Effect of occupationally phthalate exposure on pulmonary functions in Slovakian plastic industry

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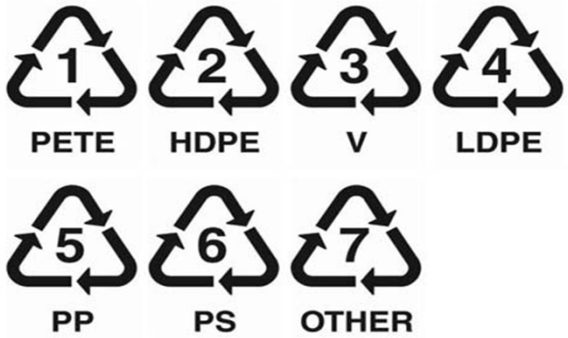
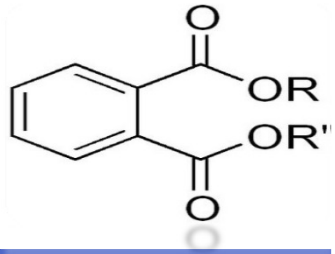
INTRODUCTION

Plastic material

- cheaper, lighter, stronger, flexible, more durable and versatile products
- 0.5 million tonnes (1950) x 360 million tonnes (2009)
- Additives
  - Phthalates
  - Bisphenol A
  - Polbrominated diphenyl ethers



Phthalates

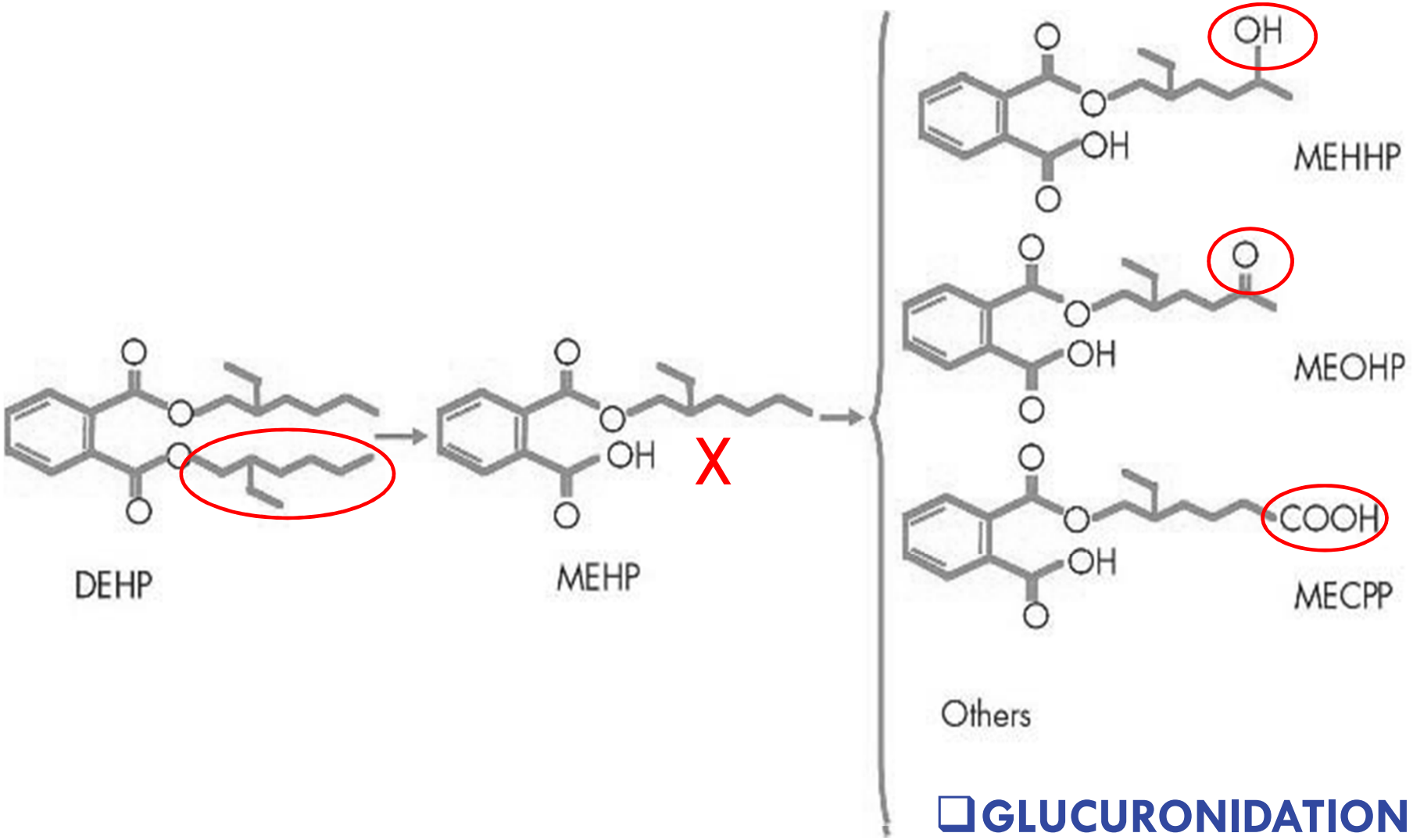


- esters of 1,2-benzene dicarboxylic acid
- Application
  - Polymeric => plasticizers
  - Non-polymeric => fixatives, detergents, lubricating oils, and solvents
- Not bounded on polymeric chains

Health outcomes

- **Endocrine disruptors**
  - Developmental anomalies (cryptorchydism, premature telarche)
  - Reproductives system (antiandrogenic effect, semen quality)
- **Respiratory system**
  - Rhinitis, wheezing, higher risk of asthma, obstructive disorders of airways

Metabolism



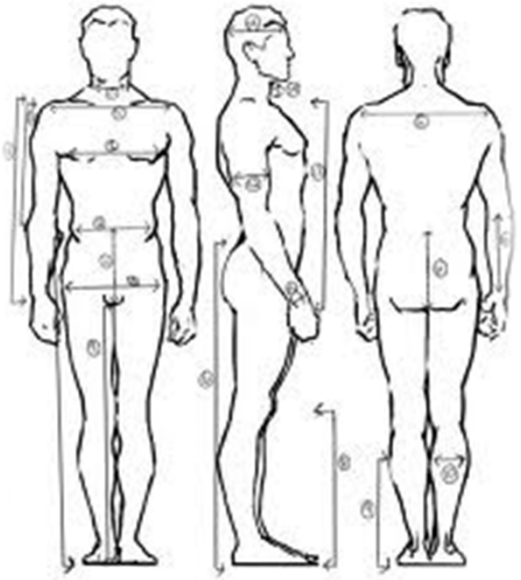
❑ **GLUCURONIDATION**

MATERIAL AND METHODS

- Plastic factory workers (n=15) control (n=25)
- Anthropometry
- Spirometry
- Urine analysis
  - Sample preparation
  - HPLC-MS/MS

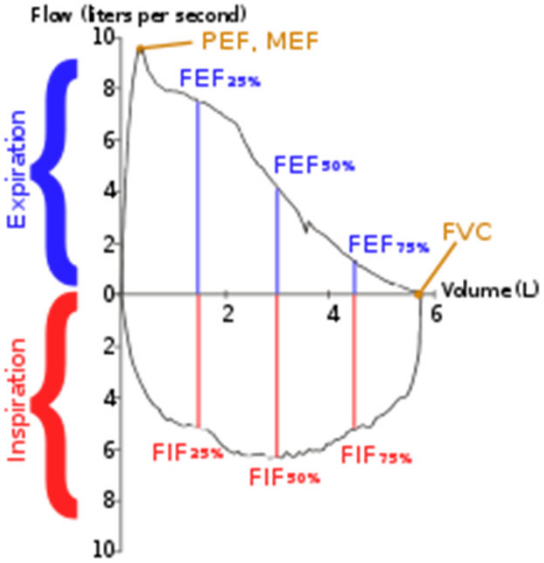
Anthropometry

- Body height
- Body weight
- Body-mass index



Spirometry

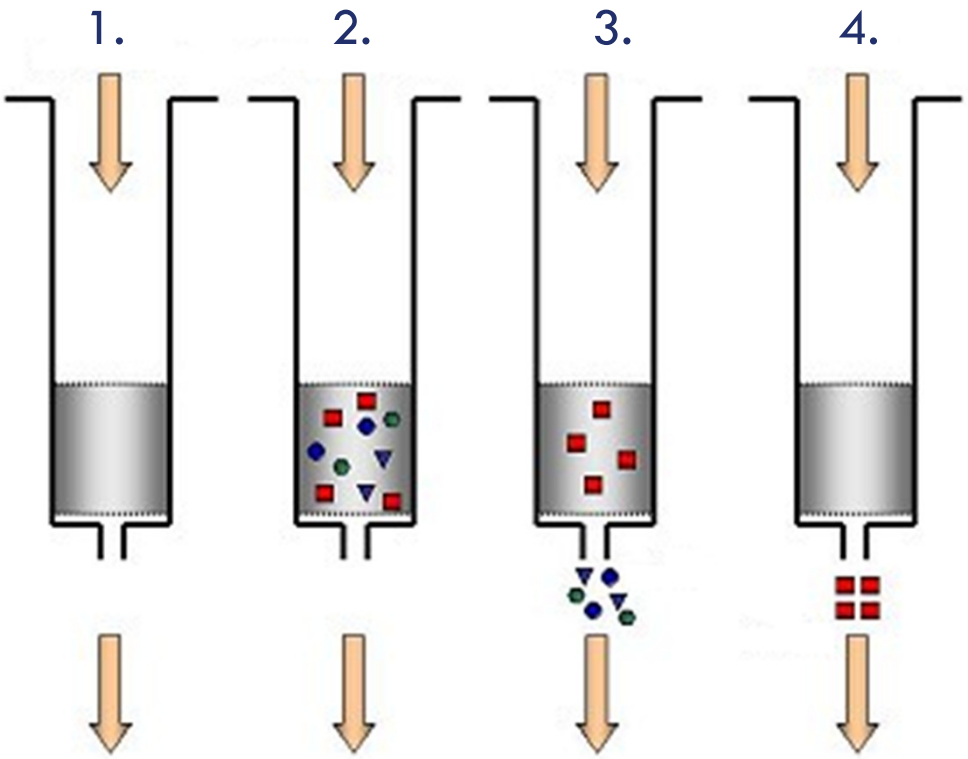
- Spirolab II
- WinSpiro PRO 4.1
- FVC, FEV_1, FEV_1/FVC, VC, MEF_{25-75}



Sample preparation

- Deglucuronidation (β-glucuronidase; E.Coli, K12)
- Solid phase extraction (ABS Elut Nexus, Agilent)

1. Conditioning (ACN/phosphate buffer)
2. Sample adition
3. Rinsing (formic acid, water)
4. Elution (ACN/EtoAc)



- Evaporation and reconstitution

HPLC-MS/MS

- High performance liquid chromatography (HPLC)
  - ZORBAX Eclipse plus phenyl-hexyl

Time, min	0	4	6	8
A%	80	50	40	10
B%	20	50	60	90

Flow rate (0.3 $ml.min^{-1}$)
mobile phase A (0.1% acetic acid in HPLC grade water)
mobile phase B (0.1% acetic acid in acetonitrile)

HPLC-MS/MS

- Tandem mass spectrometry

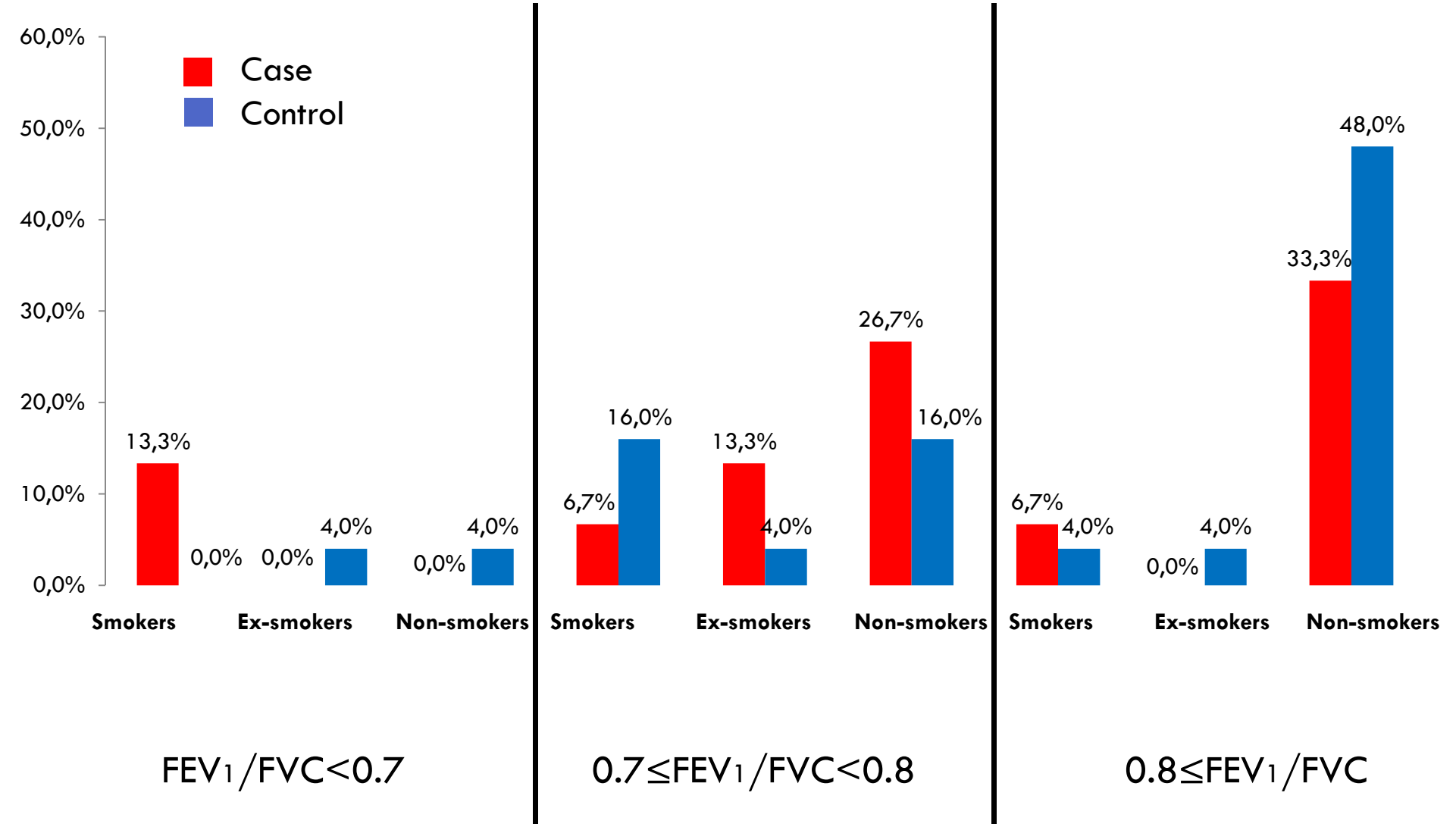
Compound Name	Precursor Ion	Product Ion	Fragmentor (V)	Collision Energy (V)	RT, min
MiNP	291,2	141,2	95	13	13,1
MEHP-C4	281,1	137,1	90	14	12,7
MEHP	277,1	133,9	90	14	12,7
MnOP	277,1	127,2	90	10	12,9
MBP-C4	225,1	78,8	90	10	8,7
MBP	221,1	76,9	90	10	8,7

Results

Baseline characteristics of study participants

	case		control	
	♂ n=3	♀ n=12	♂ n=5	♀ n=20
Age	51.67±10.12	43.04±11.36	43.00±21.43	39.1±14.09
BMI	26.27±1.36	27.44±6.27	26.33±4.27	24.13±4.06
FVC	4.02±0.34	3.17±0.4	4.92± 0.78	3.53±0.52
FEV1	3.66±0.10	2.85±0.45	4.16 ±1.09	2.89±0.58
FEV1/FVC	78.7±3.62	78.17±7.72	79.9± 9.23	81.51±7.62
MEF 25-75	3.33±0.43	2.87±0.97	4.03± 1.86	3.65±0.49
VC	3.52±0.5	3.7±0.59	5.03±0.98	3.45±0.45
p/y	1.67±2.89	2.42±4.98	9.09±21.27	5.65±24.79

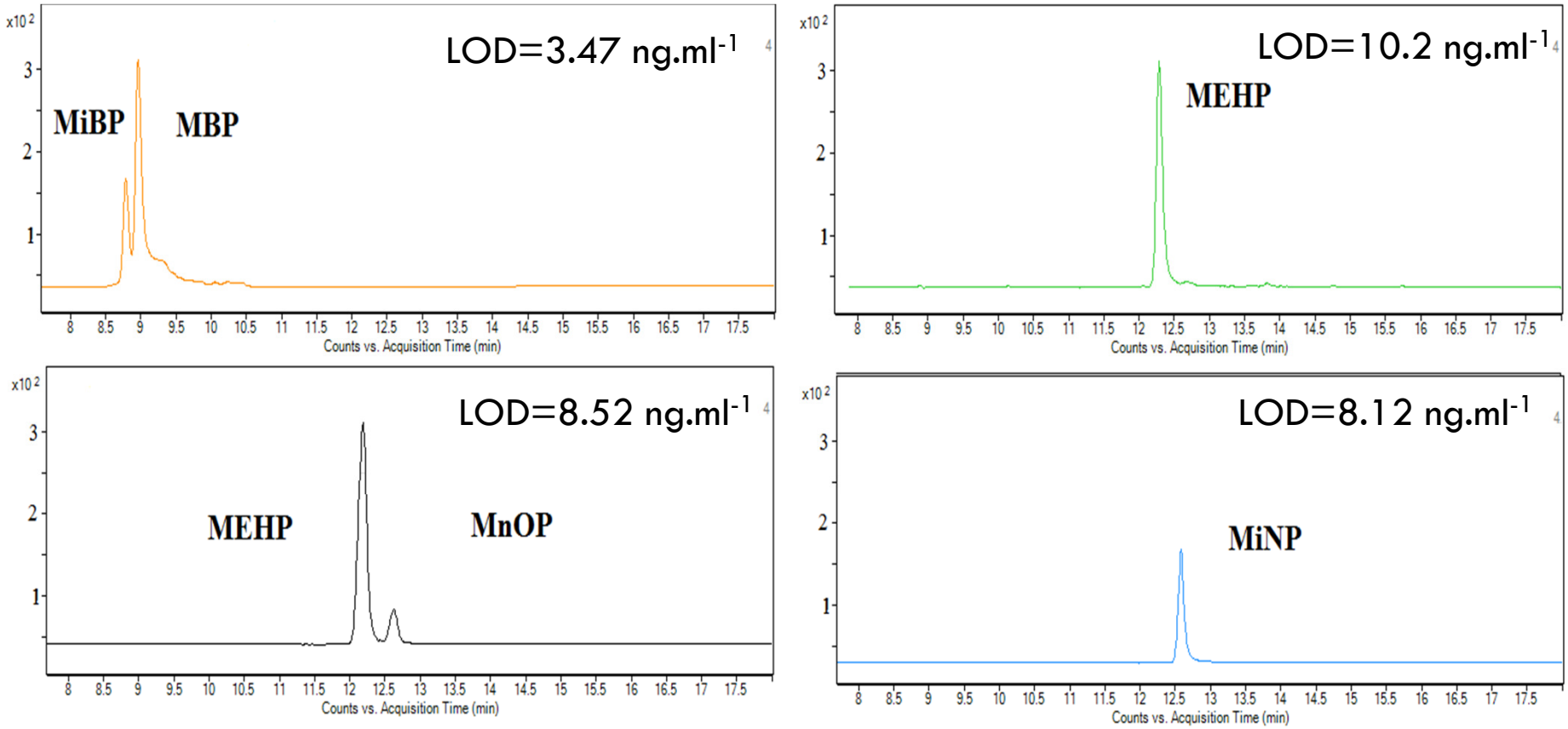
Effect of smoking



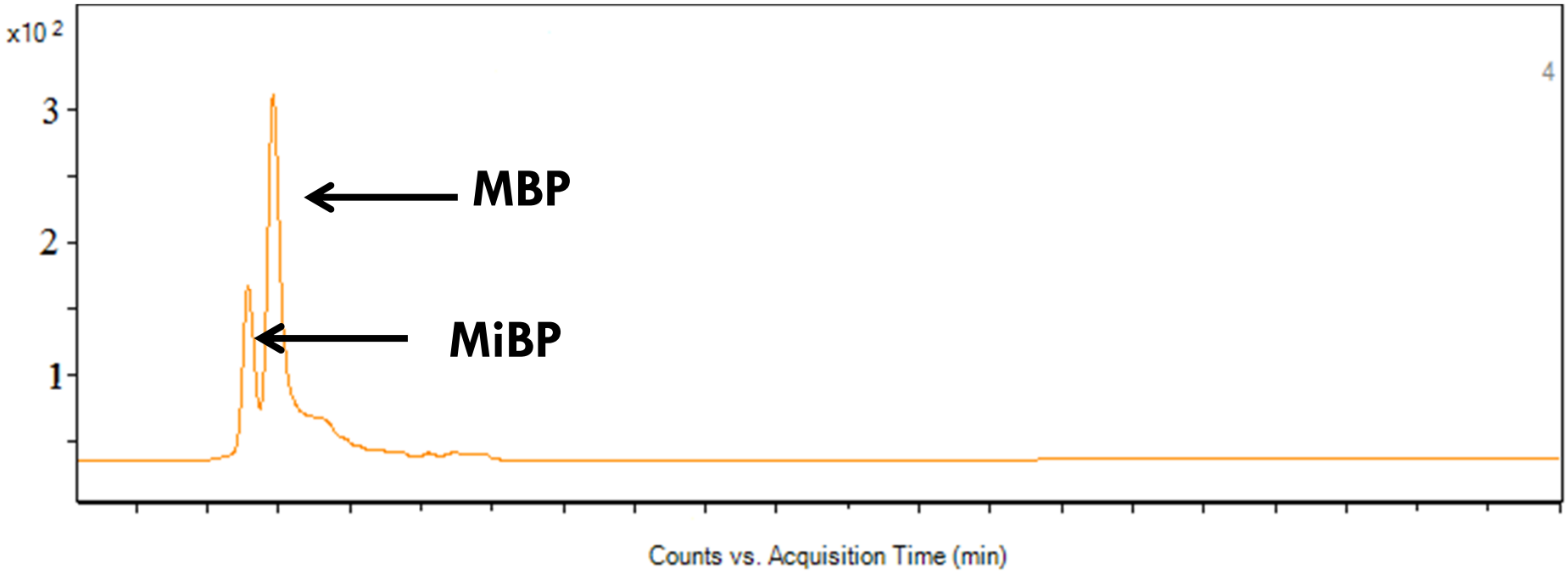
Presence of phthalate metabolites in urine samples

	case	control
MBP	100%	100%
MEHP	100%	100%
MnOP	40%	0%
MiNP	66%	28%

HPLC-MS/MS chromatogram of human urine sample



Presence of isomeric form of MBP



Conclusion

- We identified reduction of lung volumes and flow rates in plastic factory workers
- We identified higher rate of presence of some phthalate metabolites in plastic factory workers
- Following our results and other studies, we suppose that exposure to phthalates play role in development of obstructive disorders of airways. However this assumption needs to be proved by quantitative analysis of phthalate.

Thank you for your attention

ACKNOWLEDGEMENT

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