in aquatic systems (d)

Condition	DBP	BBP	DEHP	DINP	Reference
Aerobic	0.5–10.1	0.5–10.5	7.3–27.5		Yuan <i>et al.</i> , 2002 <sup>a</sup>
	1–3	2–4	2–5		Fujita <i>et al.</i> , 2005 <sup>b</sup>
	2–5	4–11	6–21	7–40	Lertsirisopon <i>et al.</i> , 2003 <sup>c</sup>
Anaerobic	8–14	14–33	> 1300		Painter and Jones, 1990 <sup>d</sup>
	11.7–18.9	9.9–25.5	29.9–39.1		Yuan <i>et al.</i> , 2002 <sup>e</sup>
	2–3	2–3	> 208	> 347	Lertsirisopon <i>et al.</i> , 2006 <sup>f</sup>

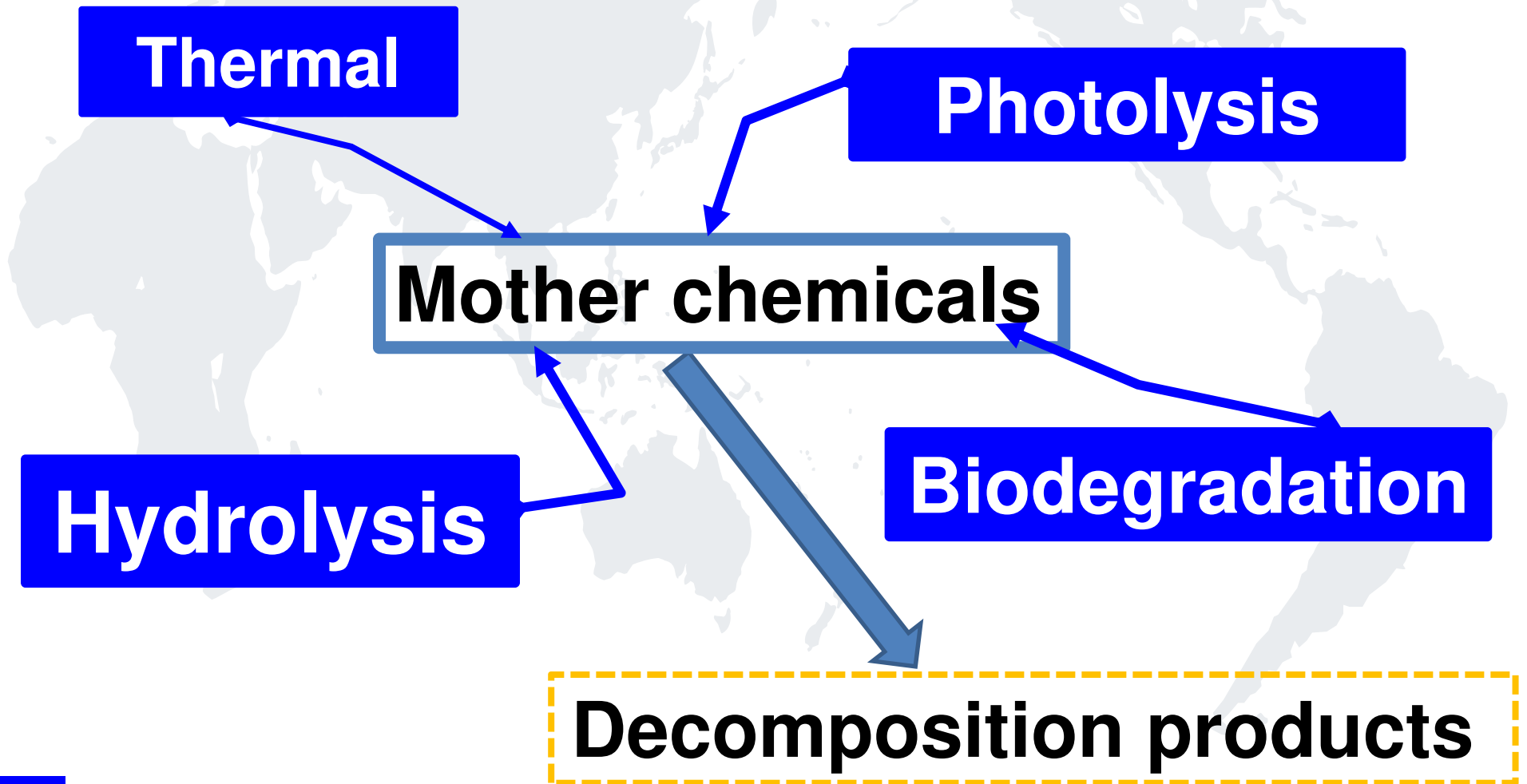
<sup>a</sup> Unacclimated river sediment samples at pH 7.0; <sup>b</sup> unacclimated river, pond, or activated sludge samples at pH 7.2, and 28°C; <sup>c</sup> unacclimated pond water samples at 28°C; <sup>d</sup> unacclimated sludge at 30°C; <sup>e</sup> unacclimated river sediment microcosms at pH 7 and 30°C; <sup>f</sup> natural sediment microcosms at pH 7 and 28°C.

“Abiotic degradation of four phthalic acid esters in aqueous phase under natural sunlight irradiation”

Ruttapol Lertsirisopon, Satoshi Soda, Kazunari Sei, Michihiko Ike *Journal of Environmental Sciences* 21(2009) 285–290.

# Scientific background of the talk

(Factors relating to stability in chemical structure of phthalates)





**JPIA Environmental Monitoring  
and Risk Assessment  
1993~**

## Objective :

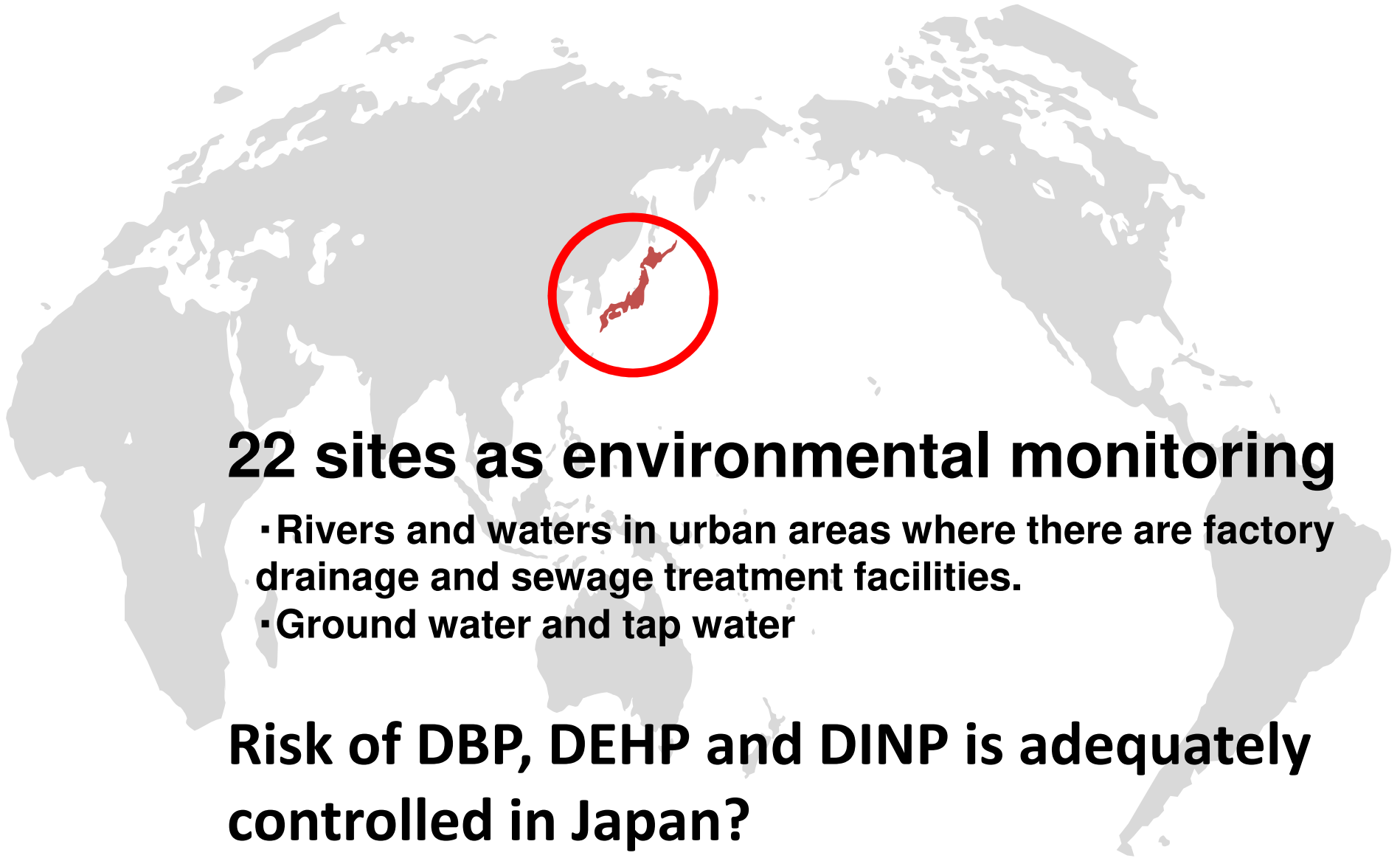
Long term Monitoring of concentration (exposure) of target chemicals in marine and river waters, and river sediments for estimation of ecological risk.

**Target chemicals:**  
DBP, DEHP, DINP

**Analytical method : GC/MS**

Detection limit (A, B(sensitive))

	Water (mg/L)	Sediment (mg/dry-g)
DBP	0.0002	0.01
DEHP	0.0002	0.01
DINP	0.001	0.05



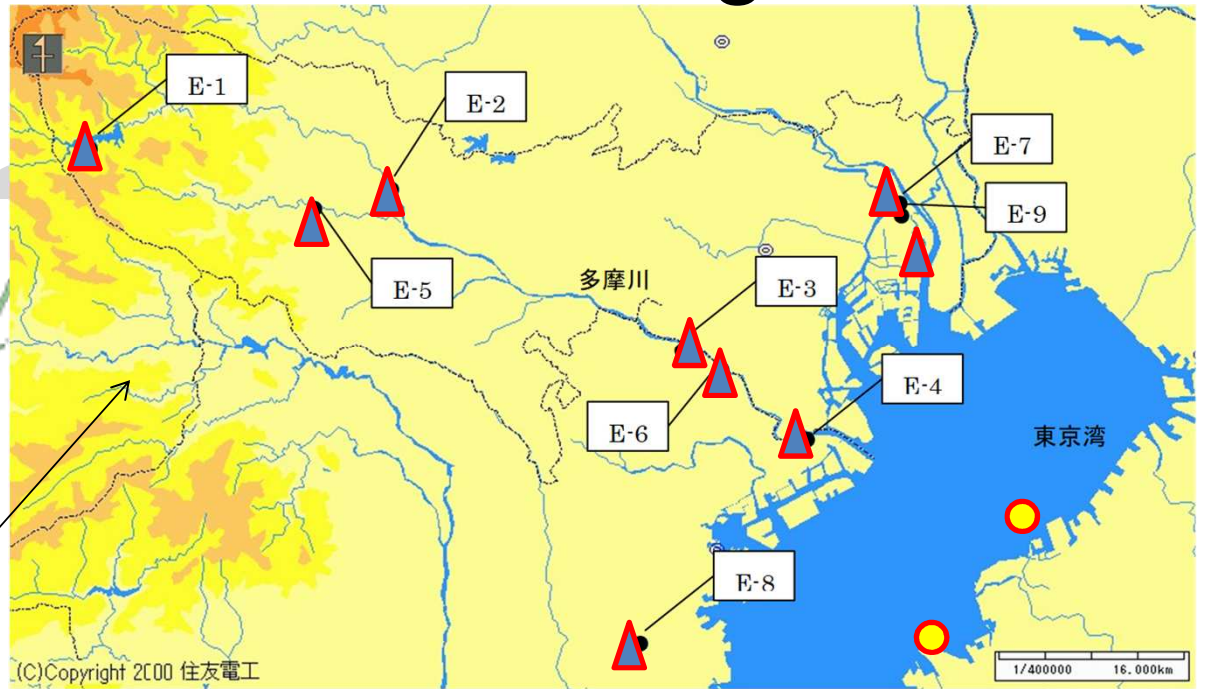
## **22 sites as environmental monitoring**

- Rivers and waters in urban areas where there are factory drainage and sewage treatment facilities.
- Ground water and tap water

**Risk of DBP, DEHP and DINP is adequately controlled in Japan?**

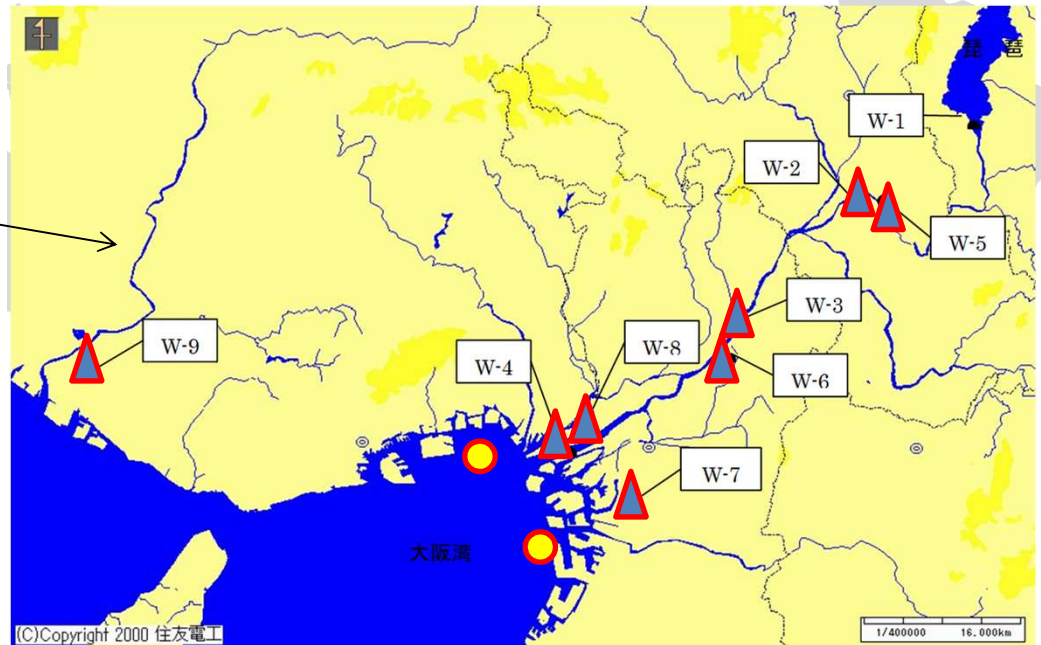
# Environmental Monitoring

Sampling sites :



East

West







**Yokohama Bay**





**Tokyo Bay**



**Rainbow Bridge**

Sites	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
E-1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
E-2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
E-3	HP.9	ND	ND	HP.3	ND	ND	HP.4	ND	ND	ND	ND	ND
E-4	ND	HP.8	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
E-5	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
E-6	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
E-7	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
E-8	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
E-9	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
E-10	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-1	BP.3	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-2	HP.5 DBP.7	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-3	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-4	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-5	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-6	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-7	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-8	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-9	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-10	ND	HP.4	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
W-11	ND	HP.3	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

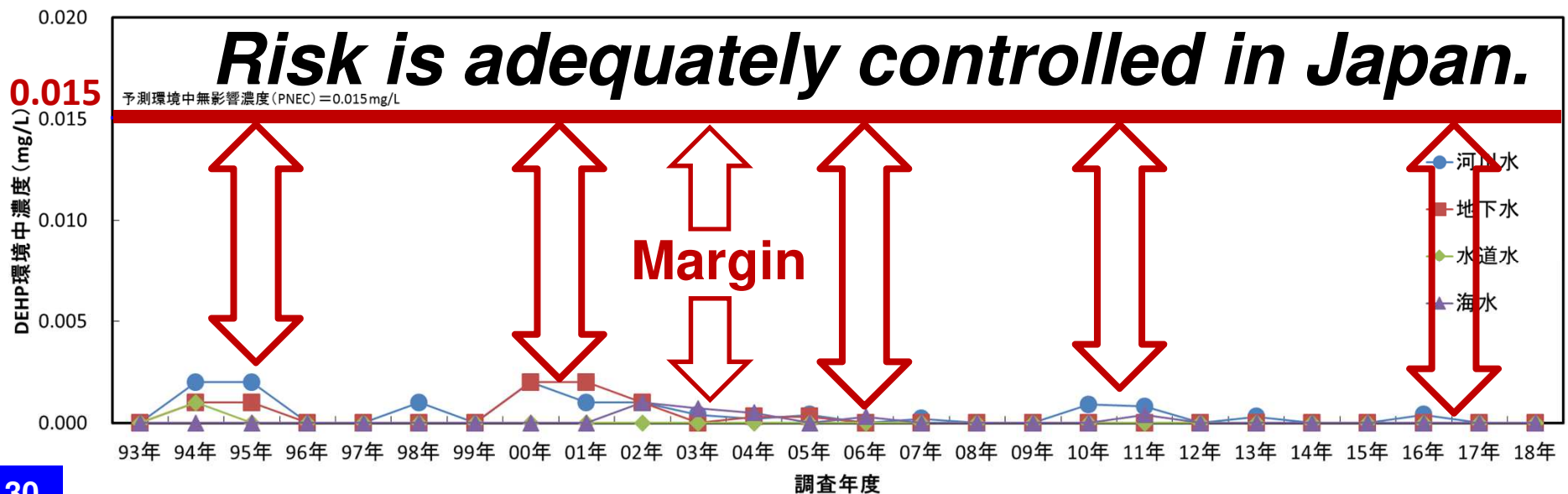
**Concentrations (exposure) level of river, sea, underground water are mostly below Detection Limit of the phthalates in these days**

**Concentration in river water : HP:DEHP, BP:DBP, unit :  $\mu\text{g/L}$**

**Management target value : 80  $\mu\text{g/L}$  for drinking water in Japan**

# Environmental risk assessment based on water monitoring data by JPIA at 1993-2019

Substance	Maximum concentration in the environment (mg/L) = PEC	PNEC (mg/L)	PEC/PNEC	Risk Concern
DEHP	0.002	0.015	0.13 <1	NO
DBP	0.002	0.004	0.5 <1	NO
DINP	<0.005 (Under detection limits)	-	( PEC/PNEC <1 )	NO

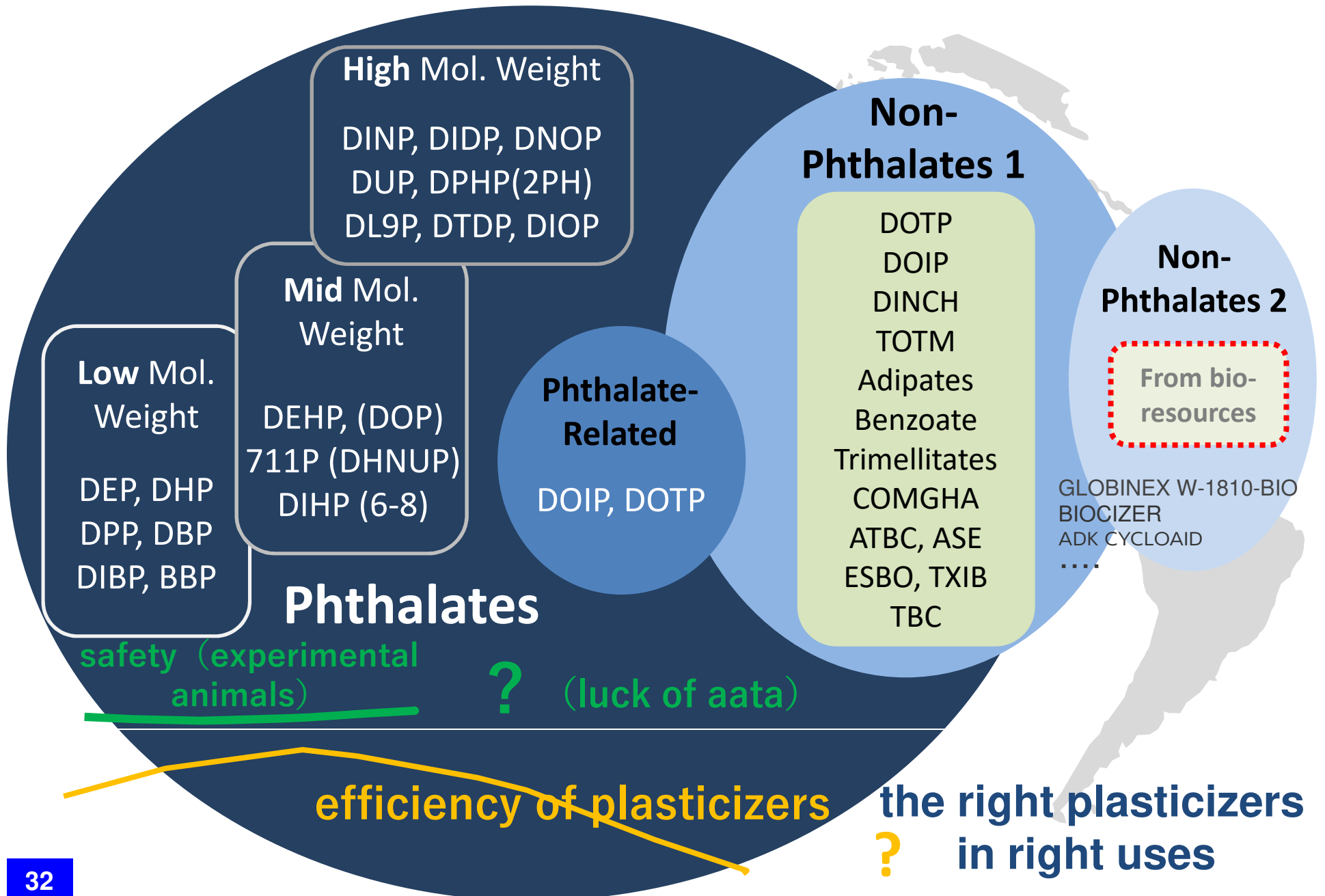




**○ Phthalates are degradable  
and not persistent  
in natural environment.**  
(The level depends on the condition.)

**○ Investigation on the property  
strengthen  
the industrial applicability and life span  
of materials for “Sustainability”.**

# Assortments of Plasticizers





# **Flexible Design for “Sustainability”**

**with coming Innovative Plasticizers**

**Novel sources  
for special uses  
not for general purpose**



# Far Reaching Subjects

## — Source Material Issue —

- **What is Green Plasticizers ?**

《Example》

### **cardanols from cashewnuts**

<http://www.packagingeurope.com/Packaging-Europe-News/64226/Placard-Biobased-Plasticizer-Tests-Show-Good-Results-.html>

- **The PLACARD project**



- This project is co-funded by the European Union within the **CIP Eco-Innovation** initiative of the Competitiveness and Innovation Framework Programme, **CIP**.

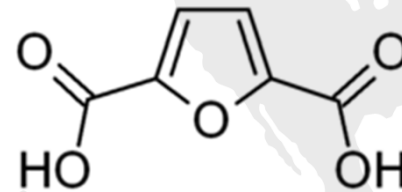
<http://www.placard-ecoinnovation.eu/>

# Far Reaching Subjects

– Source Material Issue –

- **BASF and Avantium intend to establish Joint Venture**

15 Mar 2016 | [2016, Press releases](#)



**Production and marketing of furandicarboxylic acid (FDCA) based on renewable resources, the main new building block for polyethylenefuranoate (PEF)**

**Further development and licensing of Avantium's production processes for FDCA and PEF at industrial scale**

**Intention to build a reference plant for FDCA with an annual capacity of up to 50,000 tons at BASF's Verbund site in Antwerp, Belgium.**

<https://www.avantium.com/press-releases/2016/basf-avantium-intend-establish-joint-venture/>

# Flexible Design for “Sustainability” through upper to down Stream

cooperatively, ideally

- Efficient mixing with polymer in processing  
with **less energy**
- Extraordinary plasticizer efficiency, flexible  
with much **small quantity**
- After complete mixing with polymer  
**without migration for maintaining Property**
- Reusable circularly as flexible polymers  
**without contamination for Recycable**



可塑剂工业会  
Japan Plasticizer Industry Association

**Visiting older, learn newer.**



**Thank you for your attention**

<http://www.kasozai.gr.jp/>

**Q** (ばく露量)

**TDI**

(日々許容摂取量)

$< 1 <$

**Q**  
**TDI**

**Risk 大**

**Risk 小**

[mg/体重/日]

# ■ ヒト化PBPKモデルによるHBMデータ (DEHP) からの暴露レベル $Q_{HPBPK}$ の推算

30  
(Hazard)

0.087 (GM) 1.3 (95<sup>th</sup>)  
0.059、0.456  
( $Q_{HPBPK}$ )

リスクは  
小さい。

Silva, M.J., Barr, D.B., Reidy, J.A., Malek, N.A., Hodge, C.C., Caudill, S.P., Brock, J.W., Needham, L.L., Calafat, A.M., 2004. Urinary levels of seven phthalate metabolites in the **U.S. population** from the **National Health and Nutrition Examination Survey (NHANES) 1999–2010**. *Environ. Health Perspect.* 112, 331–338.  
3.4、49.8  $\mu\text{g}/\text{L}$

日本における化学物質暴露量(環境省2015)  
2.29  $\mu\text{g}/\text{L}$  → 0.059  $\mu\text{g}/\text{kg}/\text{day}$  (GM),  
17.82  $\mu\text{g}/\text{L}$  → 0.456  $\mu\text{g}/\text{kg}/\text{day}$  (max)  
2011–2014

Koichiro Adachi, Hiroshi Suemizu, Norie Murayama, Makiko Shimizu, Hiroshi Yamazaki, \**Environmental Toxicology and Pharmacology*, 39, 1067–1073, 2015.